ABSTRACT BOOK

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19 - 22 July 2015

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The Abstract Mentor Programme provides an opportunity for early-career abstract submitters to receive feedback from experienced abstract submitters on their draft abstracts. The programme links participants to mentors within the same track to maximize the use of the mentors' expertise. Mentoring support was complemented by an online e-course on conference abstract writing.

This year, 80 mentors reviewed 156 draft abstracts for 124 researchers, offering them an opportunity to improve their submissions. 116 mentees finally submitted an abstract for IAS 2015.

Of the 156 abstracts, 34 were accepted, with the following breakdown:
• poster discussion sessions: 2
• poster exhibition: 32

We would like to extend a special thank you to the volunteer abstract mentors, listed here, whose mentoring helped early career HIV researchers improve the quality of their abstracts:

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The 8th IAS Conference on HIV Pathogenesis, Treatment and Prevention (IAS 2015) received more than 2,600 abstract submissions, which were put through a blind, peer-reviewed process carried out by an international panel of reviewers who play a critical role in designing a strong scientific programme.

More than 900 specialists from around the world volunteered their time and expertise to serve as peer reviewers, helping to ensure that the abstracts presented were selected on the basis of rigorous review and were of the highest scientific quality.

We extend our special thanks to these individuals for the time they dedicated to the success of the conference:

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SESSION CODING FOR IAS 2015 PROGRAMME

Example 1: **MOAA01** = **MO** (Weekday) – **AA** (Session type) – **01** (Session order)
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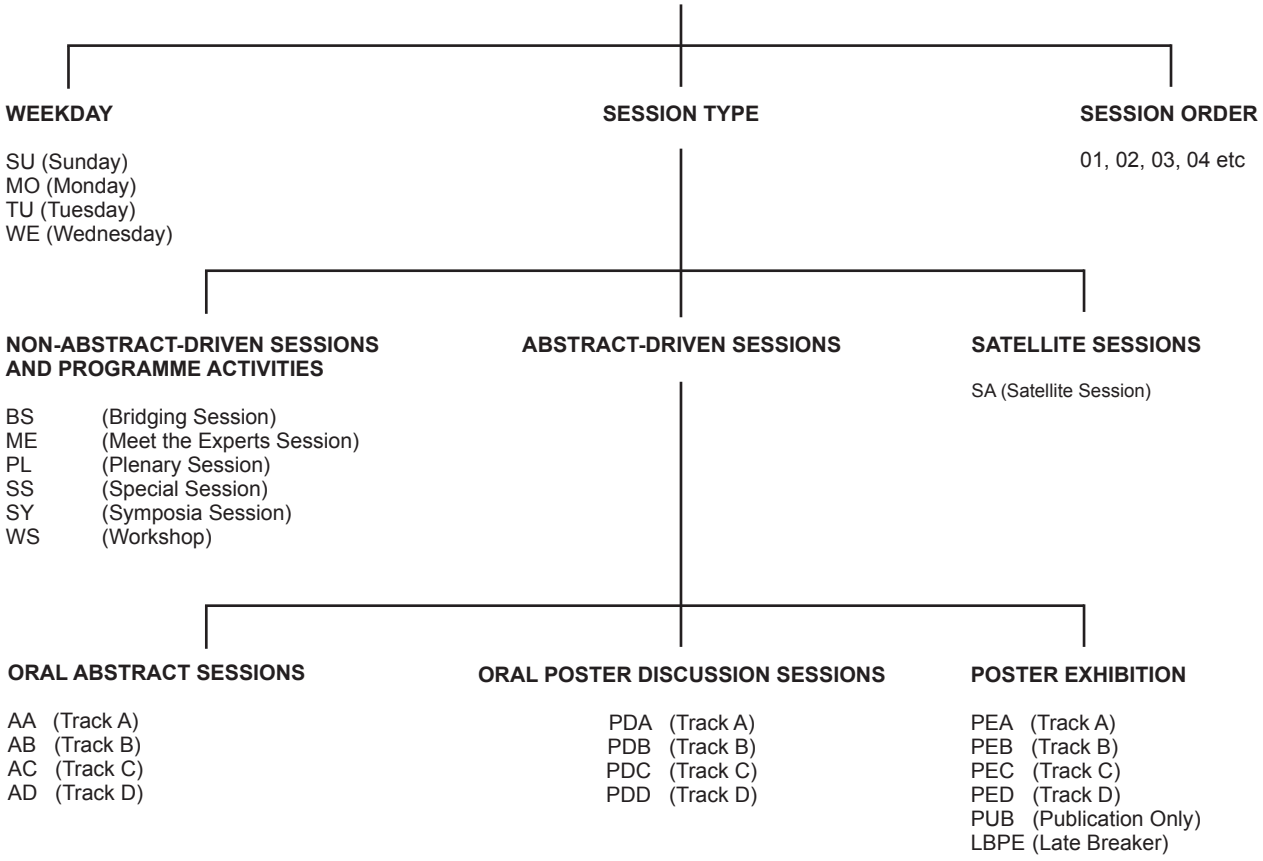
Example 3: **MOPEA001** = **MO** (poster presentation day) – **PE** (presentation type) – **A** (track)– **001** (abstract order)



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The content of oral abstracts is embargoed until the start of the session in which the abstract is being presented, with the exception of oral abstracts included in an official IAS 2015 press conference. The embargo on those abstracts lifts at the start time of the press conference in which the oral abstract is featured or the start time of the scientific session in which the abstract is presented – whichever is earlier.

The content of poster discussion and poster exhibition abstracts is embargoed until 10:00 (PDT – Pacific Daylight Time) on Friday, 17 July 2015.

Monday 20 July

Oral Abstract Sessions

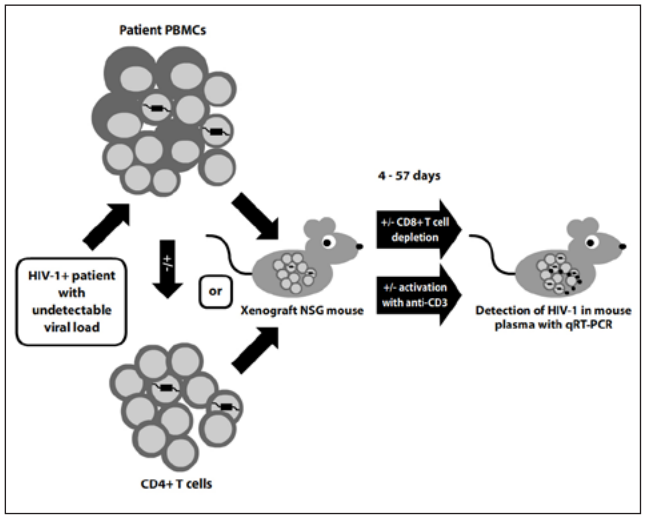
MOAA01 Persistently Seeking Virus

MOAA0101

A murine viral outgrowth assay to detect HIV in patients with undetectable viral loads

K. Metcalf Pate[1], C. Pohlmeyer[2], V. Walker-Sperling[2], J. Foote[1], K. Najarro[1], C. Cryer[1,3], M. Salgado[2,4], L. Gama[1], E. Engle[1], E. Shirk[1], S. Queen[1], S. Chioma[2], M. Vermillion[1], B. Bullock[1], M. Li[1], C. Lyons[1,5], R. Adams[1], C. Zink[1], J. Clements[1], J. Mankowski[1], J. Blankson[2]
[1]Johns Hopkins University School of Medicine, Molecular and Comparative Pathobiology, Baltimore, United States, [2]Johns Hopkins University School of Medicine, Medicine, Baltimore, United States, [3]University of Pennsylvania, School of Veterinary Medicine, Philadelphia, United States, [4]Universitat Autònoma de Barcelona, Institue IrsiCaixa, Badalona, Spain, [5]Tufts University, Cummings School of Veterinary Medicine, North Grafton, United States
Presenting author email: kpate5@jhmi.edu

Background: Sensitive assays are needed for detection of residual HIV in patients with undetectable plasma viral loads to determine if eradication strategies are effective. The gold standard quantitative viral outgrowth assay (QVOA) underestimates the magnitude of the viral reservoir, while sensitive PCR-based assays lack the ability to distinguish replication competent from defective virus. We sought to determine whether xenograft of leukocytes from HIV-1 infected patients with undetectable plasma viral loads into severely immunocompromised mice would result in viral amplification and measurable viral loads within the aberrant murine host.
Methods: We evaluated whether xenograft of 1. peripheral blood mononuclear cells (PBMCs) from 5 HIV-1+ patients on suppressive antiretroviral therapy (ART), 2. PBMCs or purified resting CD4+ T cells from 5 HIV-1+ elite suppressors (ES), or 3. PBMCs from a Simian Immunodeficiency Virus (SIV)+ pigtailed macaque on suppressive ART, all with undetectable plasma viral loads, into NOD.Cg-PrkdcscidIl2rgtm1Wjl/SzJ (NSG) mice resulted in viral amplification in the mouse. Successful xenograft of mice was confirmed by flow cytometry. Human CD8+ T cells were depleted in humanized mice with depleting antibody, and CD4+ T cells were activated in a subset of mice with activating anti-CD3. Plasma viral loads in xenografted mice were quantified using qRT-PCR, and compared to plasma viral load and QVOA results from the human or macaque donor.
Results: With this murine viral outgrowth assay (MVOA), we amplified HIV-1 from all 10 HIV+ subjects with undetectable plasma viral load, including an ES from whom we were unable to recover virus by QVOA. We detected HIV in mice an average of 20 days after xenograft with PBMCs from patients on suppressive ART, and an average of 28 days after xenograft with PBMCs or resting CD4+ T cells from ES. For 2 of the mice xenografted with CD4+ T cells from ES, we detected HIV only after activation with anti-CD3. We similarly detected SIV in macaquized mice by 7 days post-xenograft.
Conclusions: The MVOA has the potential to serve as a powerful tool to identify residual HIV-1 in patients with undetectable viral loads, such as those who have undergone promising cure therapies.



[MVOA for detection of residual virus]

MOAA0102

Virologic and immunologic correlates of viral control post-ART interruption in SIV-infected rhesus macaques

L. Micci[1], E. Ryan[1], R. Fromentin[2], C. Benne[3], N. Chomont[2], J. Lifson[4], M. Paiardini[1]
[1]Emory University, YNPRC, Atlanta, United States, [2]Université de Montréal, Montreal, Canada, [3]Case Western Reserve University, Cleveland, United States, [4]NCI/NIH, Frederick, United States
Presenting author email: mirko.paiardini@emory.edu

Background: Antiretroviral therapy (ART) does not eradicate HIV and the virus rebounds upon treatment interruption. Recently, a sustained control of HIV replication in the absence of ART has been achieved in a subset of patients starting ART early after infection, defined as post-ART treatment controllers (PTC). Unfortunately, the virologic and immunologic determinants of post-ART control of HIV replication are still unclear, particularly in tissues. Here, we used the well-established model of SIV-infection in rhesus macaques (RMs) to investigate the existence of PTC in this model and the features associated with post-ART SIV control.
Methods: 15 RMs (B*08$^-$ and B*17$^-$) were infected (i.v.) with SIV_{mac239}. All 15 animals initiated a 5-drug ART regimen 60 days after infection, which was maintained for seven months. ART was then interrupted and RMs monitored for eight additional months. Blood (PB), lymph node (LN), and colorectal (RB) biopsies were collected throughout the study. Quantitative assessment of total SIV-DNA and RNA was performed on purified blood CD4 T cells and mucosal tissues by quantitative PCR; immunological parameters were determined by flow cytometry.
Results: ART suppressed SIV-RNA to <60 copies/mL in all RMs. After ART interruption, 6 RMs controlled SIV viremia at <10^3 copies/mL up to 8 months off-ART (PTC), while 9 RMs rebounded to pre-ART levels (non-controllers, NC). At pre-ART, PTC had significantly lower plasma viremia and SIV-DNA content, as well as higher CD4 T cell counts as compared to NC. Levels of intestinal CD4 T cells were similar, but PTC had higher frequencies of Th17 cells than NC. On-ART, PTC had significantly lower levels of residual plasma viremia (3 copies/mL, limit of detection) and SIV-DNA content (both in blood and colorectum). After ART interruption, SIV-DNA content rapidly increased in NC while it progressively decreased in PTC. Finally, in PTC control of SIV rebound associated with higher CD4 T cell levels and reduced immune activation in PB and RB during the entire off-ART period.
Conclusions: Lower set point viremia, reduced cell-associated SIV-DNA, and preserved Th17 cell homeostasis associate with improved virologic response to ART and sustained viral control post-ART interruption in SIV-infected RMs.

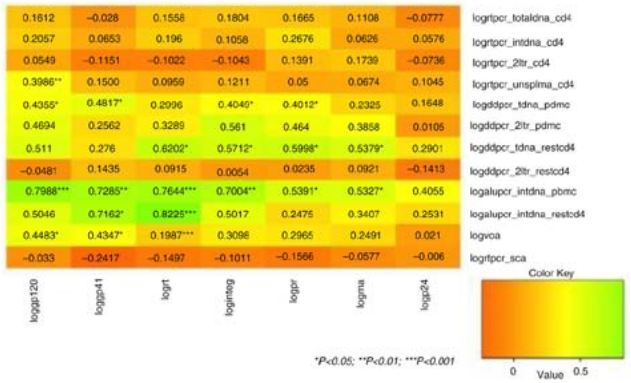
MOAA0103

Anti-HIV antibody responses reflect the quantifiable HIV reservoir size

S. Lee[1], N. Chomont[2], R. Fromentin[2], R. Silicano[3], J. Silicano[3], D. Richman[4], U. O'Doherty[5], S. Palmer[6], P. Burbelo[7], S. Deeks[1]
[1]University of California San Francisco, Medicine, San Francisco, United States, [2]University of Montreal, Immunology, Montreal, Canada, [3]Johns Hopkins University, Medicine, Baltimore, United States, [4]University of California San Diego, Medicine, La Jolla, United States, [5]University of Pennsylvania, Pathology and Laboratory Medicine, Philadelphia, United States, [6]University of Sydney, Medicine, Sydney, Australia, [7]National Institute of Dental and Craniofacial Research, Clinical Dental Research Core, Bethesda, United States
Presenting author email: sulggi.lee@ucsf.edu

Background: A major challenge to HIV eradication strategies is accurate measurement of the latent HIV reservoir. We assessed whether the host response to residual virus may be a sensitive measure of reservoir size by comparing anti-HIV antibody profiles in relation to several HIV reservoir assays.
Methods: Using a luciferase immunoprecipitation systems (LIPS) assay, we quantitatively analyzed seven anti-HIV antibody profiles from 61 patients who initiated long-term (≥3 years) antiretroviral therapy (ART) during chronic HIV infection. HIV antibody levels were evaluated in relation to twelve HIV reservoir measures: total, integrated, and 2-LTR DNA (rtPCR, N=48); unspliced RNA (rtPCR, N=44), total and 2-LTR DNA (droplet digital PCR, N=27); integrated DNA (*alu*PCR, N=16); viral outgrowth assay (VOA, N=27), and plasma HIV RNA (single copy assay, SCA, N=27). Summary estimates of the overall association between HIV reservoir measures and HIV antibody levels adjusted for multiple comparisons were obtained using permutation testing.
Results: Participants were mostly male (96%) with a median age of 56, median nadir and proximal CD4+ T cell counts of 210 and 670 cells/mm^3, respectively, and ART-suppression for a median of 11 years. Individual correlations showed that integrated and total HIV DNA levels by *alu*PCR and ddPCR were significantly associated with all antibody levels except p24 (nor matrix, for ddPCR, Figure 1). HIV reservoir size measured by VOA was associated with gp120 and gp41 levels (R=0.45, P=0.02; R=0.43, P=0.02) while HIV RNA by SCA and HIV DNA by rtPCR were not correlated with any HIV antibody responses. Permutation testing demonstrated a strong overall association between HIV reservoir size and anti-HIV antibody responses (R=0.82, P=0.04, Table 1), in particular with gp120 (R= 0.80, P=0.009), gp41 (R=0.73, P=0.04), and reverse transcriptase (R=0.82, P=0.007). Further adjustment for age, proximal CD4+ T cell count, and years of ART suppression did not significantly alter these results.

Conclusions: Anti-HIV antibody responses correlate with quantifiable reservoir size during chronic ART-mediated suppression. Epitope location (envelope proteins and reverse transcriptase, an enzyme involved in the early steps of viral replication) may determine the strength of this association. Future studies are needed to evaluate whether viral RNA or proteins are produced in cells with defective proviruses.



[Figure 1. Individual correlations matrix]

Anti-HIV Antibody Response	R	P
loggp120	0.80	0.009
loggp41	0.73	0.042
logrt	0.82	0.007
logintegrase	0.70	0.053
logpr	0.60	0.199
logma	0.54	0.340
logp24	0.41	0.679
All	0.82	0.039

[Table 1. Adjusted summary correlations]

MOAA0104

Trancriptomics and metabolomics identify inflammatory profiles that segregate subjects with high and low inducible HIV reservoir

K. Ghneim[1], J. Ahlers[2], S. Fourati[1], C. Shive[1], M. Cameron[1], P. Mukerjee[1], M. Ghannoum[1], B. Rodriguez[1], S. Deeks[3], M. Lederman[1], R. Sekaly[1]
[1]Case Western Reserve University, Pathology, Cleveland, United States, [2]VGTI-FL, Port Saint Lucie, United States, [3]University of California San Francisco, San Francisco, United States
Presenting author email: khader.ghneim@case.edu

Background: To identify mechanisms that control immune reconstitution and the size of the inducible HIV reservoir, we performed whole blood transcriptional and metabolic profiling of subjects from the CLIF and UCSF SCOPE cohorts. These cohorts included subjects who increased CD4 counts post cART (IR) or stayed < 350/mm^3 after 3 years of cART (INR).
Methods: We performed unsupervised analysis of gene expression data using hierarchical clustering to identify class and supervised analysis using statistical filtering to identify gene signatures and pathway activity differentially expressed between classes. Multivariate analysis based on Sparse Partial Least Regression was used to determine if Group membership correlated with plasma metabolites measured by LC-MS/GC-MS. A gene-based classifier was developed to identify INR groups using the pamr package.
Results: Two groups of INR subjects were identified by whole blood gene expression and pathway analysis. INR-A had the highest levels of IL-6, sCD14, FOXO3 and STAT1 expression, and highest levels of oxidative stress and mitochondrial dysfunction. Pathway analysis showed that INR-A failed to activate the NF-κB pathway, TLR- MyD88 signaling, and proinflammatory modules yet upregulated expression of the p38 MAPK pathway, IRF-3, IRF-4, and IL-10 associated with a tolerogenic myeloid response. In contrast, INR-B was characterized by an unrestrained proinflammatory response including the upregulation of multiple TLRs, STAT1, IRF1, and IRF8 associated with Type I/II IFN responses. Plasma metabolites including carnitines, bacterial metabolites and cholesterol also segregated between the 2 INR groups and correlated with gene expression including FOXO3A and STAT-1. TILDA, a measure of the inducible HIV reservoir; revealed that INR-A subjects had higher levels than INR-B and IR's. As CD4 counts and plasma biomarkers of inflammation/immune activation fail to distinguish the two INR groups, we developed a 352 gene-based classifier that accurately identified patient groups (AUC of 0.81 by ROC analysis) in an independent test cohort (UCSF SCOPE) including those that had the highest levels of HIV reservoir.
Conclusions: Identifying pathways that control immune reconstitution and the size of the inducible HIV reservoir paves the way to the development of therapeutic strategies that can lead to eradication of HIV.

MOAA0105LB

HIV-1 virological remission for more than 11 years after interruption of early initiated antiretroviral therapy in a perinatally-infected child

P. Frange[1,2,3], A. Faye[4,5], V. Avettand-Fenoel[1,2], E. Bellaton[6], D. Deschamps[7,8], M. Angin[9], S. Caillat-Zucman[10,11], G. Peytavin[12,13], J. Le Chenadec[14,15], J. Warszawski[14,15], C. Rouzioux[1,2], A. Saez-Cirion[9], ANRS EPF-CO10 Pediatric Cohort
[1]Assistance Publique - Hôpitaux de Paris (AP-HP), Hôpital Necker - Enfants malades, Laboratoire de Microbiologie clinique, Paris, France, [2]EA7327, Université Paris Descartes, Paris, France, [3]AP-HP, Hôpital Necker - Enfants malades, Unité d'Immunologie, Hématologie et Rhumatologie pédiatriques, Paris, France, [4]AP-HP, Hôpital Robert Debré, Service de Pédiatrie générale, Paris, France, [5]Université Paris 7 Denis Diderot, Paris, France, [6]AP-HP, Hôpital Robert Debré, Service d'Hématologie pédiatrique, Paris, France, [7]AP-HP, Hôpital Bichat - Claude Bernard, Laboratoire de Virologie, Paris, France, [8]INSERM UMR1137 IAME Université Paris Diderot, Paris, France, [9]Institut Pasteur, Unite de HIV inflammation et persistance, Paris, France, [10]AP-HP, Hôpital Robert Debré, Laboratoire d'Immunologie, Paris, France, [11]INSERM UMR1149, Université Paris Diderot, Paris, France, [12]AP-HP, Hôpital Bichat, Laboratoire de Pharma-Toxicologie, Paris, France, [13]IAME, INSERM UMR 1137, Université Paris Diderot, Paris, France, [14]AP-HP, Hôpital Bicêtre, Service d'Epidémiologie et de Santé publique, Le Kremlin-Bicetre, France, [15]INSERM U1018, Université Paris Sud, Le Kremlin-Bicetre, France

Background: Durable HIV-1 remission after interruption of combined antiretroviral therapy (cART) has been reported in some adults who started cART during primary HIV-1 infection. The *in utero* HIV-1-infected «Mississippi child», exhibited transient viral control after interrupting very early-initiated cART. However viremia rebounded 27 months later, leaving unclear the possibility of obtaining long-term post-treatment remission in vertically-infected children. Here we report the case of a perinatally-HIV-1-infected adolescent who shows unprecedented virological remission more than 11 years after cART discontinuation.
Methods: HIV-RNA and CD4+ T-cell counts have been monitored since birth. Ultrasensitive HIV-RNA, PBMC-associated HIV-DNA, flow-cytometry-assessed frequency of HIV-specific CD8+ T-cells, CD8+ T-cell mediated HIV-suppression, reactivation of the CD4+ T-cell reservoir were evaluated after 10 and 11 years of control off therapy. Plasma concentrations of antiretrovirals were determined by tandem mass spectrometry.
Results: One infant born from a woman with uncontrolled HIV-1 viremia received zidovudine-based prophylaxis during 6 weeks. HIV-RNA and DNA were not detected 3 and 14 days after birth. HIV-DNA was detected at 4 weeks of age. HIV-RNA reached a peak of 2.1x10^6 copies/ml at 3 months of age when cART (zidovudine, lamivudine, didanosine, ritonavir) was initiated. HIV-RNA was undetectable one month later and remained below assay-detection limits while on cART, except at 15 and 21 months of age. Between 5.8 and 6.8 years of age cART was discontinued by the family. HIV-RNA was undetectable at 6.8 years of age and cART was not resumed. HIV-RNA has remained < 50 copies/ml through 18.3 years of age, except for one blip (515 copies/ml). CD4+ T-cell counts remained stable. After 11 years of control off therapy (confirmed by undetectable plasma concentrations of antiretrovirals), HIV-RNA was below 4 copies/ml and HIV-DNA was 2.2 Log copies/10^6 PBMC. Low levels of HIV-RNA and p24 were detected upon activation of CD4+ T-cells with PHA. HLA genotype showed homozygosity at several loci (A*2301-;B*1503/4101;C*0210/0802;DRB1*1101-;DQB1*0602-). HIV-specific CD8+ T-cell responses and T-cell activation were very weak. HIV-1 western blot was positive with absence of antibodies against gp110 and p18.
Conclusions: This case provides first-time evidence that very long-term HIV-1 remission is possible in perinatally-infected-early-treated children, with similar characteristics as reported in adult post-treatment controllers.

MOAA0106LB

Time associated changes in cell-associated HIV RNA in HIV-infected subjects on suppressive antiretroviral therapy - implications for clinical trials of cure interventions

C. Chang[1,2], P. Cameron[1,2], J. Elliott[2], A. Perelson[3], M. Roche[1], A. Dantanarayana[1], A. Solomon[1], V. Naranbhai[4], S. Tenakoon[1], R. Hoh[5], J. McMahon[2], K. Sikaris[6], W. Hartogensis[7], P. Bacchetti[7], F. Hecht[8], J. Lifson[9], S. Deeks[5], S. Lewin[1,2]
[1]The University of Melbourne, Doherty Institute, Melbourne, Australia, [2]Alfred Hospital, Dept. of Infectious Diseases, Melbourne, Australia, [3]University of California, Los Alamos National Laboratory, Los Alamos, United States, [4]The University of Oxford, Nuffield Dept of Medicine, Oxford, United Kingdom, [5]University of California, San Francisco, School of Medicine, San Francisco, United States, [6]Melbourne Pathology, Melbourne, Australia, [7]University of California, San Francisco, Division of Biostatistics, San Francisco, United States, [8]University of California, San Francisco, Osher Center for Integrative Medicine, San Francisco, United States, [9]National Cancer Institute, Frederick National Laboratory for Cancer Research, Frederick, United States

Background: Cell-associated unspliced (CA-US) HIV RNA is an important marker of the HIV reservoir and a common primary endpoint in clinical trials of latency reversing agents in HIV-infected subjects on antiretroviral therapy (ART). We observed large baseline variation in CA-US HIV RNA in a recent clinical trial of disulfiram and hypothesised these changes were due to circadian-related alterations in CD4+ T-cell composition, gene regulation or anticipatory stress.
Methods: Blood was collected on three occasions (B1, B2 and B3) from HIV-infected subjects (n=30) on suppressive ART prior to any intervention. B3 was collected immediately prior to administration of disulfiram. We measured CA-US HIV RNA and DNA by real-time PCR and plasma HIV RNA (using a single copy assay) by droplet digital PCR. Plasma cortisol and thyroid stimulating hormone (TSH) levels were quantified by ELISA. PBMC were stained with live-dead dye and antibodies to CD3, CD4, CD8, CD45RA, CCR7, CD27, CD38, HLA-DR, acetylated lysine and acetylated histone-3 and were analysed by flow cytometry. Data were assessed for normality then analysed with Wilcoxon matched-pairs signed rank tests and paired-t-tests.
Results: CA-US RNA was higher in blood collected at B3 compared to B1 and B2 (median 85.63 vs. 28.14 and 34.87 copies/million CD4+ T-cell equivalents; both, p< 0.001). There were little differences in HIV DNA or plasma HIV RNA at these times. B3 was collected earlier in the day compared to B1 and B2 (mean 8.28am vs. 11.38am and 10.21am; both, p< 0.001). Other parameters that were significantly higher at B3 compared to B1 and B2 were cortisol (p=0.001 and 0.011); TSH (p=0.023 and 0.004); CD8+CD38+HLADR- T-cells (both, p< 0.001) and CD4+CD38+HLADR- T-cells, which were elevated at B3 compared to B2 (p=0.012). There were no significant differences in the percentage of T-cell subsets or histone acetylation in the blood collected at these time-points.
Conclusions: Time-associated variation in CA-US HIV RNA seen in HIV-infected subjects on suppressive ART was not associated with significant alterations in CD4+ T-cell subset composition and was suggestive of circadian changes in HIV RNA transcription. Diurnal changes in CA-US HIV RNA may need to be considered in the design of future cure intervention trials.

MOAA02 Microbiome: the Good and the Bad for HIV

MOAA0202

Treatment with anti-α4β7 integrin antibody reduces virus-mediated gastrointestinal pathology by targeting distinct mucosal tissues

S. Byrareddy[1], J. Arthos[2], C. Cicala[2], K. Reimann[3], T. Parslow[1], P. Santangelo[4], F. Villinger[1], A. Fauci[2], A. Ansari[1]
[1]Emory University, Pathology & Laboratory Medicine, Atlanta, United States, [2]National Institute of Allergy & Infectious Diseases, National Institutes of Health (NIH), Laboratory of Immunoregulation, Bethesda, United States, [3]Mass Biologics, University of Massachusetts Medical School, Boston, United States, [4]Georgia Institute of Technology and Emory University, Wallace H. Coulter Department of Biomedical Engineering, Atlanta, United States
Presenting author email: siddappa.n.byrareddy@emory.edu

Background: Our laboratory has recently demonstrated that in vivo administration of a monoclonal anti-α4β7 antibody (α4β7-mAb) during acute SIV infection following
1) intravenous,
2) intra-rectal or
3) repeated low-dose intra-vaginal SIV challenge lead to markedly lower gastro-intestinal tissue viral loads compared to rhesus macaques (RM) treated with a control mAb.
The purpose of the present study was to compare the tissues that served as primary targets of viral infection in the α4β7-mAb versus control mAb-treated RM, in order to identify mechanisms by which α4β7-mAb antibody reduces virus-mediated gastrointestinal pathology.
Methods: Groups of 12-16 RM were administered a rhesus α4β7-mAb monoclonal antibody or an isotype-matched control rhesus IgG mAb (50 mg/kg) intravenously (i.v.) starting on day -1 and then every 3 weeks after infection. Each monkey was then repeatedly challenged with a low-dose SIVmac251 intra-vaginally or a single high-dose intrarectally.
Results: i.v. administration of α4β7-mAb blocked the detection of α4β7 on CD4+ T cells in the blood, cervicovaginal tissue, and GALT throughout the period of mAb administration. Viral DNA was reduced in GALT biopsies of the α4β7-mAb treated RMs compared to those treated with control mAb treated (median 3.5 vs. 12.8 copies/ng DNA respectively, p=0.006). Furthermore, in-depth analysis performed on a subset of animals (n=4/group) indicated that proviral DNA was 5 to 25 fold more abundant in jejunum, ileum, or colon of control-treated RMs compared to those treated with a4b7-mAb. In contrast, no difference in proviral loads in the spleen and lymph nodes from various sites was noted in the 2 groups.
Immuno-PET/CT assisted analysis revealed that for animals with comparable plasma viral loads, the α4β7-mAb treated monkeys showed a lower signal in the large intestine. In addition, only the control treated monkeys showed a clear PET/CT signal in lymph nodes surrounding the genital tract suggesting that treatment with α4β7-mAb prevents viral replication in this tissue, leading to different patterns of tissue localization of the virus between the two groups.
Conclusions: The α4β7-mAb either protects or delays intravaginal SIV transmission, reduces gastrointestinal pathology following infection, and results in both quantitative and qualitative differences in the level of viremia and tissue localization of virus.

MOAA0203

Oral microbiome in HIV-infected women: aging, disease progression and opportunistic infections increase the pathogenic profile

M. George[1], B. Weiser[2,3], H. Burger[2,3], T. Lewy[1], K. Anastos[4]
[1]University of California Davis School of Medicine, Medical Microbiology and Immunology, Davis, United States, [2]University of California Davis School of Medicine, Davis, United States, [3]Sacramento Veterans Administration Medical Center, Sacramento, United States, [4]Albert Einstein College of Medicine, Bronx, United States
Presenting author email: mdgeorge@ucdavis.edu

Background: A recent marked increase in the proportion of HIV-infected individuals older than 50 highlights the need to study the impact of aging on HIV pathogenesis. HIV-Associated Non-AIDS (HANA) conditions, such as cardiovascular disease, diabetes, osteoporosis, and dementia are more prevalent in older HIV-infected populations than young adults. The microbiome in saliva and the oral cavity has been studied as a window into pathogenesis in aging populations.
Although disruption of the oral microbiome (dysbiosis) has been linked to various human conditions and diseases associated with aging, the role of age-related dysbiosis in the development of opportunistic infections and HANA conditions in HIV patients is not well understood.
Methods: We utilize 16S rRNA-based pyrosequencing to compare the salivary microbiome in 3 groups: Chronically HIV-infected women enrolled in the Women's Interagency HIV Study who are
1) >50 years old (aging), or
2) <35 years old (young adult), and
3) healthy age-matched uninfected women.
We also examine correlations between dysbiosis of the salivary microbiome, disease progression, and opportunistic oral infections.
Results: HIV infection results in dysbiosis of the salivary microbiome that is enhanced in aging individuals, and characterized by increased abundance of pathogenic bacteria and a decline in healthy probiotic microbes. Higher proportions of *Prevotella*, *Staphylococcus, Moryella, Peptostreptococcus, Ruminococcus,* and *Oribacterium* were detected in both aging and young adult HIV infected women than in uninfected controls. *Prevotella*, *Moryella*, and *Oribacterium* increases were higher in aging than in young HIV patients. HIV infection in older patients was associated with greater salivary shedding of Epstein Barr Virus (EBV). Increased EBV shedding, higher peripheral HIV burden, and reduced CD4+ T cell counts correlated with increases in *Prevotella* and decreases in probiotic *Lactobacillus*. Patients with opportunistic oral infections also showed enhanced salivary levels of *Porphyromonas, Lachnospira,* and *Actinobacillus,* and reduced *Streptococcus*.
Conclusions: Age, severity of disease progression, and emergence of opportunistic infections all contribute to various degrees in increasing the pathogenic footprint of the oral microbiome during chronic HIV infection. The study findings provide new insights into age-related dysbiosis of the salivary microbiome and its role in HIV pathogenesis and lay critical groundwork for future expanded investigations.

MOAA0204

Serum-derived bovine immunoglobulin isolate increases peripheral and mucosal CD4 T cell count in patients with HIV enteropathy

D. Asmuth[1], M. Somsouk[2], P. Hunt[2], Z.M. Ma[3,4,5], C. Miller[3,5], X.D. Li[1,4], J. Hinkle[6], A. Shaw[7], E. Weaver[8], G. Klein[7]
[1]University of California Davis Medical Center, Sacramento, United States, [2]University of California San Francisco, San Francisco, United States, [3]University of California Davis, Davis, United States, [4]Center for Comparative Medicine, Davis, United States, [5]California National Primate Research Center, Davis, United States, [6]EarlyPhase Sciences Inc., Cary, United States, [7]Entera Health Inc., Cary, United States, [8]Entera Health, Inc., Ankeny, United States,

Background: A multi-center trial in HIV-enteropathy was conducted to evaluate the impact of serum-derived bovine immunoglobulin isolate (SBI) on markers of peripheral and mucosal immunity and gastrointestinal (GI) symptoms as previously reported.
Methods: Patients (pts) on long-term suppressive ART with HIV-enteropathy were randomized to receive SBI 2.5 vs 5.0 grams (g) BID or placebo (PBO) during a 4-week lead-in phase followed by SBI 2.5 vs 5.0 g BID for 20 weeks. Evaluations included plasma biomarkers for inflammation, peripheral CD4 counts and pt-reported surveys on GI symptoms. Eight pts underwent duodenal biopsies to examine mucosal immunity.
Results: 103 pts (SBI 2.5 g; n=34; SBI 5.0 g; n=33; PBO: n=36 continued 2.5 v 5.0 g [n=18 each]) were enrolled (31% female; 61% black; mean age 51 yrs). Mean duration of HIV, ART, and enteropathy was over 15, 5 and 5 years, respectively. All cohorts showed a reduction in abnormal stool frequency (p=0.0001) from baseline (BL) to week 4; however between group analysis was not significant. This reduction was maintained for pts receiving SBI through 24 weeks. The 2.5 and 5.0 g cohorts were combined for zonulin and CD4 analysis. The mean plasma zonulin levels significantly increased (p< 0.0001) for pts receiving SBI through 24 weeks. Median peripheral CD4 counts increased significantly from BL to week 24 in patients in the lowest baseline CD4 quartile (308 to 386 cells/mL, p=0.002), while no significant change was observed among subjects in the combined SBI cohorts during this time period. This compromised subgroup also experienced greater increases in CD4 counts at week 4 than PBO pts (median +42 vs -17 cells/mL, p=0.02). Duodenal CD4 densities increased from 217 to 329 cells/mm^2 (median increase of 145 cells/mm^2 [p=0.02]) in biopsies obtained from 8 pts, consistent with earlier findings. Duodenal crypt cells expressing Ki67 decreased in 6/7 pts from 41% to 24% (p=0.08, n=7) which correlated with the decreased number of Paneth cells per crypt (p=0.048).
Conclusions: Oral SBI may be a novel strategy to restore mucosal immunity and systemic immune reconstitution among pts who have not achieved normal CD4 counts despite prolonged suppressive ART.

MOAA0205

HIV-exposure, gut microbiome, and vaccine responses in South African infants

K. Viljoen[1], J. Wendoh[1], U. Karaoz[2], E. Brodie[2], N. Mulder[3], G. Botha[3], E. Kidzeru[1], J. Butcher[4], C. Gray[1], K. Rosenthal[5], A. Abimiku[6], B. Cameron[7], A. Stintzi[4], H. Jaspan[1,8]
[1]University of CapeTown, Clinical Lab Sciences, Institute of Infectious Disease and Molecular Medicine, Cape Town, South Africa, [2]Lawrence Berkeley National Laboratory, Berkeley, United States, [3]University of Cape Town, Cape Town, South Africa, [4]Ottawa Institute of Systems Biology, Ottawa, Canada, [5]McMaster University, Hamilton, Canada, [6]Institute of Human Virology, Baltimore, United States, [7]Ottawa Hospital Research Institute, Ottawa, Canada, [8]Seattle Children's Research Insitute/ University of Washington, Pediatrics. Global Health, Seattle, United States
Presenting author email: hbjaspan@gmail.com

Background: The gut microbiome is crucial for mucosal and systemic immune development. In mice, certain bacteria are required for induction of Treg and Th17 cell development in the gut. Likewise, gut microbiota enhance immune responses to influenza vaccination in the mouse model. HIV-infected women have altered vaginal and gut microbiome, and HIV-exposed infants (HEU) and their mothers receive antibiotics for Pneumocystis pneumonia prophylaxis, therefore HEU may have altered gut microbiota. HEU have higher morbidity and mortality than HIV-unexposed (HU) infants, and respond poorly to certain infant vaccinations. We hypothesized that the etiology of this relative immune deficiency is mediated by gut dysbiosis.
Methods: HEU and HU infants were recruited at birth from informal settlements of Cape Town. Blood and stool were collected after informed consent was obtained. Stool DNA was extracted using MoBio PowerFecal DNA kit and 454 or Illumina sequencing was performed. Data was preprocessed using QIIME and UPARSE and imported into R for further analyses using phyloseq. Differential abundance testing was performed at Operational Taxonomic Unit (OTU) level using the R metagenomeSeq package. Whole blood was incubated with BCG, positive and negative controls, and proliferation and cytokine expression measured using multiparameter flow cytometry.
Results: We found substantial differences in bacterial diversity between HEU and HU infants by Shannon index. Moreover, at all taxonomic levels, there were differences between the HIV exposure groups via PCoA analysis. Several OTUs of the phylum Firmicutes were differentially abundant between HEU and HU infants, three of which were of the genus Veillonella. Several key species were significantly correlated with both proliferative and cytokine responses to BCG. For example, at 6 weeks of age, significantly decreased abundance of *Bacteroides* species, and in particular *B. fragilis,* were present in infants with high CD4+IL-2+, CD8+ki67+, and CD8+IL-17+ responses to BCG vaccination at 6 weeks of age.
Conclusions: Gut microbial composition could explain the immunological differences between HU and HEU infants. These differences should be considered in development of HIV vaccines for exposed neonates.

MOAA0206LB

SIV-induced translocation of bacterial products in the liver mobilizes myeloid dendritic and natural killer cells associated with liver damage

J. Schafer[1], T. Evans[2], H. Li[1], R.K. Reeves[3]
[1]Beth Israel Deaconess Medical Center, Center for Virology and Vaccine Research, Boston, United States, [2]Harvard University, New England Primate Research Center, Southborough, United States, [3]Harvard Medical School/Beth Israel Deaconess Medical Center, Center for Virology and Vaccine Research, Boston, United States

Background: Disruption of the mucosal epithelium during immunodeficiency lentivirus infections permits translocation of microbial products into the circulation, causing systemic immune activation and driving disease progression. However, the specific effects of microbial products in liver, as a blood-filtering organ, are unclear.
Methods: In this study we investigated the effects of simian immunodeficiency virus (SIV) infection of rhesus macaques on microbial translocation in the liver by immunohistochemistry. We also compared liver infiltration by myeloid dendritic cells (mDCs), trafficking to the liver by lymphocytes, and liver-resident natural killer (NK) cell frequencies, phenotypes, and functions in naïve and chronically SIVmac239- or SIVmac251-infected rhesus macaques using flow cytometry.
Results: In livers of normal rhesus macaques very low levels of bacteria and LPS were detectable, but increased up to 20-fold in chronically SIV-infected animals. Increased microbial products in the liver of infected macaques was associated with production of the chemoattractant, CXCL16, by mDCs. Subsequently, lymphocytes expressing the CXCL16 receptor, CXCR6, were mobilized in blood and hypercytotoxic NK cells were recruited to the liver. Microbial accumulation, mDC activation and hepatic cytotoxic NK cell frequency were all significantly correlated with markers of liver damage.
Conclusions: Collectively, these data indicate that SIV-associated accumulation of microbial products in the liver initiates a cascade of innate immune activation resulting liver damage. These findings have implications for the liver pathology associated with HIV, especially in instances of coinfection with HCV.

MOAB01 Paediatrics: Growing up on ART

MOAB0101

Field evaluation of point-of-care testing for early infant diagnosis in Cape Town, South Africa

M. Kroon[1], L. Dunning[2], M. Hsiao[3], L. Myer[2]
[1]Division of Neonatal Medicine, Department of Paediatrics & Child Health, University of Cape Town, Cape Town, South Africa, [2]Division of Epidemiology & Biostatistics, School of Public Health & Family Medicine, University of Cape Town, Cape Town, South Africa, [3]Division of Medical Virology, University of Cape Town, Cape Town, South Africa

Background: Provision of rapid early infant HIV diagnosis (EID) service remains a challenge for prevention of mother-to-child transmission programmes globally. Point-of-care (POC) EID testing may improve access and turnaround times, but while several POC technologies are in development there are few data on implementation.
Methods: We conducted an implementation study of the Alere q Detect POC system for EID at two public sector health facilities. At a maternity hospital the POC device was used to test HIV-exposed neonates soon after birth; at a primary care clinic the device was used for routine six-week EID testing. At each site infants undergoing laboratory-based HIV PCR testing per local protocols were tested on the POC device by doctors or nurses with results available within 1 hour. Analysis examined the performance of POC versus laboratory testing of the same specimen, and semi-structured interviews with providers to assess implementation issues and acceptability.
Results: Overall 476 tests were conducted: 291 birth tests in the maternity hospital (mean child age, <1 day) and 195 six-week tests in primary care (mean child age, 51 days). 12% of all tests resulted in an error with no differences by site; most error results resolved with retesting. POC EID was more sensitive (100%; lower confidence limit, 40%) and specific (100%, lower confidence limit, 98%) among older children tested in primary care compared birth testing in hospital (92%, [95% CI, 62-100%] and 99% [95% CI, 99-100%], respectively), though test performance improved with repeated lab testing and negative predictive value was high (>99%) at both sites. In interviews, providers felt that the ease of use of the device coupled with the

rapid turnaround time of POC EID results facilitated decision-making in the management of infants, but many wanted to understand better the cause of errors on the POC device to assist in repeat testing.

Conclusions: POC EID testing performs well in field implementation in health care facilities and is highly acceptable to health care providers. While further research is needed to understand POC EID implementation at scale, the rapid turnaround time of POC testing may allow immediate identification and management of HIV-infected infants.

MOAB0102

High rates of baseline NNRTI-resistance and virologic failure among ART naïve HIV-1-infected children in Mali

C.S. Crowell[1], A.I. Maiga[2], M. Sylla[3], B. Taiwo[4], N. Koné[3], R.L. Murphy[4], A.-G. Marcelin[5], B. Traore[2], D.B. Fofana[5], E.G. Chadwick[6]
[1]University of Washington, Seattle Children's Hospital, Pediatric Infectious Diseases, Seattle, United States, [2]Faculty of Pharmacy, University of Sciences Techniques and Technologies of Bamako, Unité d'Epidémiologie Moléculaire de la Résistance du VIH aux ARV, SEREFO, Bamako, Mali, [3]Centre Hospitalier Universitaire Gabriel Toure, Département de Pédiatrie, Bamako, Mali, [4]Northwestern University, Infectious Diseases, Chicago, United States, [5]Hôpital Pitié-Salpêtrière, Department of Virology, Paris, France, [6]Lurie Children's Hospital, Pediatric Infectious Diseases, Chicago, United States
Presenting author email: claudia.crowell@seattlechildrens.org

Background: Limited data exist on drug resistance and antiretroviral treatment (ART) outcomes in HIV-1 infected children in West Africa. We determined the prevalence of baseline resistance, and correlates of virologic failure (VF) and on-treatment resistance in a cohort of HIV-1 infected children in Mali.

Methods: Prospective observational study of HIV-1 infected children <10 years of age initiating first-line ART in Bamako, Mali. Assessments occurred at baseline and after 6months of ART. Genotypic resistance testing on stored baseline and 6-month samples occurred at study end. Reverse transcriptase and protease genes were sequenced using in-house methods. Resistance was defined as intermediate or high-level according to the Stanford HIV Genotypic Resistance Algorithm v7.0. VF was defined as viral load (VL) ≥1000copies/mL. Clinical and immunological failure were based on WHO criteria. Logistic regression was used to evaluate factors associated with VF and resistance.

Results: 150 children were enrolled; 60% male and mean age 3.4 years. 94% reported no PMTCT exposure. Median baseline CD4 count and VL were 633 cells/mm3 (IQR: 381-1039) and 675,651copies/mL (IQR: 40,000-1,583,200). Initial ART regimens were lopinavir/ritonavir-based (43%) or NNRTI (efavirenz or nevirapine)-based (57%). Of 141 children with amplifiable baseline samples, 28 (19.86%) had NNRTI resistance, only 2 of whom had PMTCT exposure, and none had PI resistance. Mean age of children with baseline NNRTI resistance was 2.3 years. By 6 months of ART, 11 died, 8 were lost to follow-up and 6 had missing VL data.
Among 125 remaining children, 41 (33%) had VF, 24 of whom (58%) had drug resistance (23 with NNRTI and one with PI mutations). 93% of children with VF did not meet criteria for clinical or immunological failure.
In multivariate analyses adjusting for age, gender, adherence, and ART regimen, baseline NNRTI resistance was strongly associated with VF and 6-month resistance (OR: 6.7, p=0.001; OR: 20, p<0.001).

Conclusions: Baseline NNRTI resistance was common in Malian children without prior NNRTI exposure and was associated with VF and a high resistance rate during ART. Clinical and immunologic criteria rarely detected VF. Our findings support WHO recommendations of PI-based regimens in all children <3 years, and virological monitoring.

MOAB0103

T cell activation and treatment outcomes among infants receiving early ART

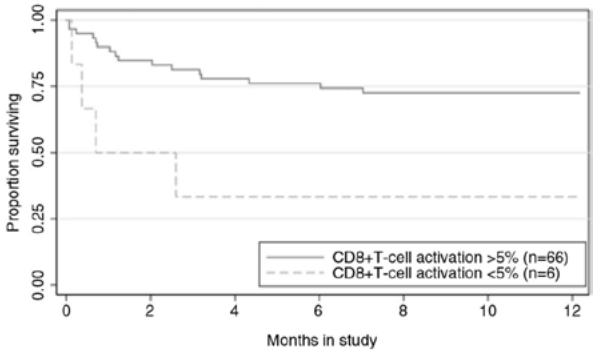
K.H. Ásbjörnsdóttir[1], J.A. Slyker[2], D. Wamalwa[3], S. De Rosa[4,5,6], J.P. Hughes[7], A. Rowhani-Rahbar[1], B.H. Chohan[8], S. Benki-Nugent[2], K. Tapia[9], G.C. John-Stewart[1,2,10]
[1]University of Washington, Epidemiology, Seattle, United States, [2]University of Washington, Global Health, Seattle, United States, [3]University of Nairobi, Paediatrics and Child Health, Nairobi, Kenya, [4]University of Washington, Laboratory Medicine, Seattle, United States, [5]University of Washington, Center for AIDS Research Immunology Core, Seattle, United States, [6]Fred Hutchinson Cancer Research Center, Vaccine and Infectious Disease Division, Seattle, United States, [7]University of Washington, Biostatistics, Seattle, United States, [8]University of Nairobi, Department of Medical Microbiology, Nairobi, Kenya, [9]University of Washington, Center for AIDS Research Biometrics Core, Seattle, United States, [10]University of Washington, Pediatrics and Medicine, Seattle, United States
Presenting author email: kasbjorn@uw.edu

Background: Chronic immune activation is associated with HIV disease progression in adults; however,data in children, especially infants, are limited. We determined levels and correlates of T-cell activation and the effect of baseline activation on response to antiretroviral treatment (ART) in HIV-infected infants.

Methods: This investigation utilized specimens from the Optimizing Pediatric HAART study of early infant ART (NCT00428116). Kenyan infants less than five months of age were enrolled between 2007-2010 and started on ART. Peripheral blood mononuclear cell (PBMC) samples collected before ART initiation were analyzed using flow cytometry and the activated (HLA-DR+/CD38^{high}) T-cell percentage quantified. Factors associated with T-cell activation at baseline were identified using Mann-Whitney U tests or linear regression. The effect of baseline activation on survival, CD4 reconstitution and HIV-1 log_{10} viral load (VL) suppression was assessed using Cox proportional hazard models.

Results: Among 72 infants, median age at enrollment was 111 days, median VL was 6.6 log_{10} copies/ml and median CD4 was 19%. Most infants had symptomatic disease; 49% were WHO stage 3/4, median weight-for-age Z-score (WAZ) was -2.5 and median length-for-age Z-score (LAZ) was -2.1. Twenty infants died, including 8 before ART initiation. Median CD8+ T-cell activation at baseline pre-ART was 17.0% (interquartile range [IQR] 10.4, 31.8) and median CD4+ T-cell activation was 3.3% (IQR 1.6, 5.8). At enrollment, CD8+ T-cell activation was associated with younger age (-0.15%/day, [95% Confidence Interval (CI) -0.28, -0.01], p=0.05) and weight-for-age Z-score (2.4%/WAZ standard deviation, [95% CI 0.64-4.2], p=0.02), but not with CD4% or VL. CD4+ T-cell activation at enrollment was inversely associated with CD4% (-0.20%/CD4% [95% CI -0.36, -0.05], p=0.01). T-cell activation pre-ART was not associated with time to CD4% reconstitution or VL suppression. Low CD8+ T-cell activation (< 5%) was associated with mortality (Hazard ratio=3.8 [95% CI 1.3, 11.4], p=0.02).

Conclusions: Contrary to findings in adults, low CD8+ T-cell activation was strongly associated with mortality in this infant cohort. Among infants, low CD8+ T-cell activation in symptomatic HIV infection may be a marker of ineffective immune response.



[Survival to one year by CD8+ T-cell activation]

MOAB0104

Changes in renal laboratory parameters and bone mineral density in treatment-naïve HIV-1-infected adolescents initiating therapy with INSTI-based single-tablet regimens containing tenofovir alafenamide (TAF) or tenofovir disoproxil fumarate (TDF)

H. Kizito[1], A. Gaur[2], W. Prasitsuebsai[3], N. Rakhmanina[4], K. Chokephaibulkit[5], J. Fourie[6], L.-G. Bekker[7], Y. Shao[8], S. Bennett[8], E. Quirk[8]
[1]Joint Clinical Research Centre, Kampala, Uganda, [2]St Jude Children's Research Hospital, Memphis, United States, [3]HIVNAT, Bangkok, Thailand, [4]Children's National Health System, Washington, United States, [5]Siriraj Hospital, Bangkok, Thailand, [6]Mpati Medical Centre, Dundee, South Africa, [7]Desmond Tutu HIV Centre, Cape Town, South Africa, [8]Gilead Sciences, Inc., Foster City, United States
Presenting author email: aditya.gaur@stjude.org

Background: EVG/COBI/FTC/TAF [E/C/F/TAF] and EVG/COBI/FTC/TDF [Stribild, STB] are integrase inhibitor (INSTI)-based single-tablet regimens (STRs) in clinical development for HIV-1-infected adolescents. Exposures of all components have been shown to be within the range associated with antiviral activity in adults. Preliminary comparative safety data through 24 weeks are reported.

Methods: Treatment-naïve 12 to < 18 year-olds weighing ≥35 kg with HIV-1 RNA ≥1000 copies/mL , CD4 >100 cells/μL and eGFR ≥90 mL/min/1.73m^2 received E/C/F/TAF or STB once daily in two ongoing 48-week, single-arm, open-label trials. Adverse events (AE), laboratory tests, bone mineral density (BMD) by dual X-ray absorptiometry and height-age adjusted (HA) Z-scores were assessed through Week 24.

Results: The E/C/F/TAF and STB trials enrolled 50 and 33 adolescents, respectively (median age 15 vs 16 years, 56% vs 30% female, 88% vs 76% Black, 22% vs 27% with baseline HIV-1 RNA > 100,000 copies/mL, median CD4 count 456 vs 407 cells/μL, median eGFR 156 vs 143 mL/min/1.73m^2). Most AEs in both trials were mild and unrelated to treatment, with no deaths or AEs leading to treatment discontinuation. At Week 24, the median increase in serum creatinine was +0.08 mg/dL in E/C/F/TAF participants, with and +0.10 mg/dL in STB participants, with median eGFR decreases of -17.0 and -18.0 mL/min/1.73m^2, respectively, consistent

with COBI's inhibition of renal tubular creatinine secretion. Proteinuria (any grade) occurred in 26% of E/C/F/TAF participants vs 52% of STB participants, with Grade 2 or higher proteinuria occurring in 4% vs 21% of participants, respectively. Of those participants with BMD measurements at Week 24, the median increase in spine BMD was +1.98% in E/C/F/TAF participants, with a decrease of ≥4% in 3/41 participants (7%), versus a median decrease of -1.29% in the STB cohort, with a decrease of ≥4% in 6/20 participants (30%). Spine HA Z-scores decreased by -0.02 and -0.21 respectively.

Conclusions: Compared with STB, E/C/F/TAF exhibited similar effects on eGFR, a lower incidence and severity of proteinuria, and a median increase in spine mineralization. Both STRs were well-tolerated through 24 weeks. These findings support INSTI-based STRs as initial HIV-1 treatment in adolescents and suggest that TAF could offer safety advantages in pediatric populations.

MOAB0105

Treatment and resistance outcomes of Asian children on second-line antiretroviral therapy

W. Prasitsuebsai[1], S. Teeraananchai[1], K.H. Truong[2], J. Ananworanich[3,4], V.C. Do[5], L.V. Nguyen[6], P. Kosalaraksa[7], N. Kurniati[8], T. Sudjaritruk[9], K. Chokephaibulkit[10], T. Singtoroj[11], S.J. Kerr[1,12], A.H. Sohn[11], TASER-Pediatrics Study
[1]HIV-NAT, Thai Red Cross - AIDS Research Centre, Bangkok, Thailand, [2]Children's Hospital 1, Ho Chi Minh City, Vietnam, [3]HIV-NAT, SEARCH, Thai Red Cross - AIDS Research Centre, Bangkok, Thailand, [4]Current address: U.S. Military HIV Research Program, Walter Reed Army Institute of Research, Silver Spring, and Henry M. Jackson Foundation for the Advancement of Military Medicine, Bethesda, Silver Spring and Bethesda, United States, [5]Children's Hospital 2, Ho Chi Minh City, Vietnam, [6]National Hospital of Pediatrics, Hanoi, Vietnam, [7]Division of Infectious Diseases, Department of Pediatrics, Khon Kaen University, Khon Kaen, Thailand, [8]Cipto Mangunkusumo General Hospital, Jakarta, Indonesia, [9]Faculty of Medicine and Research Institute for Health Sciences, Chiang Mai University, Chiang Mai, Thailand, [10]Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand, [11]TREAT Asia/amfAR, Foundation for AIDS Research, Bangkok, Thailand, [12]Amsterdam Institute of Global Health and Development (AIGHD), Amsterdam, Netherlands
Presenting author email: annette.sohn@amfar.org

Background: With limited pediatric third-line antiretroviral therapy (ART) in resource-limited settings, data on treatment efficacy and drug resistance following second-line failure are needed to guide future management.

Methods: HIV-infected children < 18 years old who were taking or switching to second-line ART were enrolled from Indonesia, Thailand, and Vietnam. Clinical and laboratory assessments were retrospectively and prospectively obtained from the time of second-line switch (baseline). Genotyping was performed upon virologic failure (VF; HIV-RNA >1000 copies/mL). Cox proportional hazards regression was used to evaluate factors predicting post-switch VF.

Results: A total of 277 children were enrolled; 41% were female. Baseline values included median (interquartile range; IQR) age 7.5 (5.3-10.3) years, CD4 count 300 (146-562) cells/mm^3, CD4 percentage 13 (7-20)%, HIV-RNA 5 (4.4-5.5) $\log_{10}$ copies/mL. The median duration of first-line ART was 2.7 (1.7-4.2) years. Resistance mutations at first-line failure were available for 156 of 277 children (all had prior non-nucleoside reverse transcriptase [NNRTI]-based regimens) and included ≥4 thymidine analogue mutations (TAMs; 18%), Q151M (8%), M184V (82%), and ≥1 NNRTI mutation (92%). Current second-line regimens contained lamivudine (90%), tenofovir (43%), zidovudine or abacavir (30%) and boosted lopinavir (LPV) or atazanavir (ATV; 98%). After a median of 3.3 (1.8-5.3) years on second-line, the median CD4 was 767 (556-1060) cells/mm^3 and 26 (20-31)%. Eighteen (7%) had WHO stage 3 or 4 events; 3 (2%) died from HIV-related illnesses. VF occurred in 73 (27%; incidence 7 per 100 person-years, 95% confidence interval [CI] 5.8-9.1), at which time 23% had < 95% adherence by pill count. Fifty of 73 with second-line VF had ≥4 TAMs (10%), Q151M (4%), M184V (55%), and ≥1 major LPV (8%), ≥6 LPV (2%), and ≥1 major ATV mutations (4%). Age >11 years (hazard ratio [HR] 4.06; 95% CI 2.15-7.66) and HIV-RNA >5 $\log_{10}$ copies/mL (HR 2.4; 95% CI 1.27-4.59) at second-line switch were predictors of VF.

Conclusions: One-fourth of children had VF while on second-line ART. However, < 10% developed major mutations to protease inhibitors, which may have been related to poor adherence or duration of VF. Greater advocacy is needed to create access to third-line antiretrovirals in resource-limited settings.

MOAB0106

Week 48 safety and efficacy of a rilpivirine (TMC278)-based regimen in HIV-infected treatment-naïve adolescents: PAINT phase II trial

J. Lombaard[1], T. Bunupuradah[2], P. Flynn[3], J. Ramapuram[4], F. Ssali[5], H. Crauwels[6], A. Hoogstoel[6], V. Van Eygen[6], M. Stevens[6], K. Boven[7]
[1]Josha Research, Bloemfontein, South Africa, [2]Thai Red Cross AIDS Research Centre, Bangkok, Thailand, [3]St Jude Children's Research Hospital, Memphis, United States, [4]Kasturba Medical College Hospital, Mangalore, India, [5]Joint Clinical Research Centre, Kampala, Uganda, [6]Janssen Infectious Diseases BVBA, Beerse, Belgium, [7]Janssen Research & Development LLC, Titusville, United States
Presenting author email: kboven@its.jnj.com

Background: Rilpivirine 25mg qd exposure was similar in adults and adolescents (Week 4 PAINT pharmacokinetic analysis). Week 48 safety and efficacy results are reported here.

Methods: PAINT (NCT00799864) is a Phase II, ongoing, open-label, single-arm trial of rilpivirine plus two investigator-selected N[t]RTIs in treatment-naïve HIV-1-infected adolescents (≥12 to < 18 years, from sites in India, Thailand, Uganda, South Africa, USA). After the adult approved indication, only patients with viral load (VL) ≤100,000 copies/mL were enrolled. Virologic response was defined as VL < 50 copies/mL (time-to-loss-of-virologic-response [TLOVR] algorithm).

Results: Of 36 patients, 20 (56%) were female, 18 (50%) aged 12-< 15 years and 32 (89%) Black/African American; 28 (78%) had baseline (BL) VL ≤100,000 copies/mL; 24 (67%) received emtricitabine/tenofovir disoproxyl fumarate (TDF), 8 (22%) lamivudine/TDF and 4 (11%) lamivudine/zidovudine.

At Week 48, 26/36 (72%) patients overall, 22/28 (79%) with BLVL ≤100,000 copies/mL and 4/8 (50%) with BLVL >100,000 copies/mL achieved virologic response. Of the ten non-responders (28%), eight were virologic failures (VFs), one was dosed although a protocol violator (screening NNRTI RAM) and withdrawn and one withdrew due to an AE (pulmonary tuberculosis). CD4$^+$ count increased by median (range) 250.5 (-135 to 740) cells/mm^3.

For 2/8 VFs, overall adherence (pill count) was < 95% (one of these also had BLVL >100,000 copies/mL). Five of eight VFs developed rilpivirine RAMs, mostly E138K (n=4), K101E (n=2) and M230L (n=2); 4/5 developed N[t]RTI RAMs, mostly M184V (n=3).

Mean (standard deviation) rilpivirine AUC_{24h} and C_{0h} were 2391 (991) ng.h/mL and 84 (39) ng/mL, respectively (population pharmacokinetic analysis). Most AEs were grade 1 or 2. Seven patients (19%) had grade 3 or 4 AEs regardless of causality, mainly malaria and depression (each n=2 and not related to rilpivirine). AEs considered at least possibly related to rilpivirine occurred in 13 (36%) patients, mainly (excluding investigations) somnolence (n=5, 14%) and nausea (n=2, 6%).

Conclusions: This 48-week analysis supports use of rilpivirine 25mg qd combined with other antiretrovirals in treatment-naïve HIV-1-infected adolescents (≥12 to < 18 years) with VL ≤100,000 copies/mL. Rilpivirine safety, virological and pharmacokinetic results were similar to those observed in adults.

MOAB0107LB

In utero tenofovir exposure is not associated with fetal long bone growth

J. Jao[1], L. Myer[2], T. Phillips[3], G. Petro[4], A. Zerbe[5], E.J. Abrams[5]
[1]Icahn School of Medicine at Mount Sinai, Department of Medicine, Department of Obstetrics, Gynecology, and Reproductive Science, New York, United States, [2]University of Cape Town, Division of Epidemiology and Biostatistics, Desmond Tutu HIV Centre, Cape Town, South Africa, [3]University of Cape Town, Division of Epidemiology and Biostatistics, Cape Town, South Africa, [4]University of Cape Town, Division of Obstetrics & Gynaecology, Cape Town, South Africa, [5]ICAP at Columbia University, New York, United States

Background: Despite widespread use of tenofovir (TDF) in pregnant and breast-feeding women, few data have been published on fetal bone development or child growth after *in utero* TDF exposure.

Methods: We evaluated fetal long bone measurements in HIV-infected pregnant woman/fetus dyads in Cape Town, South Africa. Measurements were conducted by a trained research sonographer using high-resolution ultrasound. Fetal femur (FLZ) and humerus (HLZ) length *z*-scores were compared by duration of *in utero* TDF exposure in three categories: 1) TDF-exposed since conception (TDF-C) vs. 2) TDF-exposed for ≥4 weeks and initiated after 1st trimester (TDF-E), vs. 3) TDF-exposed for < 4 weeks or TDF-unexposed (TDF-U). Ultrasounds performed at < 10 weeks gestational age (GA), twin pregnancies, and those resulting in intrauterine fetal demise were excluded. Linear mixed effects models were used to assess the effect of duration of TDF exposure category on FLZ and HLZ.

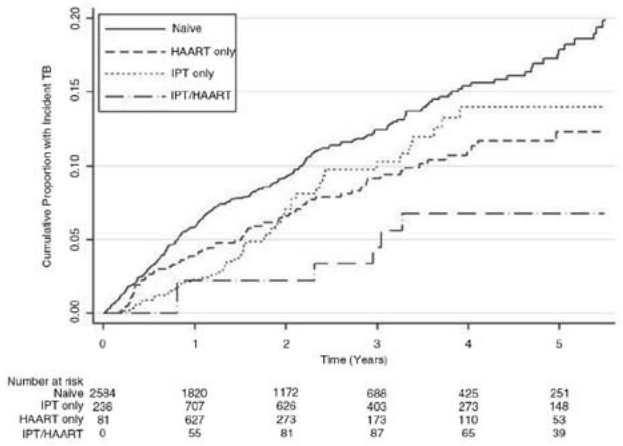
Results: A total of 1957 fetal ultrasounds (408 TDF-C, 581 TDF-E, 968 TDF-U) in 1030 women (73% of whom had ≥2 ultrasounds) were available for analysis. Women in the TDF-C group were older and had lower CD4 cell counts than women in the other categories but did not differ in anthropometry or history of low birthweight deliveries (Table). Median duration of TDF exposure was 26.9, 13.0 and 0 weeks, respectively, in the TDF-C, TDF-E and TDF-U groups. Mean FLZ and HLZ did not differ by TDF exposure category (FLZ: 0.321 vs. 0.300 vs. 0.333,

p=0.570, and HLZ: 0.130 vs. 0.318 vs. 0.048, *p*=0.832). These relationships persisted after adjusting for maternal age, gestation, gravidity, socioeconomic status, CD4 cell count, HIV RNA level, and maternal BMI (β=0.038, *p*=0.563 for TDF-C vs. TDF-U and β=-0.002, *p*=0.964 for TDF-E vs. TDF-U fetal FLZ; β=0.009, *p*=0.903 for TDF-C vs. TDF-U and β=-0.006, *p*=0.885 for TDF-E vs. TDF-U fetal HLZ). No other factors related to HIV disease severity were associated with fetal FLZ or HLZ.

Conclusions: *In utero* TDF exposure does not appear to alter fetal long bone growth. These results are reassuring and support the continued use of TDF in HIV-infected pregnant women.

CHARACTERISTICS OF PREGNANT WOMEN	TDF-exposed since conception (n=226)	TDF-exposed for >4 weeks and initiated after 1st trimester (n=232)	TDF-exposed for <4 weeks or TDF-unexposed (n=572)	p value
Age of Mother, years	31 (27-34)	27 (23-32)	28 (25-32)	<0.001
GA, weeks	20 (14-28)	21 (14-28)	21 (16-27)	0.805
Maternal BMI at enrollment, kg/m²	29.14 (25.81-33.91)	28.50 (25.00-33.75)	28.63 (25.15-34.24)	0.790
CD4 cell count, cells/mm³	399 (273-523)	360 (239-478)	340 (232-507)	0.015
Log HIV RNA level at enrollment	1.59 (1.59-1.59)	4.13 (3.52-4.57)	3.99 (3.37-4.65)	<0.001
Number of Women with >2 ultrasound scans	147 (64.8)	126 (54.3)	479 (83.6)	0.001
CHARACTERISTICS OF ULTRASOUND SCANS	(n=408)	(n=581)	(n=968)	p value
Femur Length z score	0.32 (-0.03, 0.70)	0.30 (-0.03, 0.63)	0.33 (-0.07, 0.79)	0.570
Humerus Length z score	0.13 (-0.29, 0.59)	0.32 (-0.04, 0.59)	0.05 (-0.33, 0.46)	0.832

[Characteristics of Women and Fetal Ultrasound Meas]



[Figure 1]

Time Interval	IPT Unexposed (n=2689)		IPT Exposed (n=776)		Incidence Rate Ratio (95% CI)			
Time Interval	Cases/PY	Rate/100 PY	Cases/PY	Rate/100 PY	Unadjusted	p	Adjusted	p
Overall	318/8,022	4.0 (3.6-4.4)	54/1,886	2.9 (2.2-3.7)	0.72 (0.53-0.99)	0.042	0.77 (0.57-1.0)	0.070
0-1 yr	151/2,672	5.7 (4.8-6.6)	16/615	1.6 (1.6-4.2)	0.46 (0.26-0.80)	0.006	0.60 (0.36-0.98)	0.042
≥1-2 yrs	75/2,138	3.5 (2.8-4.4)	20/519	3.9 (2.5-6.0)	1.1 (0.63-1.9)	0.740	1.1 (0.67-1.8)	0.733
≥2-3 yrs	47/1,362	3.5 (2.6-4.6)	10/301	3.3 (1.8-6.2)	0.96 (0.50-1.9)	0.880	0.95 (0.51-1.8)	0.880
≥3 yrs	45/1,851	2.4 (18-3.3)	8/451	1.8 (0.89-3.7)	0.73 (0.30-1.6)	0.413	0.73 (0.34-1.6)	0.394

[Table 1]

MOAB02 HIV and TB: Gaps and Opportunities

MOAB0201

The durability of isoniazid preventive therapy for tuberculosis: long-term follow-up from a prospective cohort of HIV-infected adults in South Africa

C. Hanrahan[1], N. Martinson[2], G. Link-Barnes[3], R. Msandiwa[2], R. Chaisson[3], J. Golub[3]
[1]Johns Hopkins Bloomberg School of Public Health, Baltimore, United States, [2]Perinatal HIV Research Unit, University of the Witwatersrand, Johannesburg, South Africa, [3]Center for TB Research, Johns Hopkins School of Medicine, Baltimore, United States
Presenting author email: chanrah1@jhmi.edu

Background: Isoniazid preventive therapy (IPT) has been demonstrated to reduce the risk of active tuberculosis (TB) in HIV-infected adults, but the effectiveness of shorter IPT regimens (6-9 months) rapidly wanes in high TB burden settings. We examined the long-term durability of 6 months of IPT among HIV-infected adults in South Africa.
Methods: We analyzed the experience of a prospective clinical cohort of HIV-infected adults at one urban and one rural hospital in South Africa. The exposures of interest were receipt of IPT and antiretroviral therapy (ART), and the primary outcome was incident TB. We used multivariate Poisson regression to examine the association of IPT and ART with risk of TB.
Results: From 2003-2010, 3,465 HIV-infected adults were followed for 9,908 person-years (PY) during which 372 incident TB cases were diagnosed (incidence rate [IR]: 3.8/100PY; 95%CI: 3.4-4.2). A total of 776 participants received IPT (median treatment length: 5 months [IQR: 2-6]). During 1,886 PY of follow-up after initiating IPT, 54 incident cases of TB were diagnosed (IR: 2.9/100 PY; 95%CI: 2.2-3.7), while during 8,022 PY of follow-up without IPT exposure, 318 incident TB cases were diagnosed (IR:4.0/100 PY; 95%CI:3.6-4.4).
After adjusting for age, sex, study site, ART use and CD4 count, IPT was associated with a 23% reduction in TB incidence over 7 years of follow-up (adjusted IRR:0.77; 95% CI:0.7-1.0, p=0.070). IPT appeared to be protective only for the first year following initial IPT exposure (aIRR: 0.46; 95%CI 0.36-0.98; p=0.042), after which the risk of TB was not significantly reduced.
Conclusions: In this prospective cohort of HIV-infected adults in South Africa, receipt of 6 months of IPT resulted in a marked (40%) reduction in risk for TB during the first year following IPT initiation, independent of ART status. No reduction in TB risk was observed beyond one year, confirming similar findings in settings of high TB burden. We demonstrate that IPT remains an important intervention for HIV-infected individuals, and that even a short regimen can provide crucial protection from TB of up to one year for those not yet initiated on highly active antiretroviral therapy.

MOAB0202

Treatment outcomes of drug-resistant TB patients in South Africa, disaggregated by HIV status, as reported in a national electronic drug-resistant TB register

D.H. Evans[1], K. Schnippel[2], E. Budgell[1], K. Shearer[1], R. Berhanu[2], L. Long[1], S. Rosen[3]
[1]Health Economics and Epidemiology Research Office, Department of Internal Medicine, School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa, [2]Right to Care, Johannesburg, South Africa, [3]Center for Global Health & Development, Boston University School of Public Health, Boston, MA, United States
Presenting author email: ebudgell@heroza.org

Background: South Africa reports the third highest number of drug-resistant TB (DR-TB) cases and the largest population living with HIV in the world. We describe treatment outcomes of patients from the South African Electronic Drug Resistant Tuberculosis Register (EDRweb), the national database of all DR-TB cases, after January 2009.
Methods: Retrospective, de-identified descriptive analysis of all patients with multidrug resistant (MDR) TB who initiated DR-TB treatment in South Africa between 01/01/09-30/09/11. During this period, guidelines specified all MDR-TB patients were admitted to specialized referral hospitals for the 6 month intensive phase of treatment or until culture conversion, then followed as outpatients for 12-18 months. Treatment outcomes included success (cured and treatment completed), failed, lost to follow-up, and died. Person-time accrued from treatment initiation until the earliest of outcome date recorded or 24 months on treatment. Cox hazard models were used to evaluate the relationship between HIV status and all-cause mortality. Models were adjusted for age, gender and previous history of TB treatment.
Results: 13,692 confirmed MDR-TB patients initiated treatment (median age 35.4 years; 53% male; 99% pulmonary TB). 81% (11,028/13,692) had an HIV status recorded; of these 66% (7,289/11,028) were co-infected with HIV.
Among those with an outcome reported (8,465/13,692; 62%), overall mortality and success rates were 24.6% [95% CI 23.7-25.6] and 42.4% [41.3 -43.4], respectively. Success was similar between HIV negative patients (42.9% [41.0-44.8]; 18.1/100 person-years (pys)) and those co-infected with HIV (42.5% [41.0-43.9]; 15.5/100 pys).
Mortality was substantially higher in the HIV positive (27.3% [26.0-28.6]; 10.1/100 pys) than the HIV negative (17.3% [15.9-18.7]; 8.0/100 pys) group (adjusted hazard ratio 1.45 [1.30-1.62]). Fewer HIV positive patients were lost to follow-up or failed treatment compared to HIV negatives (21.6% and 8.6% vs. 29.0% and 10.8%).

		Treatment success			
	Total	Cured	Completed Treatment	Died	Failed Treatment
HIV status					
HIV -ve	3739 (27.3%)	803 (21.5%)	341 (9.1%)	460 (12.3%)	289 (7.7%)
HIV +ve	7289 (53.2%)	1356 (18.6%)	576 (7.9%)	1243 (17.1%)	390 (5.4%)
Unknown	2664 (19.5%)	328 (12.3%)	184 (6.9%)	383 (14.4%)	118 (4.4%)
TB treatment history					
New	3250 (23.7%)	653 (20.1%)	291 (9.0%)	439 (13.5%)	164 (5.0%)
Relapse	2351 (17.2%)	436 (18.5%)	177 (7.5%)	328 (14.0%)	139 (5.9%)
LTF	1232 (9.0%)	132 (10.7%)	80 (6.5%)	274 (22.2%)	99 (8.1%)
Failed 1st	3959 (28.9%)	735 (18.6%)	333 (8.4%)	567 (14.3%)	186 (4.7%)
Failed 2nd	2516 (18.4%)	495 (19.7%)	197 (7.8%)	415 (16.5%)	180 (7.2%)
Other	384 (2.8%)	36 (9.3%)	23 (6.0%)	63 (16.4%)	29 (7.6%)

*LTF lost to follow-up; 1st first-line; 2nd second-line

[Table 1. Summary of treatment outcomes of MDR-TB patients in South Africa (n=13,692)]

Conclusions: In this analysis of the outcomes of MDR-TB treatment in the South African national database, the reported rate of treatment success was low (42%) and did not vary by HIV status. Mortality was high in both groups but almost 1.5 times more in HIV co-infected patients. New guidelines allowing decentralized (outpatient) treatment of some MDR-TB patients and newly available drug regimens may improve treatment results.

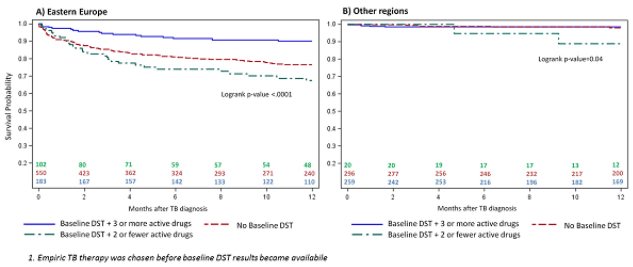
MOAB0203

Excess TB mortality in HIV patients in Eastern Europe: restructured approach to care needed

A. Schultze[1], A.M. Werlinrud Efsen[2], F.A. Post[3], A. Panteleev[4], H. Furrer[5], R. Miller[6], M.H. Losso[7], J. Toibaro[7], A. Skrahin[8], J.M. Miro[9], J.A. Caylà[10], E. Girardi[11], M. Bruyand[12], N. Obel[2], D.N. Podlekareva[2], J.D. Lundgren[2], A. Mocroft[1], O. Kirk[2], on behalf of the TB:HIV Study Group in EuroCoord

[1]University College London, Department of Infection and Population Health, London, United Kingdom, [2]University of Copenhagen, Department of Infectious Diseases and Rheumatology, CHIP, Finsencentret, Rigshospitalet, Copenhagen, Denmark, [3]King's College Hospital, Department of Sexual Health, Caldecot Centre, London, United Kingdom, [4]TB Hospital 2, Department of HIV/TB, St. Petersburg, Russian Federation, [5]Bern University Hospital and University of Bern, Department of Infectious Diseases, Bern, Switzerland, [6]University College London, Centre for Sexual Health and HIV Research, Mortimer Market Centre, London, United Kingdom, [7]Hospital J.M. Ramos Mejia, Department of Immunocompromised, Buenos Aires, Argentina, [8]Republican Research and Practical Centre for Pulmonology and TB, Clinical Department, Minsk, Belarus, [9]University of Barcelona, Infectious Diseases Service, Hospital Clinic - IDIBAPS, Barcelona, Spain, [10]Agencia de Salud Pública de Barcelona, Programa Integrado de Investigación en Tuberculosis de SEPAR (PII-TB), Centro de Investigación Biomédica en Red de Epidemiología y Salud Pública, CIBERESP, Barcelona, Spain, [11]INMI 'L. Spallanzani' Ospedale L Spallanzani, Department of Infectious Diseases, Rome, Italy, [12]INSERM, ISPED, Centre Inserm U 897- Epidemiologie-Biostatistique, Bordeaux, France
Presenting author email: a.schultze@ucl.ac.uk

Background: Management of TB in HIV patients in Eastern Europe (EE) is challenged by high MDR-TB prevalence, low rates of drug susceptibility testing (DST) and poor access to ART. We report 1-year mortality estimates from a multi-regional (EE, Western Europe (WE) and Latin America (LA)) cohort study.
Methods: Deaths within 12 months of starting TB therapy (baseline) among consecutive HIV patients with TB in 2011-2013 were classified as being TB-related or not. Risk factors for all-cause and TB-related death were assessed using standard survival analysis methods.
Results: Among 1410 patients starting TB therapy (EE=835, WE=319, LA=256), 257 (18%) died within 12 months of baseline; 170 (66%) of these were TB-related. The cumulative probability of all-cause and TB-related death at 12 months was 29%, 5% and 11% (p< .001) and 22%, 1% and 4% (p< .001) in EE, WE and LA respectively. In EE, fewer patients were on cART at 12 months (68% v 90% and 85%, p< .001), and many were treated without access to baseline DST (66% v 37% and 69% p< .001). Among those with DST, the empiric treatment regimen (composed when DST results were not yet known) included < 3 active TB-drugs in 36%, 7% and 9% (EE, WE, LA, p< .001); of those 81%, 46% and 86% had MDR-TB. Patients who started < 3 active drugs were at excess risk of dying from TB compared to patients starting ≥3 active drugs (aHR=3.20, 95%CI=1.82-5.66). Patients without DST results (and thus no option for targeting subsequent therapy) also had a greater risk of death (aHR=2.33, 1.40-3.87). This appeared driven by deaths in EE (Figure, aHR=2.37, 1.66-3.40, analyses restricted to EE), although a formal test for interaction with region was not significant (p=0.44), potentially due to few deaths outside EE.
Conclusions: There is an elevated risk of death from TB in HIV patients managed in EE compared to WE and LA. This is partly explained by modifiable risk factors including low rates of DST, hampering the optimized choice of TB drugs in a setting of high MDR-TB prevalence. Our data call for urgent action to improve the care of HIV/TB patients in EE.



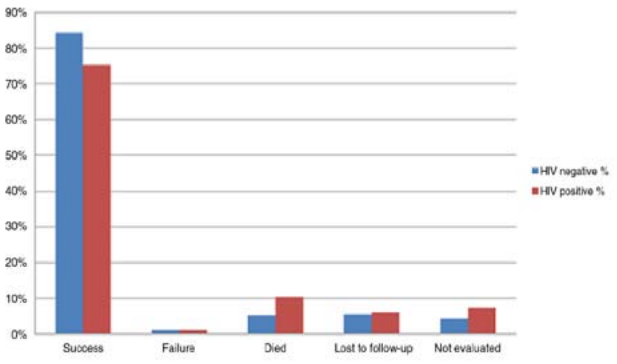
[Figure 1. TB-related death among HIV-positive patients according to the number of active drugs used as part of empiric TB therapy[1]]

MOAB0204

Missed opportunities in the TB/HIV cascade of care in 14 high burden TB/HIV African countries, 2012

A. Baddeley[1], M. Doherty[2], A. Kanchar[1], A. Matteelli[1], H. Bakir Timimi[1], H. Getahun[1]
[1]World Health Organization, Global TB Programme, Geneva, Switzerland, [2]World Health Organization, Department of HIV/AIDS, Geneva, Switzerland
Presenting author email: baddeleya@who.int

Background: Despite being preventable and curable, tuberculosis (TB) remains the leading cause of morbidity and mortality of people living with HIV (PLHIV). The past decade has seen considerable scale-up of collaborative TB/HIV activities, however, implementation remains suboptimal. Closer inspection at each stage of the cascade of TB/HIV care is warranted to assess the gaps and to identify opportunities for strengthened service delivery in order to eliminate HIV-associated TB mortality.
Methods: Data were downloaded from the Global TB Programme Database on 22/01/2015 on the latest available TB treatment outcomes (2012 cohort), disaggregated by HIV status, from reporting high TB/HIV burden countries in the WHO African Region, along with related data on the implementation of collaborative TB/HIV activities. Data were analysed and missed opportunities identified.
Results: 14 countries reported the required outcome data, accounting for some 570,000 HIV-positive incident TB cases, (Table 1), or 63% of the African burden and 49% of the global burden in 2012. More than 50,000 reported HIV-positive TB cases died or were lost to follow-up, representing 18% of evaluated cases, compared with 11% of evaluated HIV-negative TB cases, (Figure 1).



**Botswana, Burkina Faso, Burundi, Central African Republic, Ghana, Kenya, Lesotho, Mali, Namibia, Nigeria, Rwanda, South Africa, Swaziland, United Republic of Tanzania*

[Figure 1. Comparison of treatment outcomes according to HIV status in 14 African Countries 2012 cohort]*

Of the estimated HIV-positive TB cases almost 260,000 (46%) went unreported, (Table 1). Among registered TB patients, 11% (around 80,000) did not have an HIV test in the TB register. In eight countries that reported, there was a gap of over 1,700,000 reported as not having received a TB screen, (53% of the 3,300,000 people in HIV care). Among notified HIV-positive TB cases, 42% (nearly 130,000) were not reported as receiving ART. Only five of the fourteen countries reported providing Isoniazid Preventive Therapy (IPT) to people newly registered in HIV care. In the four countries that reported a denominator, 69% (some 900,000) people newly enrolled in HIV care did not receive IPT.

	Est. HIV-pos incident TB cases	% of est. HIV-pos TB cases unreported	Notified TB cases	% of TB cases with unreported HIV status	Notified TB cases with HIV-pos status	% of HIV-pos TB cases not on ART
14 High burden TB/HIV African countries	570,000	46%	695,580	11%	306,398	42%

[Table 1]

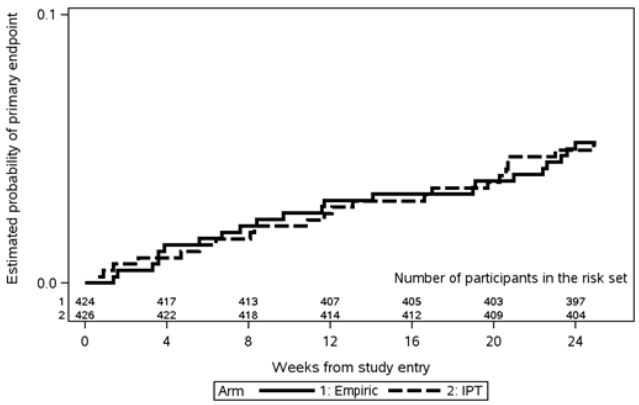
Conclusions: This analysis highlights some considerable gaps in the care cascade, resulting from suboptimal implementation and/or recording and reporting. In order to prevent disproportionate TB mortality among PLHIV, countries are encouraged to scrutinize weaknesses in the care cascade at every level to enhance early detection of HIV-associated TB, timely ART initiation and scaled-up TB prevention.

MOAB0205LB

Empiric TB therapy does not decrease early mortality compared to isoniazid preventive therapy in adults with advanced HIV initiating ART: results of ACTG A5274 (REMEMBER study)

M. Hosseinipour[1,2], G. Bisson[3], S. Miyahara[4], X. Sun[4], A. Moses[1], C. Riviere[5], F.K. Kirui[6], S. Badal-Faesen[7], D. Lagat[8], M. Nyirenda[9], K. Naidoo[10], J. Hakim[11], P. Mugyenyi[12], G. Henostroza[13], P.D. Leger[5], J.R. Lama[14], L. Mohapi[15], J. Alave[14], V. Mave[16], V.G. Veloso[17], S. Pillay[18], N. Kumarasamy[19], J. Bao[20], E. Hogg[21], L. Jones[22], A. Zolopa[23], J. Kumwenda[9], A. Gupta[24], Adult AIDS Clinical Trials Group 5274 (REMEMBER) Study Team
[1]UNC Project, Lilongwe, Malawi, [2]University of North Carolina School of Medicine, Chapel Hill, United States, [3]University of Pennsylvania, Philadelphia, United States, [4]Harvard University, Boston, United States, [5]GHESKIO, Port-au-Prince, Haiti, [6]Kenya Medical Research Institute (KEMRI), Kisumu, Kenya, [7]Clinical HIV Research Unit, Department of Medicine, University of Witwatersrand, Johannesburg, South Africa, [8]Moi University School of Medicine, Eldoret, Kenya, [9]Johns Hopkins Project, Blantyre, Malawi, [10]Centre for the AIDS Programme of Research in South Africa, Durban, South Africa, [11]University of Zimbabwe, Harare, Zimbabwe, [12]Joint Clinical Research Centre, Kampala, Uganda, [13]Centre for Infectious Diseases Research in Zambia, Lusaka, Zambia, [14]Asociacion Civil Impacta Salud y Educacion, Lima, Peru, [15]Perinatal HIV Research Unit (PHRU), Johannesburg, South Africa, [16]B.J. Medical College-Johns Hopkins Clinical Trials Unit, Pune, India, [17]Evandro Chagas National Institute of Infectious Diseases/Fiocruz, Rio de Janeiro, Brazil, [18]University of KwaZulu-Natal, Durban, South Africa, [19]YRGCARE Medical Centre,VHS, Chennai, India, [20]National Institutes of Health, Bethesda, United States, [21]Social & Scientific Systems, Silver Spring, United States, [22]Frontier Sciencies, Buffalo, United States, [23]Stanford University, Palo Alto, United States, [24]Johns Hopkins University School of Medicine, Baltimore, United States

Background: Strategies for reducing the high early mortality seen among patients initiating ART in resource-limited settings (RLS) are urgently needed. We hypothesized that given the high burden of tuberculosis (TB) in these settings, empiric TB treatment among patients at high risk for death would reduce early mortality.
Methods: REMEMBER (Reducing Early Mortality and Early Morbidity by Empiric Tuberculosis Treatment Regimens) is a multi-country randomized clinical trial comparing 2 management strategies: ART + empiric 4 drug TB therapy (Empiric) vs. ART+ isoniazid preventive therapy (IPT) in HIV infected individuals with CD4 count < 50 cells/mm^3. Participants were screened for TB prior to entry using symptom screen, locally available diagnostics per standard of care, and GeneXpert when available. The study was stratified according to CD4 count (< 25 vs. >=25 cells/mm3) and poor prognostic factors (body mass index < 18.5, Hemoglobin < 8g/dl, recent hospitalization). The primary endpoint was survival (death or unknown status) at 24 weeks post randomization, and Kaplan Meier estimates of the endpoint rates across arms were compared by the z-test.
Results: Of 1368 participants screened, 850 (62%) were randomized; 53% were male, 90% were black, and median (quartiles) age was 36 (30-42) years. The median (quartiles) CD4 count at study entry was 18 cells/mm^3 (9, 32). At week 24, both arms had the same primary endpoint rate of 5.2% (95% CI: 3.5% to 7.8% for Empiric and 3.4% to 7.8% for IPT) with an absolute risk difference of -0.06% (95% CI: -3.05% to 2.94%). Primary endpoint rates were similar across arms for the stratification factors and for other secondary outcomes: Viral load < 400 copies/ml was achieved in 84% Empiric and 85% IPT; Grade 3 or 4 symptoms occurred in 12 % Empiric and 11% IPT; Grade 3 or 4 laboratory abnormalities in 23% both arms; and new clinical events in 49% Empiric and 51% IPT.
Conclusions: Among highly TB screened participants with advanced HIV in RLS, empiric TB therapy did not reduce mortality at 24 weeks compared to IPT. The low mortality seen in both arms supports enhanced screening for TB prior to ART initiation and the routine use of IPT.



[KM graph for 5274]

MOAC01 TasP: Just Do It

MOAC0101LB

Final results of the HPTN 052 randomized controlled trial: antiretroviral therapy prevents HIV transmission

M. Cohen[1], Y. Chen[2], M. McCauley[3], T. Gamble[4], M. Hosseinipour[5,6], N. Kumarasamy[7], J. Hakim[8], N. Kumwenda[9], T. Brum[10], B. Grinsztejn[11], S. Godbole[12], S. Chariyalertsak[13], B. Riegel Santos[14], K. Mayer[15,16], I. Hoffman[17], S. Eshleman[18], E. Piwowar-Manning[18], S.-S. Ou[19], L. Cottle[20], J. Makhema[21], L. Mills[22], R. Panchia[23], S. Badal-Faesen[24], J. Eron[5], J. Gallant[25], D. Havlir[26], S. Swindells[27], V. Elharrar[28], D. Burns[28], T. Taha[29], K. Nielsen[30], D. Celentano[31], M. Essex[32,33], T. Fleming[34], HPTN 052 Study Group
[1]University of North Carolina at Chapel Hill, Medicine/Infectious Diseases, Chapel Hill, United States, [2]Fred Hutchinson Cancer Research Center, Statistical Center for HIV/AIDS Research and Prevention, Seattle, United States, [3]FHI 360, Washington, United States, [4]FHI 360, Durham, United States, [5]University of North Carolina at Chapel Hill, Institute for Global Health and Infectious Diseases, Chapel Hill, United States, [6]UNC Project-Malawi, Institute for Global Health and Infectious Diseases, Lilongwe, Malawi, [7]Y. R. Gaitonade Center for AIDS Research and Education, Chennai, India, [8]University of Zimbabwe, Harare, Zimbabwe, [9]College of Medicine-Johns Hopkins Project, Blantyre, Malawi, [10]Hospital Geral de Nova Iguacu and Laboratorio de AIDS e Imunologia Molecular-IOC/Fiocruz, Rio de Janeiro, Brazil, [11]Instituto Nacional de Infectologia Evandro Chagas-INI-Fiocruz, Rio de Janeiro, Brazil, [12]National AIDS Research Institute (ICMR), Pune, India, [13]Research Institute for Health Sciences, Chiang Mai University, Chiang Mai, Thailand, [14]Hospital Nossa Senhora da Conceição, Porto Alegre, Brazil, [15]The Fenway Institute, Boston, United States, [16]Beth Israel Deaconess Medical Center at Harvard Medical School, Boston, United States, [17]University of North Carolina Institute of Global Health and Infectious Diseases, Chapel Hill, United States, [18]Johns Hopkins University School of Medicine, Department of Pathology, Baltimore, United States, [19]Fred Hutchinson Cancer Research Center, Seattle, United States, [20]Fred Hutchinson Cancer Research Center, Statistical Center for HIV/AIDS Research & Prevention, Seattle, United States, [21]Botswana Harvard Aids Institute, Gaborone, Botswana, [22]KEMRI-CDC, Kisumu, Kenya, [23]Chris Hani Baragwanath Hospital, Soweto HPTN CRS, Soweto, South Africa, [24]University of the Witwatersrand, Clinical HIV Research Unit, Johannesburg, South Africa, [25]Southwest CARE Center, Albuquerque, United States, [26]University of California, San Francisco, United States, [27]University of Nebraska Medical Center, Omaha, United States, [28]Division of AIDS, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Clinical Prevention Research Branch/Prevention Sciences Program, Bethesda, United States, [29]Johns Hopkins University Bloomberg School of Public Health, Baltimore, United States, [30]David Geffen UCLA School of Medicine, Los Angeles, United States, [31]Johns Hopkins University Bloomberg School of Public Health, Department of Epidemiology, Baltimore, United States, [32]Harvard T.H. Chan School of Public Health AIDS Initiative, Boston, United States, [33]Botswana Harvard AIDS Institute Partnership, Gaborone, Botswana, [34]University of Washington, Department of Biostatistics, Seattle, United States

Background: The HPTN 052 trial was designed to evaluate whether antiretroviral therapy (ART) reduces sexual transmission of HIV. The trial started in April 2005 and ended in May 2015.
Methods: HPTN 052 enrolled 1,763 HIV serodiscordant couples in Malawi, Zimbabwe, South Africa, Botswana, Kenya, Thailand, India, Brazil and the US (97% heterosexual). HIV-infected index participants had CD4 cell counts between 350-550 cells/mm^3 at enrollment. Index participants were randomized to receive ART at enrollment (early arm) or when their CD4 cell count fell to ≤250 cells/mm^3 or they developed an AIDS-defining illness (delayed arm). The primary analysis was based on genetically-linked viral transmission events.
When interim analysis in May 2011 demonstrated the benefits of early ART, ART was offered

to all index participants in the delayed arm (*New Eng J Med 2011*.365:493-505); the study then continued otherwise unchanged.
Results: At the end of the trial, 1,171 (66%) of 1,763 couples remained in follow-up (603/886 early arm; 568/877 delayed arm). Index participants were followed for 9,822 person-years (py). ART was initiated by all 886 index participants in the early arm and 785 (90%) of 877 index participants in the delayed arm. Before ART was offered to all index participants, there was 1 linked infection in the early ART arm (4 total infections/1,776 py) and 35 linked infections in the delayed arm (42 total infections/1,757 py). After ART was offered to index participants in both study arms, there were 2 linked infections in the early arm (15 total infections/2,537 py) and 6 linked infections in the delayed arm (17 total infections/2,412 py). Only 7 linked infections were diagnosed while the index participant was receiving ART: 4 infections were diagnosed shortly after the index participant started ART and 3 were diagnosed after ART failure. These findings demonstrate that HIV transmission is very unlikely when viral replication is suppressed.
Conclusions: The previously reported efficacy of early ART for HIV prevention was sustained for the duration of the HPTN 052 study. ART, combined with counselling and provision of condoms provides durable, highly-effective protection from HIV transmission in serodiscordant couples.

MOAC0102

Level of viral suppression and cascade of HIV care in a South African semi-urban setting in 2012 (ANRS-12126 -12285)

K. Jean[1], A. Puren[2], E. Cutler[2], B. Singh[2], J. Bouscaillou[1], R. Rain-Taljaard[3], D. Taljjard[4], P. Lissouba[1], G. Peytavin[5], B. Auvert[1,6,7]
[1]INSERM, Villejuif, France, [2]NICD-NHLS, Johannesburg, South Africa, [3]Progressus, Johannesburg, South Africa, [4]CHAPS, Johannesburg, South Africa, [5]APHP Bichat-Cl Bernard, Paris, France, [6]University of Versailles, Versailles - Saint Quentin en Yvelines, France, [7]APHP - Hopital Ambroise Pare, Boulogne, France
Presenting author email: bertran.auvert@uvsq.fr

Background: For antiretroviral treatment (ART) programs to have a preventive impact, the proportion of HIV-infected people being treated should be high. In 2012, seven years after the beginning of ART programs in the South-African township of Orange Farm, we measured the proportion of HIV+ who were virally suppressed, especially among age groups highly exposed to HIV (women 18-29y and men 25-34y).
Methods: A community-based cross-sectional representative survey conducted in 2012 among 3293 men and 3473 women. Study procedures included a face-to-face questionnaire and collection of blood samples that were tested for HIV, 10 antiretroviral drugs (ARVs) and HIV-Viral Load (VL).
Results: HIV prevalence was 17.0% [95% Confidence Interval: 15.7-18.3%] among men and 30.1% [28.5-31.6%] among women. Overall, 59.1% [57.4-60.8%] of men and 79.5% [78.2-80.9%] of women reported having ever been tested for HIV. When controlling for age, circumcised men were more likely to ever have been tested (66.1% vs 53.6%; p<0.001).
Among HIV+ individuals, 21.0% [17.7-24.6%] of men and 30.5% [27.7-33.3%] of women tested positive for any ARV. The ratio of ARV+ people over those HIV- was 0.084. Using basic calculations, we found that if ART programs were actually treating all eligible patients since 2005, this ratio should have been 0.21-0.28, indicating an effectiveness of ART programs around 47-63%.
Among ARV+ participants, 91.9% [88.7-94.3%] had viral suppression (VL< 400cp/mL). The proportion of viral suppression among HIV+ was 27.0% [24.3-29.9%] among women and 17.5% [14.4-20.9%] among men. These proportions were lower among the highly-exposed age groups: 15.6% [12.1-19.7%] among women and 8.4% [5.0-13.1%] among men.
Conclusions: In Orange Farm, in the 2005-2012 period, ART programs were sub-optimal and, among HIV+, proportion of viral suppression was low, especially among the highly-exposed age groups. This suggests that, up to 2012, ART programs may not have substantially impacted HIV incidence. However, our study showed at community level that, when effectively taken, ARVs present a high effectiveness in suppressing VL.

MOAC0103

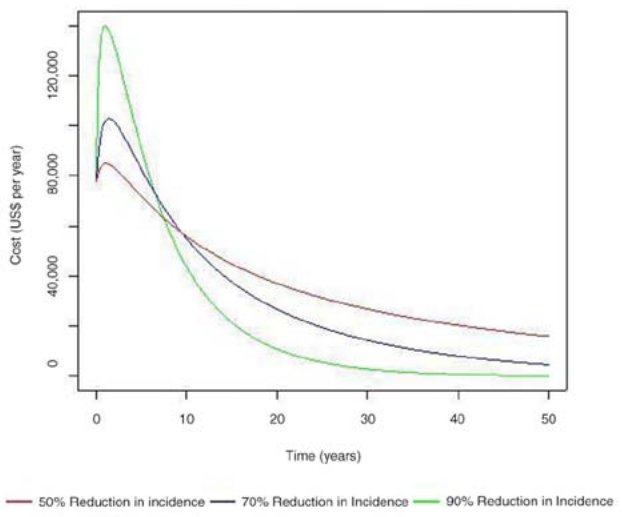
A mathematical model to determine potential costs and benefits of increasing antiretroviral therapy coverage in female sex workers: the case of Panama

L. Jenkins[1], J. Nordio[2], K. Vasarhelyi[2,3], A. Nunez[4], R. Barrios[5], A. Rutherford[2,6]
[1]University of South Florida, USF-Health and Education International Foundation, Panama, Panama, [2]Simon Fraser University, IRMACS, Burnaby, Canada, [3]Simon Fraser University, Faculty of Health Sciences, Burnaby, Canada, [4]Ministry of Health, National STI/HIV/AIDS Program, Panama, Panama, [5]British Columbia Centre for Excellence in HIV/AIDS, Vancouver, Canada, [6]Simon Fraser University, Department of Mathematics, Burnaby, Canada
Presenting author email: jenkins.lorna@yahoo.com

Background: Panama adopted Treatment as Prevention (TasP) in February 2014 and is now seeking efficient and effective ways to expand antiretroviral therapy (ART) coverage in key populations. We developed a mathematical model to determine the ART coverage and associated costs required to meet HIV incidence reduction targets for the female sex worker (FSW) population, which has a 1.6% HIV prevalence.
Methods: The Government of Panama, British Columbia Centre for Excellence in HIV/AIDS and Simon Fraser University are collaborating to develop mathematical models for informing Panama's TasP strategy. Quantitative and qualitative Information was collected from national reports, key informant interviews and focus groups with civil society to inform a compartmental HIV transmission model incorporating disease progression and treatment. The model was calibrated and validated for 2013. Estimated FSW population size is 17,000 and according to the GARP report, current ART coverage for both FSW and the hard-to-reach client population is about 47%. Annual ART cost/individual is US$625. Simulation scenarios for meeting 50%, 70% or 90% reduction in HIV incidence in FSW in 15 years assumed ART expansion either for FSW and their clients (Scenario 1) or for FSW only (Scenario 2).
Results: ART expansion for FSW costs slightly more in Scenario 1 than 2. However, overall for both populations of FSW and clients, more infections are averted and treatment program costs are lower for the strategy targeting FSW only (see table). Furthermore, initial aggressive expansion of ART coverage leads to overall cost savings and a more effective means of averting new infections (see figure). The result of no action compared to the 90% Scenario 2 strategy would be 170% more HIV infections and 50% more treatment costs over 15 years.

POPULATION	TARGET Incidence Reduction in FSW in 15Yrs	NO ART EXPANSION New Cases in 15Yrs	NO ART EXPANSION US$ Costs in 15Yrs	TasP SCENARIO 1 New Case in 15Yrs	TasP SCENARIO 1 US$ Costs in 15Yrs	TasP SCENARIO 2 New Cases in 15Yrs	TasP SCENARIO 2 US$ Costs in 15 Yrs
FSW	50%	2816	$1,240,560	2003	$911,016	2000	$1,025,737
Clients	50%	4096	$3,841,072	2878	$3,308,139	2847	$3,139,332
Both	50%	6912	$5,061,632	4881	$4,219,155	4847	$4,165,069
FSW	70%	2816	$1,240,560	1620	$863,324	1605	$1,093,578
Clients	70%	4096	$3,841,072	2331	$3,030,029	2259	$2,782,224
Both	70%	6912	$5,061,632	3951	$3,893,353	3864	$3,875,802
FSW	90%	2816	$1,240,560	1118	$777,438	1074	$1,107,593
Clients	90%	4096	$3,841,072	1615	$2,818,353	1480	$2,260,854
Both	90%	6912	$5,061,632	2733	$3,595,791	2554	$3,368,447

[Outcomes and Costs of TasP Expansion Scenarios]



[Annual Treatment Cost for FSW Population]

Conclusions: Rapid expansion of TasP for female sex workers in Panama would avert infections and treatment costs already within 15 years. Initial short-term investment to increase ART coverage would be offset by long-term savings. Since Panama adopted TasP, UNAIDS has announced the 90-90-90 targets for HIV diagnosis, treatment and suppression, which call for an even more rapid reduction in incidence. Ongoing analyses are evaluating costs and outcomes of reaching the new targets by 2020.

MOAC0104

Does a universal test and treat strategy impact ART adherence in rural South Africa? ANRS 12249 TasP cluster-randomized trial

C. Iwuji[1,2], R. Dray-Spira[3], A. Calmy[4], J. Larmarange[1,5], J. Orne-Gliemann[6], F. Dabis[6], D. Pillay[1,7], K. Porter[8]

[1]Africa Centre for Health and Population Studies, University of KwaZulu-Natal, Mtubatuba, South Africa, [2]University College London, Research Department of Infection and Population Health, London, United Kingdom, [3]INSERM-UPMC Univ Paris 06, UMR_S 1136, Paris, France, [4]Unité VIH/Sida, Hôpitaux Universitaires, Geneva, Switzerland, [5]CEPED (UMR 196 U. Paris Descartes INED IRD), Paris, France, [6]Univ. Bordeaux, ISPED, Centre INSERM U 897, Epidemiologie-Biostatistique, Bordeaux, France, [7]University College London, Infection and Immunity, London, United Kingdom, [8]MRC Clinical Trials Unit at UCL, London, United Kingdom

Presenting author email: ciwuji@yahoo.com

Background: HIV treatment guidelines are recommending ART at increasingly higher CD4 counts for maximizing individual and population benefits. However, the expansion of ART use may be at the expense of optimal adherence. We report on adherence and virological suppression when initiating ART at different CD4 thresholds within the Treatment as Prevention (ANRS 12249) trial of universal home-based testing and immediate ART initiation in rural KwaZulu-Natal.

Methods: Using data of a cluster-randomised trial of immediate ART vs. initiation according to current national guidelines (CD4≤350cells/mm^3), we compared adherence levels (≥95% vs. <95%) measured using a visual analogue scale (VAS) and pill count (PC) and virological suppression at 6 months (<400 c/mL) according to CD4 count at ART initiation through logistic regression models, adjusting for possible confounders (age, sex, marital status, education and employment).

Results: During March 2012-May 2014, 601 participants who were not on ART entered care in trial clinics; 382 initiated ART; 254 have completed ≥6 months on ART, 227 of whom had 6 months HIV RNA data and were included in analyses. 169 were women; median (IQR) age and CD4 at ART initiation were 35 years (28, 46) and 313cells/mm^3 (206, 513). Adherence ≥95% at 6 months was high (88% and 83% by PC and VAS, respectively) with no evidence that this was associated with CD4 at initiation (aOR=0.97 per 100 cells/mm^3 higher, 95%-CI: 0.83-1.12, p=0.65 for VAS; aOR 1.13 per 100cells/mm^3 higher, 0.98-1.31, p=0.09 for PC). Male sex was independently associated with < 95% adherence (2.58, 1.24-5.35, p= 0.01; ref. females). 83% (183/227) of those who started ART achieved HIV suppression by 6 months with no association with CD4 at initiation (1.13 per 100cells/mm^3 higher, 0.96-1.33, p=0.40). Compared to those with ≥95% adherence by VAS, individuals with < 95% adherence were somewhat less likely to suppress (0.44, 0.19-1.03, p=0.06).

Conclusions: We found no evidence that, among people newly entering HIV care, higher CD4 at ART initiation was associated with reduced adherence or poorer virological suppression, at least in the short-term. In this rural South African setting, motivation to adhere to ART may be independent of the presence of symptomatic HIV disease.

MOAC0105LB

Community-based HIV testing and linkage effectively delivers combination HIV prevention: results from a multisite randomized trial

R. Barnabas[1], H. van Rooyen[2], E. Tumwesigye[3], J. Brantley[1], J. Baeten[1], A. van Heerden[2], B. Turyamureeba[3], P. Joseph[4], M. Krows[1], J. Hughes[1], C. Celum[1], Linkages

[1]University of Washington, Global Health, Seattle, United States, [2]Human Sciences Research Council, KwaZulu-Natal, South Africa, [3]Integrated Community-Based Initiatives, Kabwohe, Uganda, [4]Fred Hutchinson Cancer Research Center, Vaccine and Infectious Diseases Division, Seattle, United States

Background: To have a population impact in generalized HIV epidemics in Africa, high coverage of combination HIV prevention strategies that reduce the susceptibility of uninfected persons and the infectiousness of infected persons is needed. Community-based HIV testing and counseling, with linkage to care and prevention, is a potential delivery platform for combination HIV prevention.

Methods: We conducted a multisite program of community-based HIV testing and counseling, linkage to HIV care, and demand creation for voluntary medical male circumcision (VMMC) in rural communities in KwaZulu-Natal, South Africa and Sheema district, Uganda. HIV testing was done at home or through mobile units. HIV-positive persons were randomly allocated to linkage to care strategies: clinic facilitation by lay-counselors at the initial clinic visit, lay-counselor follow-up visits at home, or standard clinic referral. HIV-negative uncircumcised men were randomized to VMMC demand creation strategies: lay counselor follow-up visits at home, SMS reminders, or standard VMMC promotion at the time of testing.

Results: Between June 2013 and February 2015, 15,332 persons received HIV testing and counseling. Among 1,325 HIV-positive persons randomized to linkage strategies, overall clinic linkage was high (93%). Compared to standard linkage, lay counselor clinic facilitation increased linkage to care (RR=1.09, 95% CI: 1.05-1.13), and home follow-up visits increased ART initiation (RR=1.23, 95% CI: 1.02-1.47). In all arms, ART initiation was limited by bottlenecks in service delivery at the clinics, although 67% of those eligible initiated ART by 9 months. Overall, 82% of persons initiating ART achieved viral suppression without significant difference between study arms.

Of 750 HIV-negative uncircumcised men randomized to VMMC promotion strategies, uptake of circumcision was 41% by month 3. Compared to standard messages, VMMC uptake was significantly higher in the SMS promotion (RR=1.72, 95% CI: 1.36-2.17) and lay counselor follow-up arms (and RR=1.67, 95% CI: 1.29-2.14).

Conclusions: Community-based HIV testing and linkage to care and prevention effectively delivers combination HIV prevention. Simple strategies, such as SMS reminders or lay-counselor visits, increase linkage for ART initiation and male circumcision. Community-based strategies require integration with efficient clinical services, and additional strategies are needed to address clinic delays that are barriers to ART delivery.

MOAC0106LB

Treatment as prevention: characterization of partner infections in the HIV Prevention Trials Network 052 trial

S.H. Eshleman[1], S.E. Hudelson[1], S.S. Ou[2], A.D. Redd[3,4], R. Swanstrom[5], S.F. Porcella[6], Y.Q. Chen[2], E. Piwowar-Manning[1], M. McCauley[7], T. Gamble[8], M. Sievers[3], C.A. Martens[6], D. Bruno[6], L.-H. Ping[9], E. Dukhovlinova[9], T.C. Quinn[3,4], J. Kumwenda[10], M. Maliwichi[11], N. Nhando[12], V. Akelo[13], S. Moyo[14], R. Panchia[15], N. Kumarasamy[16], N. Chotirosniramit[17], M.M. Rocha[18], F. Bustorff[19], B. Grinsztejn[20], K.H. Mayer[21,22], J.P. Hughes[2], M.S. Cohen[23], for the HPTN 052 Study Team

[1]Johns Hopkins Univ. School of Medicine, Dept. of Pathology, Baltimore, United States, [2]Fred Hutchinson Cancer Research Center, Vaccine and Infectious Disease Division, Seattle, United States, [3]Johns Hopkins Univ. School of Medicine, Dept. of Medicine, Baltimore, United States, [4]National Institute of Allergy and Infectious Diseases, National Institutes of Health, Laboratory of Immunoregulation, Baltimore, United States, [5]Univ. of North Carolina at Chapel Hill, Dept. of Biochemistry and Biophysics, Chapel Hill, United States, [6]National Institute of Allergy and Infectious Diseases, National Institutes of Health, Genomics Unit, Research Technologies Section, Rocky Mountain Laboratories, DIR, Hamilton, United States, [7]FHI 360, Washington, United States, [8]FHI 360, Durham, United States, [9]Univ. of North Carolina at Chapel Hill, Lineberger Comprehensive Cancer Center, Chapel Hill, United States, [10]College of Medicine-Johns Hopkins Project, Blantyre, Malawi, [11]UNC Project, Lilongwe, Malawi, [12]Univ. of Zimbabwe, Harare, Zimbabwe, [13]KEMRI-CDC, Kisumu, Kenya, [14]Botswana Harvard AIDS Institute, Gaborone, Botswana, [15]Chris Hani Baragwanath Hospital, Soweto HPTN CRS, Soweto, South Africa, [16]Y. R. Gaitonade Center for AIDS Research and Education, Chennai, India, [17]Chiang Mai University, Research Institute for Health Sciences, Chiang Mai, Thailand, [18]Hospital Nossa Senhora da Conceição, Porto Alegre RS, Brazil, [19]Hospital Geral de Nova Iguacu and Laboratorio de AIDS e Imunologia Molecular-IOC/Fiocruz, Rio de Janeiro, Brazil, [20]Instituto Nacional de Infectologia Evandro Chagas-INI-Fiocruz, Fiocruz, Rio de Janeiro, Brazil, [21]The Fenway Institute, Boston, United States, [22]Harvard Medical School/Beth Israel Deaconess Medical Center, Boston, United States, [23]Univ. of North Carolina at Chapel Hill, Dept. of Medicine, Chapel Hill, United States

Presenting author email: seshlem@jhmi.edu

Background: In 2011, results from an interim analysis of the HPTN 052 trial demonstrated that early antiretroviral therapy (ART) was highly effective for prevention of HIV transmission from HIV-infected adults (index participants) to their HIV-uninfected sexual partners. All index participants were offered ART after May, 2011; the trial ended May, 2015. This report describes the analysis of partner infections in HPTN 052.

Methods: HIV from index-partner pairs was analyzed. Phylogenetic methods were used to compare HIV *pol* sequences from index-partner pairs and controls. Linkage probability was further assessed by comparing the genetic distances between *pol* sequences (Bayesian analysis). Selected samples were also analyzed using next generation sequencing (*env* region). Three infections that occurred close to the time of index ART initiation were analyzed by BEAST and serologic methods to determine the probable timing of HIV transmission. This abstract presents provisional findings based on data available as of May, 2015.

Results: Seventy-five partner infections were confirmed (64 in Africa, 6 in Asia, 5 in the Americas), including 39 described previously (JID 2011; 204:1918-26). Linkage status was determined for 70 cases (5 cases failed analysis). Of these 70 cases, 26 (37%) were classified as unlinked (the partner was most likely infected from someone other than the index participant), and 44 (63%) were classified as linked (the index was most likely the source of the partner´s HIV infection). In 7 of the 44 linked cases, the partner seroconverted while the index was receiving study ART. In 4 of these 7 cases, the partner seroconverted shortly after the index started ART, likely before the index was virally suppressed. In the remaining 3 cases, the partner seroconverted when the index was not virally suppressed due to ART failure.

Conclusions: Laboratory and statistical methods were used to identify and characterize linked partner infections in HPTN 052. Seven linked infections were observed in partners after index participants started study ART: four occurred shortly after ART initiation and three occurred in the setting of ART failure. The timing of the linked transmission events supports the model that HIV transmission is very unlikely in the setting of viral suppression.

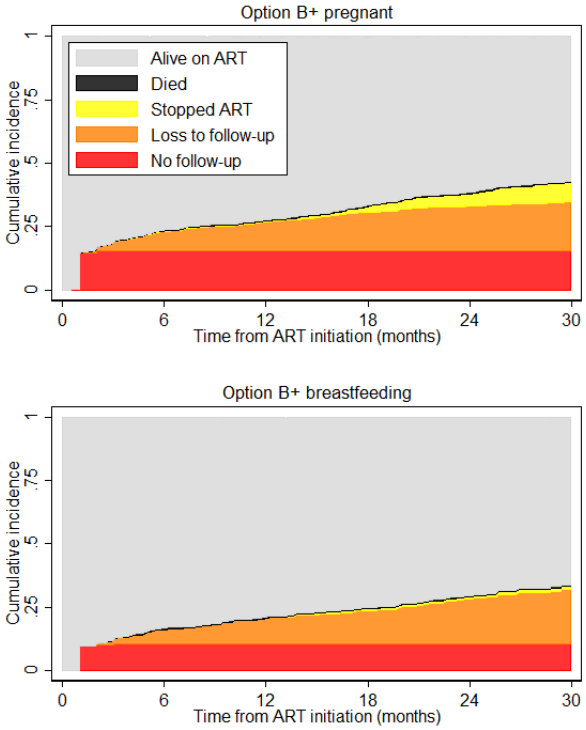
MOAC02 PMTCT: Gaps and Next Steps

MOAC0201

Post prevention of mother-to-child-transmission: 30-months outcomes in the Malawian "Option B+ programme"

A.D. Haas[1], L. Tenthani[1,2], M.T. Msukwa[1], A. Jahn[2,3], D. Midiani[3], E. Mhango[3], O. Gadabu[4], K. Tal[1], A. Spörri[1], M. Egger[1], F. Chimbwandira[3], J.J. van Oosterhout[5], O. Keiser[1]
[1]*University of Bern, Institute of Social and Preventive Medicine, Bern, Switzerland,* [2]*University of Washington, International Training and Education Centre for Health, Seattle, United States,* [3]*Ministry of Health, Department of HIV and AIDS, Lilongwe, Malawi,* [4]*Baobab Health Trust, Lilongwe, Malawi,* [5]*Dignitas International, Zomba, Malawi*
Presenting author email: andreas.haas@ispm.unibe.ch

Background: Under the Option B+ PMTCT strategy HIV-infected pregnant and breastfeeding women initiate lifelong ART. Long-term retention after weaning is unknown. We examine treatment outcomes for up to 30-months after ART initiation.
Methods: We examined cumulative incidence of mortality, no follow-up after ART initiation, loss to follow-up after the first follow-up visit (LTF), treatment discontinuation and retention in the Malawian "Option B+ programme". We analysed 24-months aggregated facility-level data (65,749 patients, 654 facilities) and 30-months individual-level data (3,225 patients; 6 large facilities) from Option B+ patients who initiated ART during 2011-2014. We excluded patients who transferred to another facility.



[Figure 1: ART outcomes for Option B+ patients]

Results: In *facility-level data* 79.9% (52,525/65,749) and 75.0% (40,509/54,029) of all patients were still in care 6 and 12 months after ART initiation. After 24 months 70.6% (17,257/24,245) were retained, 26.8% were LTF, 1.5% had died and 0.6% stopped ART.
In six large facilities with *individual-level data*, slightly more patients defaulted or discontinued treatment: 24 and 30 months after ART initiation retention was 67.2% and 62.6%. Most patients were lost early and many did not return after the first visit (Figure 1), but after 18 months, further LTF was low. Of those who started ART during *pregnancy* 15.8% (95%-CI: 14.4-17.4%) had no follow-up, 18.0% (95%-CI: 16.0 -20.0%) were LTF, 6.6% (95%-CI: 5.1-8.3%) stopped ART and 0.5% (95%-CI: 0.3-1.0%) died during 30 months of follow-up. Of those who initiated ART while *breastfeeding* 8.5% % (95%-CI: 6.8-10.4%) had no follow-up, 18.6% (95%-CI: 15.7-21.7%) were LTF, 1.9% (95%-CI: 1.0-3.5%) stopped ART and 0.6% died (95%-CI: 0.2-1.3%) (Figure 1).
Patients who collected < 85% of the prescribed drugs during the first year of ART were at higher risk of LTF between 13-30 months compared to patients who collected >95% of the prescribed drugs (aHR: 3.02; 95%-CI: 1.99-4.59).
Conclusions: Suboptimal long-term retention in care (67-70% after 2 years) needs to be addressed. Attrition rates are higher in those starting ART during pregnancy vs. breast-feeding. Poor early drug adherence predicts later LTF. If women stay in care throughout breast-feeding, retention after weaning is likely.

MOAC0202

Recruiting male partners for couple HIV counseling and testing in Malawi's Option B+ program: a randomized controlled trial

N. Rosenberg[1,2], T. Mtande[1], F. Saidi[1], C. Stanley[1], E. Jere[1], L. Mwangomba[1], K. Kumwenda[1], I. Mofolo[1], M. Mwale[3], A. Chauma[3], W.C. Miller[2], I. Hoffman[2], M.C. Hosseinipour[1,2]
[1]*UNC Project, Lilongwe, Malawi,* [2]*University of North Carolina, Chapel Hill, United States,* [3]*District Health Office, Lilongwe, Malawi*
Presenting author email: nora_rosenberg@unc.edu

Background: In Malawi's antenatal program, HIV counseling and testing (HCT) for pregnant women is nearly universal, but couple HCT (cHCT) is uncommon, even though it is included in the Option B+ guidelines. CHCT is critical for HIV-infected women: many have HIV-infected partners in need of HIV diagnosis and treatment or HIV-uninfected partners in need of HIV prevention. CHCT may also increase Option B+ retention. Two partner recruitment strategies were assessed for cHCT uptake, male HIV status, female Option B+ retention, and consistent condom use.
Methods: Newly diagnosed HIV-infected pregnant women ≥16 years with male partners in Lilongwe were recruited from Bwaila District Hospital Antenatal Unit from March-October 2014 to participate in a randomized controlled trial. Women in the "invitation only" arm received an invitation inviting male partners to antenatal care; women in the "invitation plus tracing" arm received the same invitation but male partners were traced by phone and/or home visit if they failed to present within one week. Women were assessed one month later. Analyses were conducted using Chi-squared tests
Results: Of 220 eligible women, 200 (90%) consented and enrolled. CHCT uptake was 52% in the invitation only arm and 74% in the invitation plus tracing arm (p=0.001). Among the 126 men who presented for cHCT, 25% already knew they were HIV-infected, 47% learned they were HIV-infected for the first time, and 25% were HIV-uninfected with no difference by arm (p=0.8). There was a trend towards greater one-month retention among women in the invitation plus tracing arm (91%) compared to the invitation only arm (83%) (p=0.09). Among HIV-discordant couples, unprotected sex declined from 94% to 23% (p<0.001) following cHCT. Participation did not lead to intimate partner violence in either arm.
Conclusions: The invitation plus tracing strategy was extremely effective for recruiting male partners for cHCT and substantially more effective than the invitation only strategy. Both strategies identified many HIV-infected men and HIV-discordant couples. CHCT resulted in higher ART retention, declines in unprotected sex in HIV-discordant couples, and no intimate partner violence. Scaling up an invitation plus tracing strategy within the Option B+ program would have substantial public health benefits.

MOAC0203

Zimbabwe approaching virtual elimination of mother to child transmission of HIV following implementation of Option A

R. Buzdugan[1], S.I. McCoy[1], C. Watadzaushe[2], M.-S. Kang Dufour[3], M. Petersen[1], J. Dirawo[2], A. Mushavi[4], H.A. Mujuru[5], A. Mahomva[6], B. Engelsmann[7], A. Hakobyan[8], O. Mugurungi[4], F.M. Cowan[2,9], N.S. Padian[1]
[1]*University of California, Berkeley, United States,* [2]*Centre for Sexual Health and HIV Research Zimbabwe, Harare, Zimbabwe,* [3]*University of California, San Francisco, United States,* [4]*Ministry of Health and Child Care, Harare, Zimbabwe,* [5]*University of Zimbabwe, Harare, Zimbabwe,* [6]*Elizabeth Glaser Pediatric AIDS Foundation, Harare, Zimbabwe,* [7]*Organization for Public Health Interventions and Development, Harare, Zimbabwe,* [8]*Children's Investment Fund Foundation, London, United Kingdom,* [9]*University College London, London, United Kingdom*
Presenting author email: f.cowan@ucl.ac.uk

Background: We evaluated the impact of Option A, rolled out in August-December 2011, on HIV-free infant survival and mother-to-child transmission (MTCT) in Zimbabwe.
Methods: In 2012 and 2014 we conducted cross-sectional community-based serosurveys of mother-infants pairs residing in the catchment areas of 157 health facilities randomly selected from 5 of 10 provinces in Zimbabwe. Eligible infants (alive or deceased) were born 9-18 months before each survey to mothers ≥16 years old. We randomly selected mother-infant pairs and conducted questionnaires and verbal autopsies and collected blood samples. The impact analysis was limited to 113 catchment areas *unexposed* to Option A activities at baseline according to facility records; we estimated the HIV-free infant survival and MTCT rate within each catchment area and compared the 2012 and 2014 estimates using a paired t-test.

Results: We enrolled 8568 mother-infant pairs with viable maternal specimens in 2012 and 9619 in 2014, of whom 1107 (12.9%) and 1176 (12.2%) mothers respectively were HIV-infected. Among infants born to HIV-infected mothers, 90.6% (95% confidence interval (CI): 88.8, 92.3) of infants were alive and HIV-uninfected at 9-18 months in 2012, compared to 94.7% (95%CI: 93.4, 96.0) of infants in 2014 (p=0.001); MTCT was 9.0% (95%CI: 7.3, 10.7) in 2012 and 5.3% (95%CI: 4.0, 6.6) in 2014. In the 113 catchment areas where Option A was implemented *after* the infants surveyed in 2012 were born, there was a 6.5 percentage point (95%CI: 3.3, 9.7) mean increase in HIV-free infant survival (89.8% to 96.3%, p<0.001), and 6.2 percentage point (95%CI: 3.0, 9.4) mean decrease in MTCT (9.9% to 3.7%, p< 0.001).
Conclusions: We found a substantial and statistically significant increase in HIV-free infant survival and decrease in MTCT among infants aged 9-18 months following the implementation of Option A in Zimbabwe. Our estimates capture transmissions during pregnancy, delivery and the first 9-18 months of breastfeeding. Notably, 72% of HIV-exposed infants were still breastfeeding at baseline and 78% at endline, so additional infections may occur. The 2014 survey also provides a baseline for evaluating Option B+, which has been recently rolled out in Zimbabwe and should further accelerate efforts to eliminate MTCT.

MOAC0204

Antiretroviral intensification to prevent intrapartum HIV transmission in late comers

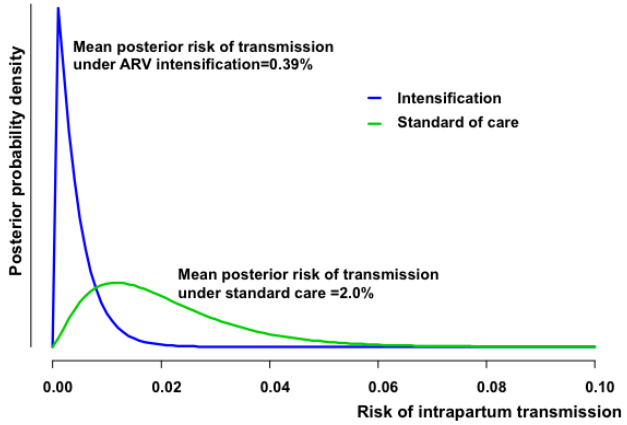
M. Lallemant[1,2,3], B. Amzal[1,4], S. Urien[5,6], P. Sripan[1,7], T. Cressey[1,2,3], N. Ngo-Giang-Huong[1,2,3], B. Rawangban[8], P. Sabsanong[9], T. Siriwachirachai[10], T. Jarupanich[10], P. Kanjanavikai[11], P. Wanasiri[12], S. Koetsawang[13], G. Jourdain[1,2,3], S. Le Cœur[1,2,14], PHPT-5 Study Team
[1]IRD174/PHPT, Chiang Mai, Thailand, [2]Harvard Chan School of Public Health, Immunology and Infectious Diseases, Boston, United States, [3]Chiang Mai University, Faculty of Associated Medical Sciences, Chiang Mai, Thailand, [4]LASER Analytica, London, United Kingdom, [5]Université Paris Descartes, Sorbonne Paris Cité, EA 08, Paris, France, [6]URC Paris Centre Necker Cochin, 0901 INSERM, Paris, France, [7]Kasetsart University, Department of Statistics, Faculty of Science, Bangkok, Thailand, [8]Nopparat Rajathanee Hospital, Bangkok, Thailand, [9]Samutprakarn Hospital, Samutprakarn, Thailand, [10]Khon Kaen Hospital, Khon Kaen, Thailand, [11]Banglamung Hospital, Chonburi, Thailand, [12]Kalasin Hospital, Kalasin, Thailand, [13]Mahidol University, Family Health Research Center, Bangkok, Thailand, [14]Institut National d'Etudes Démographiques (INED), Paris, France

Background: Infants born to HIV-infected pregnant women presenting late are at high risk of intrapartum infection. Mother/infant antiretroviral (ARV) intensification may substantially reduce this risk.
Methods: In a multicenter, phase 3, adaptive single-arm trial in Thailand, pregnant women with < 8 weeks of standard ARVs [zidovudine (ZDV)+lamivudine (3TC)+lopinavir/ritonavir] and their infants received 'ARV intensification' to prevent transmission at delivery: women took a single nevirapine (NVP) dose in labor and continued ARVs for 4 weeks; formula-fed neonates received 2 weeks AZT+3TC+NVP followed by 2 weeks AZT+3TC, instead of standard 1-week ZDV. Infants were tested for HIV at birth, 1, 2, 4, 6 months. A negative DNA PCR < 48 hours, followed by a confirmed positive PCR defined intrapartum transmission.
Data from 3,965 mother/infant pairs (84 intrapartum transmissions) in 3 PHPT randomized perinatal HIV prevention trials (NCT00386230, NCT00398684, NCT00409591) conducted in the same setting were used to define an historical control and build an intrapartum transmission model. viral load (VL) during pregnancy was modeled as a function of ARVs exposure and intrapartum transmission was predicted through a logistic model with VL, maternal/infant ARVs, delivery mode and prematurity status as covariates. The Bayesian estimation of the risks of intrapartum transmission with/without intensification used all historical information and decision rules to stop for futility or superiority of ARV intensification over standard of care (risk ratio RR< 1) were determined for 3 interim analyses. Prior intrapartum transmission probabilities were subsequently updated using the results of the intensification trial to derive posterior probabilities (Credibility interval, CrI) as well as probability distributions of RR< 1 and RR< 0.5.
Results: At first interim analysis, the DSMB recommended stopping enrollment and reporting intensification efficacy. Overall 88 mother/infant pairs received intensification with no intrapartum transmission.

Characteristics	Historical data	Intensification
N	3,965	88
Age (IQR) - years	25.7 (22.5-29.7)	26.3 (22.3-33.0)
CD4 (IQR) - cells/mm3	380 (260-527)	368 (255-503)
VL baseline (IQR) - log10 copies/ml	4.0 (3.4-4.6)	4.3 (3.7-4.7)
VL delivery (IQR) - log10 copies/ml	3.2 (2.3- 4.0)	2.2 (1.8-2.9)
GA delivery (IQR) - weeks	38.7 (37.9-39.7)	38.6 (38.0-39.3)
C/section (%)	(21%)	(36%)

[Women's baseline characteristics]

The posterior probability of intrapartum transmission was 0.4% (95%CrI 0.1%-1.4%) with intensification compared to 2.0% (0.3%-5.2%) without. The probability of superiority of intensification over standard of care (RR< 1) was 94.1%, and that of at least a 2-fold reduction of risk (RR< 0.5) was 82.9%. ARV intensification appeared safe.



[Intrapartum transmission posterior probabilities]

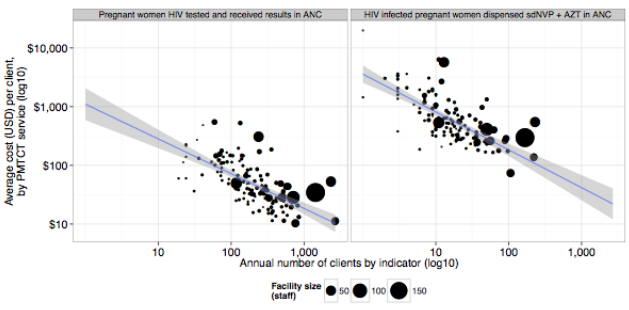
Conclusions: ARV intensification is very effective in preventing intrapartum transmission in pregnant women receiving a short course antepartum ARVs before delivery.

MOAC0205LB

Costs of Zimbabwe's accelerated prevention of mother-to-child transmission of HIV program

I. Ochoa-Moreno[1], C. Mangenah[2], R. Buzdugan[3], N.S. Padian[3], S.I. Mccoy[3], F.M. Cowan[2,4], S. Bautista-Arredondo[1]
[1]National Institute of Public Health, Cuernavaca, Mexico, [2]Centre for Sexual Health and HIV/ AIDS Research, Harare, Zimbabwe, [3]University of California, Berkeley, United States, [4]University College London, London, United Kingdom

Background: In 2010 and 2013, World Health Organization issued revised guidelines on the recommended approaches for prevention of mother-to-child transmission of HIV (PMTCT) (Options A, B, B+). Estimating the cost of these PMTCT regimens is essential. We estimated the cost of Option A in Zimbabwe, which was rolled out in 2011. These data also represent baseline estimates to assess the cost-effectiveness of Option B+, rolled out in Zimbabwe in late 2013.
Methods: We conducted a cross-sectional survey of 157 randomly selected health facilities offering PMTCT services in 5 of 10 provinces in Zimbabwe. In each facility we collected data on the output and cost of PMTCT services, including staff and supplies for the whole year and for each month of 2013. We also assessed the time allocation of staff providing these services. We estimated the average cost of PMTCT services per facility and for specific services in the PMTCT cascade such as HIV testing and antiretroviral prophylaxis. We also examined the variation in costs by the type of provider.
Results: We estimated that the average cost of PMTCT services is approximately US$13,600 (median US$9,074) per facility-year, which varies widely by facility size and type. On average, 80% of the overall cost corresponds to staff (US$10,900) and the remaining 20% to supplies (US$2,700). The average cost per pregnant woman tested was US$75 (median US$44) and the average cost per HIV-infected pregnant woman on antiretroviral prophylaxis or treatment was US$1,040 (median US$527) per year. Scale was associated with cost; 40% of the variation in the cost per pregnant woman tested can be explained by number of HIV+ women on ART/ARV, as was 50% of the variation in prophylaxis and treatment costs (see figure).
Conclusions: These findings are the first empirical estimations of PMTCT programs costs in Zimbabwe. Given limited resources, calls for the elimination of MTCT have challenged the international community to optimize the use of resources to increase coverage of PMTCT priority services. Information about costs is essential to determine the highest possible quality HIV services at the lowest feasible cost and thus maximize efficiency



[PMTCT_ZIM]

MOAC03 HIV prevention interventions and missed opportunities for prevention

MOAC0301LB

Increasing uptake of voluntary medical male circumcision (VMMC) among men aged 20-34 years in Njombe & Tabora regions, Tanzania: a cluster randomised controlled trial

M. Wambura[1], R. Hayes[2], J. Grund[3], S. Kapiga[4], H. Mahler[5], G. Mshana[1], E. Kuringe[1], M. Plotkin[5], N. Bock[3], N. Larke[2], J. Changalucha[1], H. Weiss[2], VMMC Tanzania Study Group
[1]NIMR, Mwanza, Tanzania, United Republic of, [2]LSHTM, London, United Kingdom, [3]CDC/CGH/DGHA, Atlanta, United States, [4]MITU/LSHTM, Mwanza, Tanzania, United Republic of, [5]Jhpiego/Tanzania, Dar es Salaam, Tanzania, United Republic of

Background: Tanzania introduced voluntary medical male circumcision (VMMC) in 2009 as part of its national HIV prevention strategy. Reaching men aged 20-34 years with circumcision may affect the most immediate reduction in HIV incidence. However, approximately 80% of VMMC clients in Tabora and Njombe regions are aged 10-19 years. This study evaluated the effect of a strategy to increase VMMC uptake among men aged 20-34 years in Njombe and Tabora.
Methods: A cluster-randomized controlled trial at 20 VMMC outreach sites was conducted in Njombe and Tabora, focusing on increasing VMMC uptake. The intervention, which was informed by formative research, included i) additional demand-creation messages (non-HIV benefits of VMMC, voluntary nature of HIV testing) ii) involvement of recently circumcised men as auxiliary peer promoters, iii) separate waiting and education areas for men aged >20 years, and iv) sessions on wound healing and post-circumcision abstinence targeting female partners. Analysis was based on cluster-level summary measures.
Results: Overall, 6251 men were enrolled in 10 intervention sites (1809 Njombe, 4442 Tabora) and 3968 men in the 10 control sites (1035 Njombe, 2933 Tabora). The proportion of clients aged 20-34 was greater in intervention sites compared to control sites (17.7% vs 13.0%; RR=1.4; 95%CI: 0.9-2.0; p=0.11) and was associated with a greater number of clients in both regions (overall mean difference=227; 95%CI 33-420; p=0.03). The effect of the intervention varied by region: in Njombe, there was little difference in attendance between control and intervention sites (11.3% vs 14.7%; RR=0.77, 95%CI 0.4-1.6;p=0.43) while in Tabora there was over a two-fold difference (27.5% vs 11.5%; RR=2.39, 95%CI 1.7-3.4;p=0.03). Similarly, the mean number of clients aged 20-34 was greater in intervention facilities in Tabora (mean difference=182; 95%CI 5-359; p=0.05) and there was little difference in Njombe (mean difference=12; 95%CI:-13-36; p=0.31).
Conclusions: The intervention was associated with a significant increase in the proportion of VMMC clients aged 20-34 years in Tabora but not in Njombe. The lack of intervention effect in Njombe may be due to saturation, as VMMC has been available for longer. The results suggest the intervention may be more likely to be effective in areas newly targeted for VMMC.

MOAC0302LB

Acceptability and feasibility of a novel approach to promote HIV testing in sexual and social networks using HIV self-tests

H. Thirumurthy[1,2], I. Akello[3], K. Murray[2], S. Masters[3], S. Maman[4], E. Omanga[3], K. Agot[3]
[1]University of North Carolina at Chapel Hill, Department of Health Policy and Management, Chapel Hill, United States, [2]University of North Carolina at Chapel Hill, Carolina Population Center, Chapel Hill, United States, [3]Impact Research and Development Organization, Kisumu, Kenya, [4]University of North Carolina at Chapel Hill, Department of Health Behavior, Chapel Hill, United States

Background: Identifying interventions to increase men's uptake of HIV testing in sub-Saharan Africa is essential for the success of combination prevention strategies, including treatment as prevention. HIV self-testing is an emerging approach with high acceptability, but limited evidence exists on optimal strategies for distributing self-tests and reaching men in particular. This study explored a novel approach of providing *multiple* self-tests to women with high HIV incidence in order to promote HIV testing among their sexual partners.
Methods: HIV-uninfected women aged 18-39 years were recruited at two sites in Kisumu, Kenya between January-March 2015: a drop-in center for female sex workers (FSWs) and a health facility with antenatal and postpartum clinics. Following informed consent and instructions on using the OraQuick Rapid HIV 1/2 Test, index participants (IPs) enrolled at the health facility and drop-in center received 3 and 5 self-tests, respectively. Structured interviews were conducted with IPs at enrollment and multiple times over 3 months in order to determine how self-tests were used. Key outcomes included the proportion of IPs reporting their primary sexual partner used a self-test.
Results: A total of 278 IPs were enrolled (101 FSWs, 61 antenatal, 116 postpartum). Follow-up interviews were completed with 262 IPs (94.2%) by May 9, 2015. Most self-tests provided at enrollment were either used by the IP or given to other persons (mean 2.7 [90%] for antenatal and postpartum IPs, 4.7 [94%] for FSWs). All but 2 IPs gave ≥1 self-tests to other persons, and a large majority gave a self-test to their primary sexual partner (77% FSWs, 91.8% antenatal, 86% postpartum). Ninety-eight percent of self-tests given to other persons were reported to be used. Among 367 persons who received self-tests from FSWs and used them, commercial sex clients were the largest group (211, 57%). In total, 10.6% (72/681) of those who received self-tests from IPs and used them were reported to obtain an HIV-positive result; 55% of them sought confirmatory testing.
Conclusions: Provision of multiple HIV self-tests to sub-populations of women with high HIV incidence was successful in promoting HIV testing among their sexual partners. This novel strategy warrants further consideration as countries develop self-testing policies.

MOAC0303LB

Community outbreak of HIV infection linked to injection drug use of oxymorphone - Indiana, 2015

J. Duwve[1,2], K. Hoover[3], C. Conrad[1], R. Galang[3], D. Hillman[1], B. Hoots[3], M. Patel[3], P. Peters[3], P. Pontones[1], J. Roseberry[1], J. Shields[4], D. Waterhouse[4], P. Weidle[3]
[1]Indiana State Department of Health, Indianapolis, United States, [2]Indiana University Richard M. Fairbanks School of Public Health, Indianapolis, United States, [3]Centers for Disease Control and Prevention, Atlanta, United States, [4]Clark County Health Department, Jeffersonville, United States

Background: On January 23, 2015 the Indiana State Department of Health began investigating an outbreak of HIV infection after disease intervention specialists (DIS) reported 11 confirmed HIV cases traced to a rural community in southeastern Indiana that had reported five HIV cases between 2004 and 2013. From 2009-2013, the community (population 4,200) had substantial unemployment (8.9%), many adults without high school diplomas (21.3%), a substantial proportion living in poverty (19%), and limited healthcare access. A public health emergency was declared on March 26 by executive order. We report on efforts to diagnose HIV infection in this community.
Methods: For individuals newly diagnosed with HIV infection, partner services interviews elicited information about needle-sharing and sex partners and social contacts (who could benefit from an HIV test) within the past 12 months. HIV testing was offered to all contacts who could be located.
Results: DIS identified 491 unique individuals during contact tracing, and as of May 13, 390/491 (79%) persons were located, assessed for risk and tested for HIV. Overall 153/390 (39%) persons were diagnosed with HIV infection. There was no difference in age and sex between HIV-positive and HIV-negative tested persons (Table). Compared with HIV-negative contacts (n=239), the 153 HIV-infected individuals were more likely to be named as needle-sharing partners (81% vs. 52%; p< 0.0001) and less likely to be named as sexual partners only (1% vs. 15%; p< 0.0001) during contract tracing. All individuals reporting injection drug use described practices including crushing, dissolving, and cooking OPANA® ER or extended-release generic oxymorphone. The reported daily numbers of injections ranged from 4 to 15, and the number of injection partners ranged from 1 to 6 per injection event. Individuals reported that injection drug use in this community is a multi-generational activity with family and community members injecting together, frequently sharing syringes and drug preparation equipment.

	HIV-positive N (%)	HIV-negative N (%)	Total N (%)
Overall	153	237	390
Male sex	88 (58)	132 (56)	220 (56)
Median age (range)	34 (18-57)	35 (13-75)	34 (13-75)
HIV risk factor			
Sexual risk only	2 (1)	36 (15)	38 (10)
Needle-sharing risk only	65 (42)	87 (37)	152 (39)
Sexual and needle-sharing risk	59 (39)	36 (15)	95 (24)
Unknown	27 (18)	78 (33)	105 (27)

[HIV Cases and Contacts Identified during Investiga]

Conclusions: This outbreak highlights the vulnerability of rural, resource-poor populations to drug use, misuse, and addiction; the importance of timely HIV surveillance activities and rapid response to interrupt disease transmission; and the need for expanded mental health and substance use treatment programs in medically underserved rural areas.

MOAC0304LB

HIV-1 and HCV molecular epidemiology of a large community outbreak of HIV-1 infection linked to injection drug use of oxymorphone - Indiana, 2015

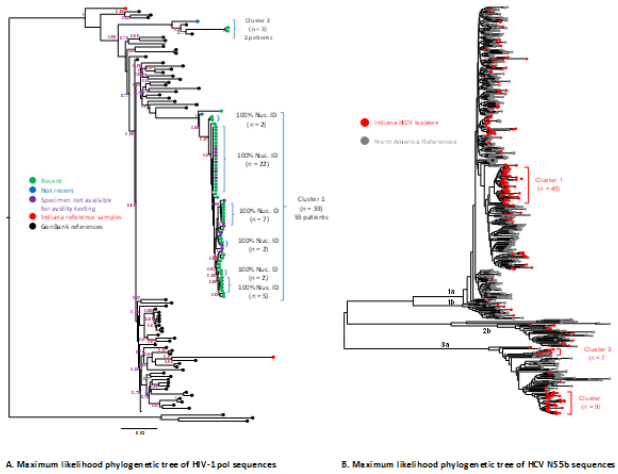
R.R. Galang[1,2], J. Gentry[3], P.J. Peters[1], S.J. Blosser[3], E.L. Chapman[3], C. Conrad[3], J.M. Duwve[3,4], L. Ganova-Raeva[5], W. Heneine[1], D. Hillman[3], H. Jia[1], L. Liu[3], W. Luo[1], J. Lovchik[3], S. Masciotra[1], S.M. Owen[1], A. Perez[3], P. Peyrani[6], P. Pontones[3], S. Ramachandran[5], J.C. Roseberry[3], M. Sandoval[1,3], A. Shankar[1], H. Thai[5], G. Xia[5], Y. Khudyakov[5], W.M. Switzer[1]

[1]CDC, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Division of HIV/AIDS Prevention, Atlanta, United States, [2]CDC, Epidemic Intelligence Service, Atlanta, United States, [3]Indiana State Department of Health, Indianapolis, United States, [4]Indiana University Richard M. Fairbanks School of Public Health, Indianapolis, United States, [5]CDC, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Division of Viral Hepatitis, Atlanta, United States, [6]University of Louisville, Division of Infectious Diseases, Louisville, United States

Background: In January 2015, a cluster of HIV-1 infections was detected in a rural county in southeastern Indiana among persons who reported injection of the prescription opioid oxymorphone. As of May 13, 2015, HIV-1 infection has been diagnosed in 153 individuals. We compare molecular analyses of HIV-1 and HCV sequences among a subset of individuals in this outbreak to infer the timing of HIV transmission relative to HCV.

Methods: Serum and plasma samples were collected from November 2014 - April 2015. HIV polymerase (*pol*) gene sequences from persons with newly diagnosed HIV infection were phylogenetically analyzed. Phylogenetic clusters were defined when HIV-1 *pol* sequences were highly genetically related (>97% nucleotide identity) and statistical evidence supporting relatedness was high (Shimodaira-Hasegawa probabilities >0.99). Recency of HIV infection was determined by avidity testing using a modified Bio-Rad HIV 1/2 plus O assay (BRAI). HCV NS5B gene sequences were phylogenetically analyzed to determine the number of clusters of independent HCV strains within this population.

Results: The *pol* gene was sequenced for 57 HIV-1-infected persons. Two clusters of HIV-1 subtype B infection were identified (Cluster 1, n= 55; Cluster 2, n =2; figure panel A). Among 49 specimens available for BRAI testing, 45 (91.8%) were recent infections. Of 36 HIV-infected specimens with HCV antibody results, 34 (94%) were HCV co-infected. The NS5B gene was sequenced for 119 HCV-infected persons. Genotype 1a (n=82) was most common, followed by genotype 3a (n=29), 2b (n=5), and 1b (n=3).Three unique clusters of HCV strains were identified (Cluster 1, n = 45; Cluster 2, n =9; Cluster 3, n = 7; figure panel B). Of 118 HCV-infected specimens with HIV antibody results, 38 (32.2%) were HIV co-infected.



[Figure. Maximum Likelihood Phylogenetic Trees]

Conclusions: In this prescription opioid injection-associated outbreak, a single strain of HIV-1 was introduced into a population infected with multiple HCV strains. In contrast to the homogeneity of HIV strains observed in this cohort, the heterogeneity of HCV strains (clustering and non-clustering) suggests earlier introduction of HCV compared with HIV. These data demonstrate the outbreak potential with introduction of HIV-1 into a community where HCV prevalence is high among persons who inject prescription opioids.

MOAC0305LB

HPTN 067/ADAPT study: a comparison of daily and intermittent pre-exposure prophylaxis (PrEP) dosing for HIV prevention in men who have sex with men and transgender women in New York city

S. Mannheimer[1,2,3], Y. Hirsch-Moverman[2,3], A. Loquere[3], J. Franks[3], J. Hughes[4,5], S.-S. Ou[5], K.R. Amico[6], C. Hendrix[7], B.J. Dye[8], E. Piwowar-Manning[9], M. Marzinke[9], V. Elharrar[10], M. Stirratt[11], R.M. Grant[12], HPTN 067/ADAPT Harlem Study Team

[1]Harlem Hospital / Columbia University, Medicine, New York, United States, [2]Columbia University Mailman School of Public Health, Epidemiology, New York, United States, [3]Columbia University Mailman School of Public Health, ICAP, New York, United States, [4]University of Washington, Department of Biostatistics, Seattle, United States, [5]Fred Hutchinson Cancer Research Center, Seattle, United States, [6]University of Michigan, Department of Health Behavior and Health Education, Ann Arbor, United States, [7]Johns Hopkins University, Department of Medicine, Baltimore, United States, [8]FHI 360, Durham, United States, [9]Johns Hopkins University, Department of Pathology, Baltimore, United States, [10]PSP/DAIDS/NIAID/NIH, Clinical Prevention Research Branch, Bethesda, United States, [11]National Institute of Mental Health, Division of AIDS Research, Bethesda, United States, [12]University of California, San Francisco, Gladstone Institutes, San Francisco, United States

Background: Daily oral FTC/TDF (Truvada) is US FDA-approved for HIV pre-exposure prophylaxis (PrEP). HPTN 067/ADAPT, a phase II randomized, open-label PrEP trial, assessed the feasibility of intermittent FTC/TDF-based PrEP for HIV prevention among men who have sex with men (MSM) and transgender women (TGW) in New York City (NYC).

Methods: MSM and TGW were eligible if: male at birth, and reported anal intercourse and ≥1 other HIV risk factor in the past 6 months. Exclusion criteria included HIV infection, hepatitis B infection, acute HIV symptoms, and abnormal renal function. Following 6 weeks of once/week directly observed dosing, participants were randomly assigned 1:1:1 to 24 weeks of PrEP dosed: daily (D), twice weekly plus one post-sex dose (time-driven [T]), or one pre- and one post-sex dose (event-driven [E]). Regimens were compared for prophylactic coverage (PrEP within 4 days pre- and 24 hours post-sex) of sex events, pills taken, side effects, and plasma drug levels. Adherence and coverage were assessed using electronic monitoring adjusted by self-reported sex and pill taking behavior collected in detailed weekly interviews.

Results: 179 participants were randomized: 176 MSM, 3 TGW; median age 30 years; 70% black, 13% white, 25% Hispanic. D arm participants had significantly higher complete coverage of sex acts (66% D, 47% T, 52% E; p=0.03; Table 1) and highest adherence to regimen (65% D, 46% T, 41% E; p < 0.001). Significantly fewer pills were used with intermittent (T and E) PrEP (p < 0.001). Side effects were similar across arms, with gastrointestinal and neurologic symptoms most common. Participants reporting recent sex in all PrEP dosing arms achieved similar rates of detectable plasma tenofovir levels and of concentrations associated with effective PrEP dose frequency.

Characteristic	Study Regimen Daily (D) N=59	Study Regimen Time (T) N=60	Study Regimen Event (E) N=60	p-value
Number of sex events during study, excluding oral sex	1083	1311	1502	0.20
% total sex events with complete coverage (or for sex events with partial coverage % pre-sex only, % post-sex only)	66 (24, 2)	47 (30, 8)	52 (29, 6)	0.03
Total number of required pills taken	5370	1708	1063	<0.001
Total % PrEP adherence	65	46	41	<0.001
% Participants with neurologic side effects (e.g., headache, dizzy, lightheaded)	24	20	18	0.64
% Participants with gastrointestinal side effects (e.g., nausea, vomiting, diarrhea, bloating, gas)	39	18	28	0.51
% Participants with detectable tenofovir (TFV) (> 0.31 ng/ml) in plasma when reporting sex in last 7 days at 10 weeks, at 30 weeks	74, 61	76, 56	64, 50	0.58
Median plasma TFV concentration (ng/ml) in plasma when reporting sex in last 7 days at 10 weeks, at 30 weeks	83, 31	24, 11	15, 1	0.49
% achieving effective plasma TFV concentration (> 5 ng/ml) when reporting sex in last 7 days at 10 weeks, at 30 weeks	63, 56	72, 50	61, 39	0.65

[Table 1]

Conclusions: While this cohort of mostly black MSM in NYC reported higher prophylactic coverage of sex acts and higher adherence to daily PrEP, non-daily PrEP users who reported recent sex achieved comparable rates of effective tenofovir plasma concentrations. Intermittent PrEP required substantially fewer pills, although side effects were similar. This study demonstrates the feasibility of intermittent PrEP, a potentially more cost-effective alternative to daily PrEP, among US black MSM.

MOAC0306LB

HPTN 067/ADAPT study: a comparison of daily and non-daily pre-exposure prophylaxis dosing in Thai men who have sex with men, Bangkok, Thailand

T.H. Holtz[1,2], A. Chitwarakorn[3], M.E. Curlin[1,2], J. Hughes[4,5], K.R. Amico[6], C. Hendrix[7], B.J. Dye[8], P.L. Anderson[9], S.-S. Ou[5], V. Elharrar[10], S.H. Eshleman[11], M. Stirratt[12], R.M. Grant[13], Bangkok HPTN 067/ADAPT Study Team

[1]Thailand Ministry of Public Health - U.S. Centers for Disease Control and Prevention Collaboration, HIV/STD Research Program, Bangkok, Thailand, [2]U.S. Centers for Disease Control and Prevention, Division of HIV/AIDS Prevention, Atlanta, United States, [3]Ministry of Public Health, Department of Disease Control, Nonthaburi, Thailand, [4]University of Washington, Department of Biostatistics, Seattle, United States, [5]Fred Hutchinson Cancer Research Center, Seattle, United States, [6]University of Michigan, Department of Health Behavior and Health Education, Ann Arbor, United States, [7]Johns Hopkins University, Department of Medicine, Baltimore, United States, [8]FHI 360, Durham, United States, [9]University of Colorado, Department of Pharmaceutical Sciences, Aurora, United States, [10]PSP/DAIDS/NIAID/NIH, Clinical Prevention Research Branch, Bethesda, United States, [11]Johns Hopkins University, Department of Pathology, Baltimore, United States, [12]National Institute of Mental Health, Division of AIDS Research, Bethesda, United States, [13]University of California, Gladstone Institutes, San Francisco, United States

Background: Oral FTC/TDF PrEP is effective for preventing sexual HIV acquisition when used daily. An alternate dosing (non-daily) regimen was effective in the IPERGAY trial. Daily and non-daily regimens have not been compared directly with respect to prophylactic coverage for sexual exposure.

Methods: We enrolled men who have sex with men (MSM) into a phase 2, randomized, open-label trial of oral FTC/TDF PrEP in Bangkok, Thailand. We randomly assigned participants to one of three self-administered dosing regimens for 24 weeks: daily (D); time-driven twice weekly with a post-sex dose (T); or event-driven before and after sex (E). We contacted participants weekly to collect dates/times of PrEP use (monitored electronically by Wisepill™) and sex events. We defined adherence as the proportion of tablets taken as recommended, and coverage as taking ≥1 tablet in the four days before sex and ≥1 tablet within 24 hours after sex.

Results: We randomized 178 MSM (median age 31 years). PrEP coverages were similar in arms D and T (85% vs 84%, p=0.79) and both were greater than in arm E (74%) (p< 0.05). Adherence was greater in D (85%) compared with T (79%) or E (65%) (p< 0.001). Compared with D, the number of doses required for full adherence was reduced by 57% in T and by 80% in E (p< 0.001). Among MSM reporting sex in the past week, PBMC tenofovir diphosphate was detectable (≥9.1 fmol/million cells) among 31/31 (100%) in D, 28/29 (96.6%) in T, and 28/30 (93.3%) in E at week 10 on study, and in 21/23 (91.3%), 18/19 (94.7%), and 12/14 (85.7%) at week 30, respectively (p=0.54). Median PBMC drug concentrations at week 30 were highest among men in D (102.0 vs. 46.8 vs. 32.9 fmol/million cells for D, T, and E, respectively, p< 0.001). No HIV infections occurred after randomization.

Characteristic	Daily (D)	Time-driven (T)	Event-driven (E)	Total	p value
N	60	59	59	178	--
Median age	31	28	31	31	--
Number of sex events over full study, not including oral sex	1485	1337	1018	--	0.16
% total events fully covered	85	84	74	--	See text
Total required tablets actually taken	8047	3272	1255	--	<0.001
Total tablets required	9420	4121	1928	--	<0.001
Total % adherence	85	79	65	--	<0.001
% detectable (>9.1 fmol/million) in PBMCs when reporting sex in last 7 days (at 10 weeks of follow up; at 30 weeks of follow up)	100; 91.3	96.6; 94.7	93.3; 85.7	96.7; 91.1	0.54
Median drug concentration in PBMCs (fmol/million cells) when reporting sex in last 7 days (at 10 weeks of follow up; at 30 weeks of follow up)	81.1; 102.0	35.3; 46.8	26.4; 32.9	45.5; 60.7	<0.001

[Results from Bangkok HPTN 067/ADAPT study (N=178)]

Conclusions: Compared with the daily regimen, the time-driven dosing regimens offered comparably high PrEP coverage for sex acts for Thai MSM, despite slightly less adherence, while requiring fewer tablets. However, since non-daily dosing results in significantly lower PBMC drug concentrations, stricter adherence is required under these regimens to maintain prophylactic drug concentrations.

MOAD01 90-90-90: Delivering on the Targets

MOAD0101

Rapid uptake and adoption of the WHO 2013 Consolidated ARV guideline recommendations: paving the way to achieving the 90/90/90 global target

M. Doherty[1], M. Beusenberg[1], E. Asamoah-Odei[2], F. Lule[2], R. Pendse[3], M. Ghidinelli[4], Y.-R. Lo[5], G. Reidner[6], M. Donoghoe[7], M. Vitoria[1], G. Hirnschall[1]

[1]World Health Organization, HIV / Hepatitis Department, Geneva, Switzerland, [2]World Health Organization, AFRO, Brazzaville, Congo, Republic of the, [3]World Health Organization, SEARO, New Delhi, India, [4]PAHO/WHO, Washington, United States, [5]World Health Organization, WPRO, Manila, Philippines, [6]World Health Organization, EMRO, Cairo, Egypt, [7]World Health Organization, EURO, Copenhagen, Denmark

Presenting author email: dohertym@who.int

Background: Progress towards the ending the AIDS epidemic by 2030 critically depends on adoption of global guidelines that address evidenced based proven approaches to optimally treat all people living with HIV (PLWHIV) and how to best deliver interventions.

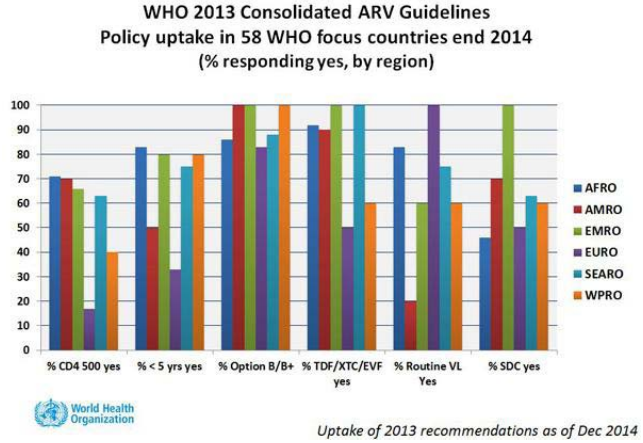
With the *2013 Consolidated ARV Guidelines*, WHO successfully launched new policy recommendations on the clinical, operational, programmatic and M&E aspects of HIV treatment and care.

Methods: WHO HQ with regional and country offices, held 9 capacity building and dissemination consultations for >100 countries from 2013-2014. Through triangulation of baseline surveys, e-surveys with the country MoH HIV focal point and data compiled from the 2014 Global AIDS Response Progress Reporting (GARPr), we have documented the adoption of priority HIV treatment policies within the 58 WHO focal countries.

Data is presented through end 2014.

Results: Within 18 months of the launch of the 2013 consolidated ARV guidelines, 44 of 58 (76%) of focus countries adopted at least one of the major recommendations; globally another 25 countries were in the process of adopting. 60% of focus countries adopted a CD4 count initiation of ≤500 cells/mm3, while Brazil, Thailand and Yemen offer treatment to all adults regardless of CD4 cell count. 71% adopted a policy to treat all children with HIV <5 years; Ethiopia treats all children <15 years. More than 90% of countries adopted PMTCT Option B/B+; 59% adopted treatment for all HIV serodiscordant couples; and 86% adopted the use of TDF + 3TC (or FTC) + EFV as the preferred first-line therapy, granting more people access to better treatment regimens; and 69% planned to implement routine viral load monitoring. Adoption varied by WHO region (Figure 1).

An update on the country implementation of these policies will be available in April 2015.



[WHO ARV Guidelines Adoption by region]

Conclusions: With the *2013 Consolidated ARV Guidelines*, WHO brought together 56 new recommendations across the continuum of HIV treatment and care, and supported countries to more rapidly adopt new policies than ever before; if fully implemented, countries can achieve the 90/90/90 global target.

MOAD0102

Can the UNAIDS 90-90-90 target be reached? Analysis of 12 national level HIV treatment cascades

J. Levi[1], A. Raymond[1], A. Pozniak[2], P. Vernazza[3], P. Kohler[4], N. Ford[5], A. Hill[2]
[1]Imperial College London, School of Public Health, London, United Kingdom, [2]St Stephens Centre, Chelsea and Westminster Hospital, London, United Kingdom, [3]Cantonal Hospital, St Gallen, Switzerland, [4]University Hospital, Zurich, Switzerland, [5]World Health Organization, Geneva, Switzerland
Presenting author email: jacob.levi11@imperial.ac.uk

Background: UNAIDS has set the "90-90-90" target for all countries: to diagnose 90% of all HIV positive people, provide antiretrovirals for 90% of those diagnosed and achieve undetectable HIV RNA for 90% of those treated, in every country worldwide by 2020. This translates to at least 73% of all HIV positive people achieving undetectable HIV RNA in every country. We used national level HIV treatment cascades to analyse whether countries have achieved these targets.
Methods: We compared published estimates of HIV treatment cascades across 12 countries in Western and Eastern Europe, North and South America, Australia and sub-Saharan Africa. Cascades were selected based on reliable, generalizable, recently published results from large cross-sectional and longitudinal study cohorts. Data were analysed in six stages; 1-HIV positive people, 2-Diagnosed, 3-Linked to care, 4-Retained in care, 5-On antiretroviral treatment, 6-Undetectable HIV RNA. Each country level cascade was analysed to identify whether each stage of the 90-90-90 target was met.
Results: The percentage of HIV positive people who both received antiretroviral treatment and achieved undetectable HIV-RNA ranged from 9% (Russia) to 73% (Switzerland). None of the 12 countries met the UNAIDS target of 90% of HIV positive people diagnosed. One country (Switzerland) met the target of 90% of diagnosed people on antiretroviral treatment. Five countries (Switzerland, Australia, UK, Denmark, Netherlands) met the target of 90% of treated people with undetectable HIV RNA. While five Western European countries achieved >50% undetectable HIV-RNA, three Eastern European countries achieved under < 20%. USA achieved undetectable HIV-RNA for 30% overall, the lowest amongst high-income countries, comparable to sub-Saharan Africa (29%). The largest fall between stages in the treatment cascades was between prevalence and diagnosis for Switzerland, UK, Netherlands, Sub-Saharan Africa, and Russia; from diagnosis to receiving ART for Australia, Brazil, USA, Georgia and Estonia, and between treatment and achieving undetectable HIV RNA for France and Canada.

Country	% Diagnosed	% On ART	% Undetectable HIV RNA		Country	% Diagnosed	% On ART	% Undetectable HIV RNA
UNAIDS 90-90-90 Targets for 2020	90%	82%	73%		Brazil (2013)	80%	48%	40%
Switzerland (2012)	84%	71%	68%		Canada (BC) (2011)	71%	51%	35%
Australia (2013)	86%	66%	62%		USA (2013)	86%	37%	30%
United Kingdom (2013)	76%	68%	61%		Sub-Saharan Africa (2013)	45%	39%	29%
Denmark (2010)	85%	62%	59%		Georgia (2012)	52%	26%	20%
Netherlands (2013)	76%	64%	58%		Estonia (2013)	87%	29%	19%
France (2010)	81%	60%	52%		Russia (2013)	49%	11%	9%

[Country level cascades versus 90-90-90 target]

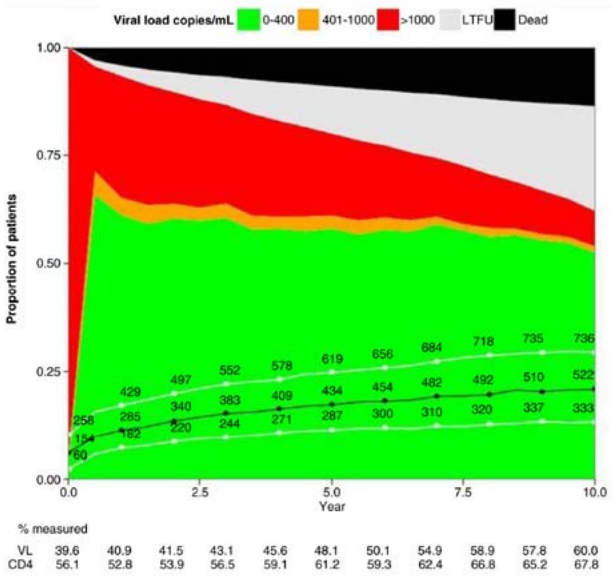
Conclusions: Only one of the 12 countries analysed achieved the UNAIDS 90-90-90 coverage target of 73% of HIV positive people with undetectable HIV RNA. There were disparities between countries. A standardized reporting method should be implemented to facilitate comparisons between countries to better identify gaps and inform policy.

MOAD0103

Major outcomes of early HAART programs at CCASAnet sites: "First Wave of HAART" study

M. Wolff[1], C.P. Cortes[1], B.E. Shepherd[2], M. Giganti[2], C. McGowan[2],
Caribbean, Central America and South America Network (CCASAnet)
[1]University of Chile, School of Medicine, Santiago, Chile, [2]Vanderbilt University, Nashville, United States
Presenting author email: marcewolff@yahoo.com

Background: Expanded access to HAART in Latin America began slowly in the late 1990s and faster in early 2000s; many antiretrovirals used then, are now outdated and most patients presented with advanced disease stages. Characterizing these patients' major outcomes (death, loss to follow-up [LTFU], viral suppression, CD4+ cell [CD4] count evolution, and regimen changes) after a decade of HAART- not well defined at present- may provide insights into their present and future situation, and provide information relevant for the management of patients who initiated HAART more recently.
Methods: The study included adults from 6 CCASAnet sites: Argentina, Brazil, Chile, Haiti, Honduras and Mexico who initiated HAART before 2004, without exclusion of non ART-naïve. Status (active, LTFU, or dead) for each patient was registered at 6-month intervals for up to 10 years, as well as CD4 and viral load (VL) in active patients. The proportions of patients in first, second, third or further HAART regimen or not on HAART were also measured.
Results: 4,975 patients (66% male) met inclusion criteria. At HAART initiation the median age was 35 years, 23% had AIDS, and 45% were not ART-naïve. At 1, 3, 5, 7 and 10 years, overall rates of mortality were 4.2%, 6.8%, 9.0%, 10.8%, and 13.6% respectively. LTFU rates for the same periods were 2.4%, 6.8%, 10.9%, 14.8%, and 24.2% respectively; 62% remained in active care at 10 years (Figure). At the end of follow up, 85% of active patients had VL <400 copies/mL (Haiti excluded because VL not regularly measured) and median CD4 increased from 153 to 517 cells/mm^3 After 10 years, only 11% of patients remained active and on their first HAART regimen, 13% were on their second, 12% were on their third, and 23% were on their fourth or more regimen. Heterogeneity in outcomes between sites was substantial.



[Major Outcomes of Early HAART Programs at CCASAnet]

Conclusions: Despite advanced disease and use of mostly old antiretrovirals, a large proportion of first HAART initiators in these Latin American cohorts were alive, in active control, with substantial immune recovery and virologic suppression after 10 years. Early death was a problem as well as persistent LTFU and frequent change of therapy.

MOAD0104

Integrating HIV-care into primary care clinics improved access to treatment and did not compromise primary health care: province-wide trend analysis over four years during implementation in Free State, South Africa

A. Rawat[1], K.E. Uebel[2], D. Moore[3], A. Yassi[1]
[1]University of British Columbia, School of Population and Public Health, Vancouver, Canada, [2]Free State Department of Health, Bloemfontien, South Africa, [3]British Columbia Centre for Excellence in HIV/AIDS, Vancouver, Canada
Presenting author email: angelirawat@gmail.com

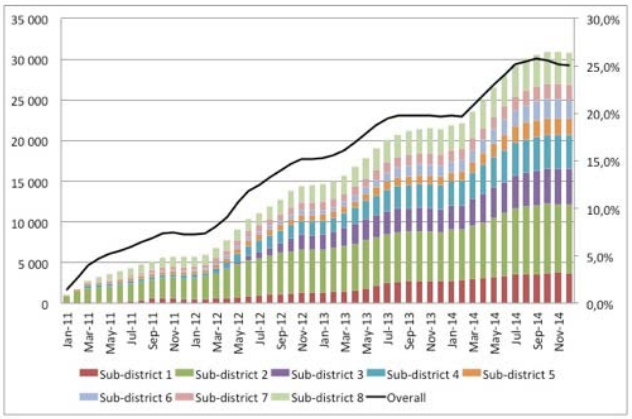
Background: The integration of HIV-care into primary health care (PHC) clinics is a strategy to expand access to antiretroviral therapy (ART). However, integration may compromise PHC service delivery within weak health systems. We designed a study to examine changes in PHC service provision (pre and post-integration) in public-sector PHC clinics in Free State, South Africa.
Methods: We analysed administrative data on 15 PHC indicators. The data were collected monthly over a critical four year period as integration was implemented into 131 PHC clinics representing a catchment population of 1.5 million. We defined integration as the month and year the PHC clinic provided comprehensive HIV-care, from testing to treatment to follow-up. We utilised interrupted time series analysis at ± 18 and ± 30 months from HIV integration in each clinic to identify changes in PHC services post-integration. We conducted sensitivity analyses with linear mixed effect models to study the relationship between HIV service indicators and the PHC indicators.
Results: The number of patients receiving ART in the 131 PHC clinics studied increased from 121 (April 2009) to 57, 958 (March 2013). We did not observe any changes in service indicators for 11 of the 15 PHC indicators we examined, However, we did observe decreases in population-level immunisation coverage after integration by 0.98% (SE=0.25 , p< 0.001) at ±18 months and by 1.31%
(SE0.16, p< 0.001) at ±30 months. Clinic level immunisation coverage also decreased by 33 infants per 100,000 patients (SE=8, p< 0.001) at ±30 months. None of these changes were associated with the number of HIV patients at the clinics. We also observed decreases in total clinic visits per year for adults and children under 5 years old.
Conclusions: Despite an extraordinary increase in patients accessing ART in PHC clinics during our study period, the vast majority of PHC indicators remained unchanged. Our findings suggest that the integration of HIV-care into public-sector PHC clinics is a viable strategy through which to expand access to ART. However, further research is needed to understand how immunisation coverage is affected.

MOAD0105LB

Implementation scale up of the Adherence Club model of care to 30,000 stable antiretroviral therapy patients in the Cape Metro: 2011-2014

L. Wilkinson[1], B. Harley[2], S. Jacobs[3], C. Cragg[3], E. Kriel[3], S. Solomon[1], N. Peton[3], K. Jennings[2], M. Youngleson[4], A. Grimsrud[5]
[1]Médecins Sans Frontières, Cape Town, South Africa, [2]City Health, Cape Town Municipality, Cape Town, South Africa, [3]Department of Health, Western Cape Government, Cape Town, South Africa, [4]Institute for Healthcare Improvement, Boston, United States, [5]University of Cape Town, Cape Town, South Africa

Background: The Adherence Club (AC) model of care was piloted by Médecins Sans Frontières starting in 2007. Adherence Clubs are groups of ~30 stable antiretroviral therapy (ART) patients who met every 8 weeks for group support, brief symptom screen and collection of pre-packed ART facilitated by a lay healthcare worker. Following good pilot outcomes, from 2011 the Cape Metro health district in turn piloted, using a collaborative quality improvement approach and then adopted the model of care.
Few data on large-scale implementation of novel models of care exist. We describe the implementation scale up across the district highlighting key efficiencies and context specific adaptations to the model.
Methods: We describe the scale-up from January 2011 - December 2014. Data from routine electronic monitoring of the ART programme provides the total number of ART patients retained in care (RIC) while monitoring of Adherence Club participation is reported monthly by each Adherence Club.
Results: AC implementation expanded over the 4-year period with the number of patients retained in AC care increasing annually from 5,675 in December 2011 to 30,790 in December 2014 (Figure 1). By December 2014, ACs were offered at 76.1% of ART facilities (51/76) with only 7.5% of ART patients in care at a facility where ACs were not operating. The proportion of patients receiving ART within an AC grew from 7.3% in 2011 to 25.0% by the end of 2014 (Figure 1).



[Figure 1. Number of patients receiving care within an Adherence Club and the proportion of all ART patients in the Cape Metro health district receiving care within an Adherence Club, January 2011 - December 2014]

Conclusions: Over a 4-year period, the AC model of care was widely accepted and expanded to support a quarter of all patients receiving ART in the district. Adaptations to the model of care supported implementation within the various facility contexts. Some facilities offered ACs at the facility while others decentralized the model to outreach, community and home venues. Most used various lay cadres of staff, while some used nurses to facilitate the groups. The model offered efficiencies both to patients and the health system. For ACs to expand to provide quality care to a greater proportion of ART patients, appropriate resources are required. Further research is needed to evaluate the outcomes of AC patients.

Monday 20 July

Oral Poster Discussions

MOPDA01 From Pathogenesis to Persistence

MOPDA0101

Within-host evolution of X4 HIV-1 in a rare transmission pair revealed by phylogenetic reconstruction of deep-sequence data

A. Le[1], J. Taylor[2], W. Dong[2], R. McCloskey[2], C. Woods[2], K. Hayashi[2], M.-J. Milloy[2], P.R. Harrigan[2], A.F.Y. Poon[2], Z.L. Brumme[1,2]
[1]Simon Fraser University, Health Sciences, Burnaby, Canada, [2]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada
Presenting author email: qal@sfu.ca

Background: A putative case of transmission of an X4 HIV strain from a CCR5wt/wt donor to a homozygous CCR5Δ32/Δ32 recipient was retrospectively identified in the Vancouver Injection Drug Users Study. We collected longitudinal intrahost deep-sequence data and applied ancestral phylogenetic reconstruction methods to characterize HIV transmission and evolution in this rare event.
Methods: Pairwise genetic distances separating donor and recipient bulk plasma HIV *gag, pol, nef,* and *env-V3* sequences were the lowest in the cohort (*e.g.* 0.0027 substitutions/nuc site in Gag vs. cohort median 0.06), identifying them as a putative transmission pair. The estimated transmission date (ETD), calculated as the midpoint of the recipient's last HIV-negative and first positive dates, was Aug/01. Donor plasma/PBMCs were available at -13, -7, -1, and +35 months from ETD; recipient plasma/PBMCs were available +5, +6, and +12 months from ETD. *Env-V3* from plasma-RNA and PBMC-DNA were triplicate amplified, pooled equally and deep-sequenced (Roche 454). BEAST and HyPhy were used to reconstruct phylogenies, estimate multiplicity of infection and reconstruct transmitted/founder (T/F) viruses from plasma-derived deep sequences from donor and recipient.
Results: Despite infection with the same X4 HIV strain, donor CD4 count was 20 cells/mm^3 within 1.5 years of infection whereas the recipient's remained >270 cells/mm^3. Donor/recipient plasma viral loads were comparable (~4.5 Log). All 10 ancestral reconstructions were consistent with transmission of a single X4 T/F virus between May-Aug 2001. The estimated T/F virus sequence was identical to the co-dominant variant (36%) observed in the recipient's first (+5 month) timepoint. This sequence was also observed in 0.09% of donor plasma and 33.5% of PBMC at month -1, suggesting minority variant transmission. In the donor, reversion of ~60% of the total plasma virus population to an R5 phenotype occurred by 50 months post-infection; in contrast, the recipient's dominant V3 sequence steadily diversified over time but remained consistently X4.
Conclusions: Results highlight the utility of phylogenetic reconstruction applied to deep-sequence data to characterize T/F viruses and intra-host evolution in transmission pairs. Differential CD4 depletion and V3 evolution in these individuals, despite acquisition of a near-identical X4 strain, underscores the critical role of host genetics on HIV evolution/pathogenesis.

MOPDA0102

Genetic ancestry component proportions are correlated with HIV disease progression

D. Garrido-Rodriguez[1], S. Avila-Rios[1], H. Valenzuela-Ponce[1], T. García-Tellez[1], V. Quiroz-Morales[1], C. García-Morales[1], M. Soto-Nava[1], A. Murakami-Ogasawara[1], J.C. Fernandez-Lopez[2], G. Reyes Terán[1]
[1]National Institute of Respiratory Diseases, Centre for Research in Infectious Diseases, Mexico City, Mexico, [2]National Institute of Genomic Medicine, Mexico City, Mexico
Presenting author email: danni.garrido@gmail.com

Background: Genetic stratification within specific populations may explain differences in HIV control. We explore the influence of genetic diversity on HIV disease progression in a cohort of mestizo individuals with different proportions of European (EUR), Amerindian (AMI) and African (AFR) genetic ancestry components.
Methods: We estimated individual ancestry proportions in a cohort of 565 HIV clade-B infected, antiretroviral treatment-naïve Mexican individuals using a panel of 128 ancestry informative markers. HLA alleles and KIR genes were genotyped for each participant in order to control for already known associations with HIV control and to describe putative novel associations in different genetic context.
Results: The mean ancestral component proportions in the study cohort were 0.594 AMI, 0.38 EUR and 0.026 AFR, as previously observed in Mexican mestizo populations. We observed a negative correlation between the proportion of AMI ancestry component (p=0.0014) and a positive correlation between the proportion of EUR ancestry component (p=0.0004) and CD4 T cell counts. To try to explain these observations, we evaluated differences in frequency and effects on CD4 T cell counts of specific HLA alleles, KIR genes or HLA-KIR combinations in EUR 60% vs. AMI 60% individuals. A*31:01, B*39:05, B*44:03, and C*07:02 showed protective effects in individuals with high EUR component, but risk effects in individuals with high AMI component (p< 0.05). Most KIR genes were more protective for EUR individuals than for AMI individuals. KIR+HLA-Bw4 combinations were more frequent in individuals with EUR component (p< 0.05) while KIR+HLA-C1 combinations were more frequent in AMI individuals (p< 0.05). Interestingly, the previously observed protective associations KIR3DS1/3DL1+HLA-Bw4^{80Ile} were not evident, neither in the entire cohort, nor in EUR individuals. KIR2DS4 in combination with HLA-C1 seemed to be protective for individuals with higher EUR component.
Conclusions: This is the first time that differences in HIV disease progression associated with genetic stratification are shown in a single population. Further studies involving fine stratification of genetically diverse populations, exploring expression of other genes involved in HIV control are warranted to understand differences observed in this study.

MOPDA0103

Dasatinib preserves SAMHD1 antiviral activity in CD4+ T cells treated with IL-7

J. Alcami[1], M. Bermejo[1], B. Descours[2], E. Mateos[1], M.M. Lederman[3], M. Benkirane[2], M. Coiras[1]
[1]Instituto de Salud Carlos III, Microbiology, Majadahonda, Spain, [2]Institute of Human Genetics, Montpellier, France, [3]Case Western Reserve University School of Medicine, Cleveland, United States
Presenting author email: ppalcami@isciii.es

Background: HIV-1 post-integration latency in quiescent CD4+ T cells is responsible for viral persistence despite antiretroviral treatment. It was proposed that the increase in proviral load in HIV-infected patients after IL-7 treatment was due to homeostatic proliferation of memory CD4+ T cells. We determined previously that IL-7 increased HIV-1 infection through phosphorylation and subsequent inactivation of the restriction factor SAMHD1. Now we analysed SAMHD1 phosphorylation in PBMC from patients enrolled in ACTG 5214 study (NTC00099671), in order to elucidate the role of IL-7 in HIV-1 proviral integration and persistence and whether this could be related to SAMHD1 inactivation. In addition, we determined that the tyrosine-kinase inhibitor Dasatinib preserved SAMHD1 antiviral activity, avoiding IL-7-mediated HIV-1 infection.
Methods: PBMC samples obtained from 10 patients enrolled in ACTG 5214 study (NTC00099671), collected before (day 0) and 4 after administration of IL-7. PBMCs obtained from 2 patients diagnosed with chronic myeloid leukemia (CML), on chronic treatment with Dasatinib. Resting CD4+ T cells from healthy donors obtained by negative selection from PBMCs. Phosphorylation of SAMHD1 at T592 was determined by immunoblotting and flow cytometry. Proviral integration was analyzed by TaqMan qPCR. Dasatinib (BMS-354825, Sprycel) was provided by Bristol-Meyers Squibb.
Results: 1) IL-7 (1nM) induced SAMHD1 phosphorylation, interfering with its antiviral activity. 2) IL-7-mediated SAMHD1 phosphorylation greatly increased HIV-1 infection in purified CD4+ T cells, increasing early and late retrotranscription, as well as proviral integration. 3) A significant increase in pSAMHD1 was observed in central memory CD4+ T cells from HIV-infected patients treated with IL-7 (ACTG 5214). 4) Dasatinib completely inhibited SAMHD1 phosphorylation at 75nM, interfering with HIV-1 retrotranscription and consequently, with proviral integration. 5) CD4+ T cells from patients with CML treated with Dasatinib showed lower expression of SAMHD1 phosphorylated.
Conclusions: By inducing SAMHD1 phosphorylation, IL-7 increases susceptibility of resting CD4+ T lymphocytes to infection, leading to HIV persistence. SAMHD1 regulation plays a central role in the establishment of HIV-1 reservoirs and represents a major target for therapeutic intervention. Dasatinib is the first compound currently used in clinic that has been described to preserve the antiviral function of an innate factor such as SAMHD1.

MOPDA0104

HIV-specific latency reversing therapies that exploit novel pathways for suboptimal Tat protein expression

D. Purcell[1], J. Jacobson[1], L. Harty[1], K. Jarman[2], K. Lackovic[2], G. Khoury[1], T. Mota[1], M. Lee[1], G. Bernardi[1], S. Saleh[3], S. Sonza[1], S. Lewin[3]
[1]University of Melbourne, Microbiology and Immunology at the Peter Doherty Institute, Melbourne, Australia, [2]The Walter and Eliza Hall Institute of Medical Research, Parkville, Australia, [3]Peter Doherty Institute, University of Melbourne, Melbourne, Australia
Presenting author email: dfjp@unimelb.edu.au

Background: We have identified a footprint of viral Tat expression in latent HIV infected cells. Suboptimal levels of Tat arise from an IRES-mediated translation of chimeric cell-HIV mRNAs that arise from alternative splicing of read-through mRNA transcripts from cellular promoters adjacent to latent integrated provirus. To simulate the role of RNA-processing pathways in HIV latency we recapitulated the low level Tat-expression from cellular-provirus read-through transcripts present in HIV latency reporter cells that express low-level Tat using the native

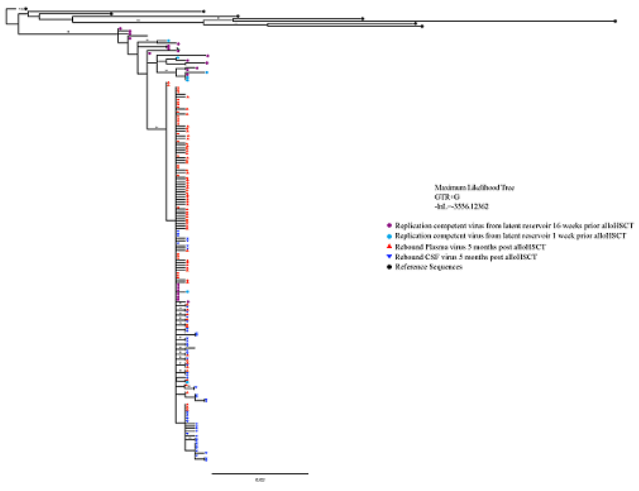
IRES that underlies the first coding tat exon and a second, different Click-Beetle-Luciferase, expressed from a CMV-IE promoter to test specificity. Novel compounds and drug combinations were screened to identify HIV-specific drugs that synergize with this latent-viral signature. HIV-specific activation was further examined in
T-cell models.
Methods: We screened 5,600 compounds in a known drug library and a library comprising of 114,000 drug-like compounds using a 293.IRES HIV-specific reporter cell line that contained CMV-CBG/LTR-CBR luciferase reporter system. Hits were identified that activated the LTR-CBR while having a minimal effect on the CMV-CBG reporter. A rigorous selection verification included 11-point titration in the normal and counter-screen assay cell lines, in dsRED-expressing J-Lat cells, and activity in primary cell models of latent HIV.
Results: From this screening cascade two known BET bromodomain and four HDAC inhibitors were found to significantly and specifically activate LTR promoter whereas compounds such as Vorinostat exhibited non-specific activity and increased global transcription. Several drug combinations that target different mechanisms implicated in HIV-1 latency were found to synergistically reactivate the virus with high potency. Importantly, seven novel compound classes were identified in the 114,000 compound library screen. Analogues of these seven classes were obtained and examined in 11-point assay with CMV-CBG/LTR-CBR reporter cell lines and 106 compounds gave a clear indication of early structure-activity relationships.
Conclusions: Seven novel classes of HIV-specific latency purging drugs were found that activate HIV provirus in synergy with a low intrinsic expression of HIV RNA and Tat. These novel small molecule leads warrant further development to iteratively enhance their HIV-1 specificity and potency. We also identified new drug combinations that synergistically activate expression from the latent HIV-1 LTR.

MOPDA0105

HIV rebound and meningoencephalitis following ART interruption after allogeneic hematopoietic stem cell transplant: an investigation of the source of HIV rebound

A. Capoferri[1,2], M. Sievers[2], A. Redd[2,3], A. Cash[2], D. Xu[2], S.F. Porcella[3,4], T. Quinn[2,3], R.F. Siliciano[1,2], M. Levis[2,5], R.F. Ambinder[2,5], C.M. Durand[2,5]
[1]Howard Hughes Medical Institute, Baltimore, United States, [2]Johns Hopkins University, Department of Medicine, Baltimore, United States, [3]National Institute of Allergy and Infectious Disease, National Institutes of Health, Division of Intramural Research, Bethesda, United States, [4]Rocky Mountain Laboratories, Genomics Unit, Research Technologies Branch, Hamilton, United States, [5]Sidney Kimmel Cancer Center, Baltimore, United States
Presenting author email: alongwi2@jhmi.edu

Background: Allogeneic hematopoietic stem cell transplant (alloHSCT) with uninterrupted antiretroviral therapy (ART) is being investigated as a component of HIV eradication strategies. In the two "Boston patients", alloHSCT resulted in the disappearance of HIV in peripheral blood. However, after analytical ART interruption, viral rebound occurred. Proposed sources of HIV rebound include the latent reservoir in resting CD4+ T cells and tissue macrophages. We present the case of an HIV-infected patient who received alloHSCT for leukemia and experienced acute retroviral syndrome after self-discontinuing ART post-alloHSCT.
Methods: Resting memory CD4+ T-cells obtained 16 and 1 week prior to alloHSCT were used in a limiting-dilution viral outgrowth assay (VOA) in which each well that demonstrates viral growth contains a single replication-competent viral clone. The *pol* region of virus from positive VOA supernatants was sequenced. Rebound virus from blood and cerebrospinal fluid (CSF) was also analyzed using deep-sequencing (Roche 454) of *pol*. Sequences were aligned and maximum likelihood analysis was performed using the GTR+G model of evolution with 100 bootstrapping pseudoreplicates.



[2015 IAS Abstract Case Study ML Tree]

Results: The patient had undetectable plasma HIV and achieved 100% donor chimerism at week 12 post-alloHSCT, but then became non-adherent with ART. At 5 months, the patient presented with fever and meningoencephalitis. Plasma and CSF HIV levels were 25,500 and 17,000 copies/ml, respectively. Before alloHSCT, 31 sequences were isolated from the VOA. At rebound, 14,645 and 5,003 sequence reads were obtained from CSF and blood respectively, and were combined into consensus sequences using a cut-off of >0.2% of total sequence reads. An identical sequence found at both pre-alloHSCT timepoints accounted for 9/31 (29%) of independent VOA sequences. This sequence grouped with the plasma and CSF viral rebound sequences in a monophyletic clade with high sequence homology.
Conclusions: Despite 100% donor chimerism in peripheral blood, ART interruption led to HIV rebound in plasma and CSF. Rebound virus was identical to a pre-alloHSCT isolate which compromised nearly 1/3 of the latent CD4+ T-cell reservoir sampled. This unique case suggests that recipient cells persist at early time-points after alloHSCT and that a single viral population latent in resting memory CD4+ T cells can re-establish infection.

MOPDA0106LB

Assay to measure the latent reservoir of replication-competent HIV-1 in suppressed patients based on ultra deep sequencing

S.-K. Lee[1], S. Zhou[1], N. Archin[2], D. Margolis[2], R. Swanstrom[1]
[1]University of North Carolina, Department of Biochemistry and Biophysics, and the UNC Center for AIDS Research, Chapel Hill, United States, [2]University of North Carolina, Department of Medicine, Chapel Hill, United States

Background: Viral outgrowth assay (VOA) is a widely used culture assay to measure the latent HIV-1 reservoir harboring replication-competent HIV-1 in resting CD4+ T cells in patients on HAART. However, the assay is costly, and both labor and resource intensive. To overcome some of these issues with the VOA, we designed an assay using ultra deep sequencing (UDS), which directly analyzes the number of different sequences of the induced viruses to score the number of latently HIV-infected resting CD4+ T cells. In this study, we tested the premise whether the viral sequences derived from two different proviruses are genetically distinct, since the assay involves a bulk culture.
Methods: To analyze viruses derived from different VOA culture wells scored as p24 positive, the viral samples derived from different culture wells were assigned with a specific Barcode and subjected to sequence analysis of the V1-V3 region of env sequences using the Primer ID-based paired-end MiSeq platform. A total of nine patient samples, two acute and seven chronic, were analyzed by UDS. Phylogenetic trees were generated by using consensus sequences created from sequences with the identical Primer ID and were used to detect distinct viral lineages present in the individual culture supernatant. For chronic patient samples, IUPM values were determined by using distinct viral lineages detected and the adjusted number of patient-derived resting CD4+ T cells used for VOA.
Results: Approximately 50% of the viral lineages derived from each chronic patient were distinct. In contrast, all viral lineages derived from each acute patient were homogeneous. When IUPM values determined by UDS analysis were compared to the IUPM values obtained from VOA, we observed approximately 2-fold higher IUPM values than the IUPM values determined by VOA. We also observed a significant positive correlation between the number of viral lineages observed per well and the number of resting T cells present per well.
Conclusions: The results suggest that approximately 50% of the viral lineages induced from different cells derived from chronic patients were distinct. Thus, the UDS assay is applicable for samples derived from chronic patients. The multiplexing ability of the assay improves the efficiency for the throughput capacity.

MOPDB01 Women and Children First

MOPDB0101

Bacterial vaginosis, intravaginal practices and HIV genital shedding: implications for HIV transmission

M. Alcaide[1], M. Chisembele[2], E. Malupande[2], K. Arheart[1], D. Jones[1], M. Fischl[1]
[1]University of Miami Miller School of Medicine, Miami, United States, [2]University of Zambia, Lusaka, Zambia
Presenting author email: malcaide@med.miami.edu

Background: Bacterial vaginosis (BV) is associated with an increased risk of HIV transmission and intravaginal practices (IVP), the practice of cleansing the vagina for hygienic, health or sexuality reasons, is the primary risk factor for developing BV. This study examines the relationship between BV, IVP and lower genital HIV shedding in HIV infected women in Zambia.
Methods: Participants were HIV-1 infected women, older than 18 years, and living in Lusaka, Zambia. Participants completed audio computer administered self-interviews questionnaires assessing demographic, sexual risk factors and IVP. BV was diagnosed by gram stain

of vaginal secretions using Nugent criteria. HIV-1 plasma viremia and genital shedding was assessed by measuring HIV-1 RNA in plasma and cervico vaginal lavages using real time PCR.
Results: One hundred and twenty eight HIV-1 infected women were enrolled. Mean age was 37 years (range 24-60). Most had a stable male sex partner (126,98%), and the majority of male partners had HIV infection (86,67%). About one third (44,34%) reported more than one partner in the prior year. All participants had engaged in IVP in the prior month, and over 90% used IVP daily. Ninety eight participants (76%) had abnormal vaginal flora (Nugent score of 4-10); and 80 (62%) had BV (Nugent score 7-10). HIV-1 plasma viremia was detected in 26 participants (20%) (median=8.4 log copies/ml, range=3.9-14.5). HIV-1 genital shedding was detected in 18 participants (14%) (median=6.7 log copies/ml, range=3.6-12.7). In multivariate analysis, daily IVP were associated with BV (OR=7.9, CI=1.54-40.8, p< 0.01) and plasma viremia was associated with HIV-1 genital shedding (OR=7.23, CI=2.43-21.37, p< 0.01). Demographic, sexual risk factors, IVP or BV were not associated with HIV genital shedding.
Conclusions: BV was common in this sample of women with HIV infection and occurred in women engaging in frequent IVP. Neither BV nor IVP increased HIV genital shedding in women on suppressive antiretrovirals. Effective antiretroviral therapy remains the main strategy to prevent HIV female genital shedding and risk of subsequent HIV transmission. Further research in women with detectable plasma viremia is needed to examine how IVP and BV affect the vaginal mucosa and increase HIV transmission.
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MOPDB0102

IUD use in HIV-positive women

L.A. Vicol[1], A. Hornsberger[1], N. Pick[1], J. Van Schalkwyk[1], D. Bloomenthal[1], J. Christilaw[1], D. Money[2]
[1]PHSA, BCWH, Oak Tree Clinic, Vancouver, Canada, [2]PHSA, BCWH, WHRI, Oak Tree Clinic, Vancouver, Canada
Presenting author email: lvicol@cw.bc.ca

Background: 80% of HIV-positive (HIV+) women are of childbearing age, therefore access to effective, safe contraception is essential. Generally, IUDs provide safe, effective contraception but historically, IUDs were contraindicated in HIV+ women due to concerns regarding infection. Data in HIV+ women is scarce. The goal was to assess rate of complications for IUS insertion in HIV+ women.
Methods: IUDs insertions in HIV+ women were offered at Oak Tree Clinic (the provincial referral center for HIV+ women and children) since 2009, following strict clinical evaluations for eligibility. Criteria used for insertion were: not planning a pregnancy for at least one year; requesting a reversible contraceptive, wanted/needed to avoid estrogen-based methods, and CD4 > 150. STD screening was done in all cases. Demographic information collected included: age, CD4, ARV at insertion, and purpose of IUD (contraception vs cycle control).
Results: Data was reviewed from 44 sequential women given IUDs from 2009 to 2014 with ages 17- 48. CD4 count160-1230 (median 590); 32/44(73%) had viral loads < 40 c/ml, 9 women had detectable VL between 89-126,908 c/ml. 7 were not on ARV therapy. 2 were on ARV but struggled with adherence and were detectable. 3/44 had a copper IUD. 40/44 had a hormonal IUD. 1 had a hormonal followed by a copper IUD. 3 IUDs were inserted for menorrhagia. 1 IUD was for combined therapeutic and contraceptive purposes. 5 requested the hormonal IUD removed not related to reproductive plans. 1 refused reinsertion when the expired hormonal IUD was removed. Complications included 4 IUD expulsions (9%) (3 spontaneous; 1 partial within the cervix). The rate of expulsion in general population is 6%.1 IUD was removed by hysteroscopy due to upward migration of strings and myometrial embedment. 1 IUD accidentally pulled out during intercourse and required emergent reinsertion of a new device. No IUD related infections or other serious complications occurred, regardless of CD4 count.
Conclusions: In this small series of HIV+ women, IUDs were safe and well tolerated. This method of contraception should remain an option for HIV+ women if close follow up of short and long term complications can be followed.

MOPDB0103

Effectiveness of contraception for HIV-infected women using antiretroviral therapy: combined data from 3 longitudinal studies

M. Pyra[1,2], R. Heffron[1,2], N.R. Mugo[1,3,4], K. Nanda[5], K.K. Thomas[2], C. Celum[1,2,6], A.P. Kourtis[7], J.M. Baeten[1,2,6], Partners in Prevention HSV/HIV Transmission Study and Partners PrEP Study Teams
[1]University of Washington, Department of Global Health, Seattle, United States, [2]University of Washington, Department of Epidemiology, Seattle, United States, [3]University of Nairobi, Department of Obstetrics and Gynaecology, Nairobi, Kenya, [4]Kenya Medical Research Institute, Sexual, Reproductive, Adolescent and Child Health Research Program, Nairobi, Kenya, [5]FHI 360, Integrated Health Sciences, Research Triangle Park, United States, [6]University of Washington, Department of Medicine, Seattle, United States, [7]Centers for Disease Control and Prevention, Division of Reproductive Health, National Center for Chronic Disease Prevention and Health Promotion, Atlanta, United States
Presenting author email: mpyra99@uw.edu

Background: Ensuring safe, effective contraception for women with HIV-1 is a public health imperative. Some data suggest that antiretroviral therapy (ART) may diminish the effectiveness of certain contraceptive methods, particularly implants.
Methods: Combining data from 5282 HIV-infected women participating in three longitudinal studies (Partners in Prevention HSV/HIV Transmission Study, Couples Observation Study, and Partners PrEP Study) from seven countries in Africa between 2004-2012, we calculated incident pregnancy rates among women using different contraceptive methods (implant, injectable, oral) and compared those to rates among women using no contraception. Multivariable Cox regression models controlled for confounding factors, and the interaction between each contraceptive method and ART use was tested to assess if ART diminished contraceptive effectiveness.
Results: During follow-up (median 1.8 years, IQR 1.2-2.3), 9% of women ever used implant, 41% used injectables (primarily DMPA), 15% used oral pills, and 47% never used hormonal contraception. Additionally, 31% of women ever used ART during follow-up, including 23% using nevirapine and 5% using efavirenz. Among women not using contraception, pregnancy rates were 13.2 and 22.5 per 100 women-years for those on and not on ART, respectively. Use of implants reduced the risk of pregnancy by more than 90%, both among women on ART (aHR 0.06, 95% CI 0.01-0.45) and not on ART (aHR 0.05, 95% CI 0.02-0.11). Likewise, injectables reduced pregnancy risk (aHR 0.18, 95% CI 0.09-0.35 on ART and aHR 0.20, 95% CI 0.16-0.24 not on ART), as did oral contraceptives by a lesser degree (aHR 0.37, 95% CI 0.15-0.91 on ART and aHR 0.36, 95% CI 0.28-0.47 not on ART). We found no statistical evidence that ART use diminished contraceptive effectiveness, including for nevirapine and efavirenz, although sample size was limited for assessing specific ART agents.

Progestin Use	ART Use	# Pregnancies	Person-Years	Incidence Rate (per 100 pyears)	aHR* (95% CI), reference no contraception	p-value for interaction term
No Contraception	On ART	111	843.5	13.2	--	--
No Contraception	No ART	1067	4733.6	22.5	--	--
Implant	On ART	1	94.1	1.1	0.06 (0.01, 0.45)	0.73
Implant	No ART	7	507.8	1.4	0.05 (0.02, 0.11)	
Injectable	On ART	11	332.8	3.3	0.18 (0.094, 0.35)	0.79
Injectable	No ART	111	2100.2	5.3	0.20 (0.16, 0.24)	
Oral Pills	On ART	5	81.2	6.2	0.37 (0.15, 0.91)	0.97
Oral Pills	No ART	63	573.1	11.0	0.36 (0.28, 0.47)	
TOTAL		1376	9266.3	14.8	--	--

[Contraceptive Effectiveness, By ART Status & Type]

Conclusions: In this large prospective evaluation of three studies, modern contraceptive methods were highly effective in reducing pregnancy risk in HIV-infected women, including those concurrently using ART. While limited evidence from other studies suggests that some ART agents could diminish the effectiveness of contraceptive implants, these data emphasize that implantable contraception is highly effective compared to no contraception and more so than shorter-acting methods such as injectables and oral pills.

MOPDB0104

Importance of programmatic longitudinal surveillance for identification of congenital anomalies among infants exposed to HIV-1 and antiretrovirals: findings from the Mpepu Study, Botswana

G. Ajibola[1], R. Shapiro[2,3], R. Zash[1,3], L. Holmes[4], O. Batlang[1], K. Ramogothobeng[1], F. Chilisa[1], K. Bennett[5], J. Makhema[1], S. Lockman[1,2,6], K. Powis[1,2,7]
[1]Botswana Harvard AIDS Institute Partnership, Gaborone, Botswana, [2]Harvard School of Public Health, Department of Immunology and Infectious Diseases, Boston, United States, [3]Beth Israel Deaconess Medical Center, Division of Infectious Diseases, Boston, United States, [4]Massachusetts General Hospital, Department of Pediatrics, Boston, United States, [5]Bennett Statistical Consulting, Ballston Lake, United States, [6]Brigham and Women's Hospital, Infectious Disease Unit, Boston, United States, [7]Massachusetts General Hospital, Department of Internal Medicine, Boston, United States

Background: A large and increasing number of HIV-infected women are conceiving while taking antiretrovirals (ARVs) globally. In resource-limited settings, surveillance systems, if present, often are limited to the initial birth exam.
Methods: We used pre-randomization data from May 2011-Dec 2014 from an ongoing clinical trial of infant cotrimoxazole prophylaxis in Botswana. Enrollments of live-born infants of HIV-infected women occurred after delivery, so long as the mother consented to infant participation and no infant life-threatening conditions were identified at birth. Infants were examined by study staff at delivery, and monthly in the first 3 months of life, and congenital anomalies were documented. We present a descriptive analysis of anomalies identified after the initial birth exam.
Results: Of 2,935 HIV-infected women enrolled in the Mpepu study who delivered live-born infants, newborn exams were documented on 2,900 (99%) infants. ART from conception was documented for 1088 (38%) women; 1147 (40%) started ARVs during pregnancy; 442 (15%) women received AZT monotherapy; and 223 (7%) received no ARVs during pregnancy. A total of 28 congenital anomalies were identified, and 8 (29%) were first diagnosed at a visit after the initial birth exam (Table 1). No differences were identified in the number of infants with or without congenital abnormalities by ARV exposure group in pregnancy, but the study was underpowered to detect differences in rare outcomes. Identification of congenital anomalies after the birth exam occurred either because the anomaly was not readily apparent at birth (e.g. biliary atresia), or because an externally-identifiable anomaly was overlooked at birth but subsequent parental concern led to documentation and management of the anomaly.
Conclusions: ARV use in pregnancy warrants ongoing surveillance monitoring for teratogenicity, particularly for regimens such as EFV/FTC/TDF with insufficient safety data in pregnancy. Nearly one third of birth anomalies detected in this cohort of well children were diagnosed after the initial birth exam. Our findings highlight the importance of incorporating, where possible, longitudinal assessment and reporting for detection of congenital anomalies that may not be identifiable at the birth exam.

Case #	Description of Congenital Anomaly	Presenting symptom	Timing of Diagnosis from Birth
1	Anovestibular Fistula	Stool in urine	42 days
2	Biliary Atresia	Jaundice at birth	48 days
3	Biliary Atresia	Jaundice at birth	38 days
4	Congenital Lymphedema	Bilateral leg swelling	15 days
5	Jejunal Atresia	Failure to pass stool with abdominal distension and vomiting	5 days
6	Macrocephaly	Widening of fontanelle and increasing head size	85 days
7	Pyloric Stenosis	Projectile vomiting	25 days
8	Talipes Equino Valgus	Concern expressed by mother about position of foot	60 days

[Table 1 - Congenital Anomalies]

MOPDC01 HIV Testing: The Gateway for Everything

MOPDC0101

Communities can mobilize to test: findings from a community randomized trial of a theory-based community mobilization (CM) intervention in South Africa

S.A. Lippman[1], A.P. Pettifor[2,3], T.B. Neilands[1], C. MacPhail[3,4], D. Peacock[5], S. Maman[2], R. Twine[6], A. Selin[2], K. Kahn[6,7]
[1]University of California, Center for AIDS Prevention Studies, Department of Medicine, San Francisco, United States, [2]University of North Carolina at Chapel Hill, Gillings School of Global Public Health, Chapel Hill, United States, [3]University of the Witwatersrand, Wits Reproductive Health and HIV Institute (WRHI), School of Clinical Medicine, Faculty of Health Sciences, Johannesburg, South Africa, [4]University of New England, School of Health, Armidale, Australia, [5]Sonke Gender Justice, Cape Town, South Africa, [6]University of the Witwatersrand, MRC/Wits Rural Public Health and Health Transitions Research Unit (Agincourt), School of Public Health, Faculty of Health Sciences, Johannesburg, South Africa, [7]Umeå University, Centre for Global Health Research, Division of Epidemiology and Global Health, Umeå, Sweden
Presenting author email: sheri.lippman@ucsf.edu

Background: While Community mobilization (CM) is a powerful tool to increase and sustain demand for HIV testing services, few rigorous trials of CM interventions have been conducted. We implemented a theory-driven CM intervention in order to improve HIV outcomes in 22 communities participating in a community randomized trial (CRT) in a rural area of Mpumalanga Province, South Africa. The mobilization activities were designed to improve community collaboration to address HIV and inequitable gender norms.
Methods: Cross-sectional surveys were conducted with 50-55 residents ages 18-35 in each village prior to (n=1181, 2012) and following (n=1174, 2014) two years of intensive intervention activities in half of the villages. Intervention activities mapped onto six domains of CM: 1) shared concern around HIV, 2) community consciousness, 3) organizational structures, 4) leadership, 5) community cohesion, and 6) collective action. Validated domain measures were included in the surveys and mean community CM scores were computed and used to predict HIV testing in the past year for each domain and for total CM scores. We used GEE logistic regression analysis to assess the effect of village level CM domain scores on individual-level testing outcomes and included interaction terms to assess intervention effects at follow-up.
Results: The overall CM score as well as three of six CM domains, including consciousness, concerns, collective action, were significantly associated with HIV testing following the intervention and interacted with intervention assignment. For example, for every standard deviation increase in community consciousness, the odds of HIV testing increased for intervention village participants (OR:1.36, p=< .01) but not for control village participants. Similar findings for total CM score (OR: 1.51), shared concerns (OR:1.62), and collective action (OR:1.45) indicate that the intervention successfully improved HIV testing. Leadership, presence of organizations, and community cohesion were not significantly associated with HIV testing at endline.
Conclusions: To our knowledge this is the first CRT assessing a theory-based CM intervention including quantitative measures of CM domains over time. While not all of the six domains were associated with HIV testing uptake, we found clear evidence that communities can be mobilized and that CM measures are associated with improved engagement in HIV testing.

MOPDC0102

Reducing stigma and increasing HIV testing with a health information intervention, a cluster-randomized trial from Malawi

L. Derksen[1], A. Muula[2], J. van Oosterhout[2,3], M. van Lettow[3], A. Matengeni[3], S. Sodhi[3,4]
[1]London School of Economics, Economics, London, United Kingdom, [2]University of Malawi, College of Medicine, Blantyre, Malawi, [3]Dignitas International, Zomba, Malawi, [4]University Health Network, Toronto Western Hospital, Toronto, Canada
Presenting author email: l.c.derksen@lse.ac.uk

Background: Despite widespread availability of antiretroviral therapy (ART), demand for HIV testing remains low across southern Africa. HIV testing may be viewed as a signal of HIV status. Those who seek an HIV test may be rejected by potential sexual partners who fear contracting HIV. This could discourage HIV testing, and encourage travel far from home for HIV testing to avoid being seen. Such stigma may be exacerbated by unawareness of the public benefit of ART, i.e. its capacity to reduce HIV transmission by 96%. We evaluated an information experiment designed to increase HIV testing rates by reducing stigma.
Methods: We conducted a cluster-randomized controlled trial in Malawi. We held community health information meetings in all villages. In control villages (n=62), we provided information on the private benefits of ART, including its potential to prolong life and reverse AIDS symptoms. In intervention villages (n=60), the public benefit of ART was discussed in addition to the control message.

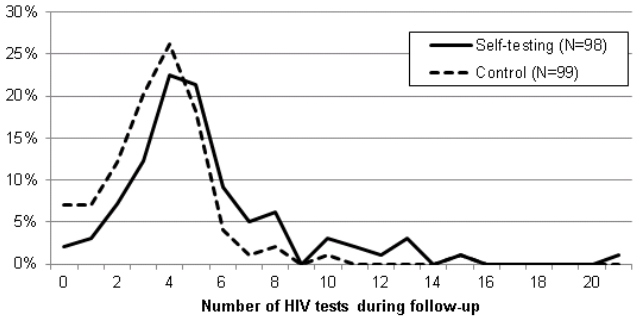
Results: Among those aged 15-49, there was a significantly larger uptake of HIV testing in the intervention villages (intervention 2.6% vs. control 1.6%; p=0.0035), according to routinely collected data from 18 health facilities over a period of 3 months after the intervention. This effect was significant for men and women, and larger when corrected for spill-overs.The intervention led to a large shift in beliefs about ART, as measured by a survey five months after the intervention. Respondents in intervention villages were more likely to report accepting attitudes towards sexual partners on ART. High beliefs about the public benefit of ART were associated with significantly more tests at nearby clinics. HIV testing decisions were predicted by a respondent's perception of his/her community's beliefs about ART. These observations strongly suggest that the effect of the intervention on HIV testing uptake is mediated by a reduction in stigma.
Conclusions: The results demonstrate that stigma between sexual partners is a significant barrier to HIV testing, and that providing new information on the effect of ART on HIV transmission can increase testing uptake.

MOPDC0103

HIV self-testing increases HIV testing frequency among high-risk men who have sex with men: a randomized controlled trial

D. Katz[1,2], M. Golden[1,2], J. Hughes[1], C. Farquhar[1], J. Stekler[1]
[1]University of Washington, Seattle, United States, [2]Public Health - Seattle & King County, Seattle, United States
Presenting author email: dkatz7@u.washington.edu

Background: HIV self-testing has the potential to increase HIV testing and thereby decrease the time persons living with HIV are unaware of their status, but the absence of counseling may result in increased risk of HIV acquisition.
Methods: In Seattle, Washington, we randomly assigned 230 HIV-negative men who have sex with men (MSM) at high risk for HIV acquisition in a 1:1 ratio to have access to HIV self-testing using the OraQuick ADVANCE Rapid HIV-1/2 Antibody Test on oral fluids or to testing as usual for 15 months. Men randomized to self-testing were trained to use the test and provided a self-test at baseline; they could contact the study for additional tests as needed up to once a month. All participants were advised to test quarterly, offered testing reminders, and could test through any existing HIV testing source. The primary outcome was self-reported number of HIV tests during follow-up. To evaluate potential adverse effects of self-testing, we compared the following between the two arms: non-concordant condomless anal intercourse (CAI) and number of male CAI partners in the last 3 months (measured at 9 and 15 months) and diagnosis with a bacterial sexually transmitted infection (STI) at the final study visit (15 months).
Results: Men randomized to self-testing reported significantly more HIV tests during follow-up (mean=5.3, 95%CI=4.7-6.0) than those in the control arm (3.6, 3.2-4.0; p< .0001), representing an average increase of 1.7 tests per participant over 15 months. Men randomized to self-testing reported using an average of 3.9 self-tests during follow-up. Self-testing was non-inferior to clinic-based testing with respect to markers of HIV acquisition risk. At the final study visit, 5.4% of MSM randomized to self-testing were diagnosed with a bacterial STI compared with 12.2% of control participants (risk difference= -6.8%; 95%CI= -16 to +1.6%). There were no significant differences between the two arms in the proportion of men reporting non-concordant CAI or the reported number of male CAI partners in the last 3 months at 9 and 15 months.



[Distribution of self-reported HIV tests by arm]

Conclusions: Access to free HIV self-testing increased testing frequency among high risk MSM and did not impact sexual risk behavior or STI acquisition.

MOPDC0104

Home HIV testing among transgender women in San Francisco: a pilot feasibility and acceptability study

S.A. Lippman[1], M.E. Moran[1], A. Ventura[1], L.S. Castillo[1,2], S. Buchbinder[3], S. Treves-Kagan[1], J.M. Sevelius[1]
[1]University of California, Center for AIDS Prevention Studies, San Francisco, United States, [2]University of Calfornia, School of Public Health, Berkeley, United States, [3]San Francisco Department of Public Health, Bridge HIV, San Francisco, United States
Presenting author email: sheri.lippman@ucsf.edu

Background: Transgender women are the population most impacted by HIV in the United States, with prevalence approximately 40 times higher than the general population. The rates of HIV antibody testing in the transgender community are not commensurate with risk. Development of alternative testing strategies to ensure early detection, care, and prevention of infection is critical.
Methods: We conducted a pilot study to explore feasibility and acceptability of offering home-based, self-conducted HIV testing for transwomen. Fifty HIV-negative transwomen in San Francisco were provided with *OraQuick* oral HIV self-test kits and asked to utilize the tests once a month for three months. Survey data were collected at baseline, 1 month, and 3 months. In-depth-interviews (IDIs) were conducted with 11 participants at their final visit to learn more about self-testing experiences, barriers to self-testing, and how the self-test might fit into an expanded pool of testing options.
Results: Self-testing was both feasible and acceptable: following the first test 94% reported the test easy to use; 93% said the results were easy to read; and 91% said they would recommend the self-test to others. Acceptability remained high at three months. Approximately 25% used the test kit with others present and 68% reported preference for self-tests vs. clinic-based testing. IDIs revealed tension between a desire for the privacy afforded by self-testing and a desire for the social and resource support offered at health facilities. While most participants were comfortable accessing services and had been tested recently (88% in the past year), IDIs revealed apprehension about being seen at HIV-testing clinics. Qualitative data also indicated that partner testing was of interest and that the cost of the kits could discourage future utilization.
Conclusions: The home-based, self-conducted HIV test provides a viable option for populations who prefer to avoid the clinic environment. To increase acceptability, enhanced linkage strategies to social and resource support should be considered. The current price point is inaccessible for populations that experience disproportionate economic marginalization. Interest in partner testing could represent an opportunity to package tests in pairs and an expanded opportunity for testing uptake. Additional research should focus on expanding delivery options and implementation strategies.

MOPDC0105

Supervised HIV self-testing to inform implementation and scale up of self-testing in Zimbabwe

S. Napierala Mavedzenge[1], E. Sibanda[2], Y. Mavengere[2], K. Hatzold[3], O. Mugurungi[4], G. Ncube[4], F. Cowan[2,5]
[1]RTI International, Women's Global Health Imperative, San Francisco, United States, [2]Centre for Sexual Health and HIV/AIDS Research, Harare, Zimbabwe, [3]Population Services International, Harare, Zimbabwe, [4]Zimbabwe Ministry of Health and Child Care, Harare, Zimbabwe, [5]University College London, London, United Kingdom
Presenting author email: smavedzenge@rti.org

Background: HIV self-testing (HIVST) can potentially increase uptake of testing in a low-cost, confidential and non-stigmatizing manner. Rigorous evaluation of instructional materials for accurate self-testing has rarely been conducted. In preparation for implementation and scale-up of HIVST in Zimbabwe, we have adapted and iteratively refined instructional materials to support self-testing. Here we present results from our evaluation of these materials through supervised self-testing.
Methods: Participants were recruited at an HIV testing clinic using convenience sampling. They were given the instructional materials and left alone to complete their self-test and record the result. Confirmatory rapid testing after HIVST, and pre- and post-test questionnaires to evaluate their experience were conducted. The testing process was video recorded and videos analyzed using checklists. Data were evaluated weekly and IEC materials iteratively refined accordingly to optimize accuracy.
Results: We conducted 172 supervised self-tests among participants in urban Harare, with mean age of 30 (range 18-70), 53% female and 20% first-time testers. Overall 93% read their result accurately, in some cases despite failing to follow instructions as determined by video. Six percent were unable to determine their result. 1% got inaccurate results, including one HIV+ individual on ART who followed instructions correctly as determined by video. While most (88%) reported the test was not hard to use, 23% said some instructions were unclear, resulting in modifications to the materials. Common sources of confusion were in interpreting results, the purpose of the test kit desiccant, and unclear images/language. Low literacy was associated with unsure/invalid results, prompting revision of the materials for a rural, less literate setting.

There, among 29 participants, 3% were unable to determine their results and 31% got an inaccurate result. Materials have been further revised making them almost entirely pictorial, and supervised self-testing is on-going.

Conclusions: Though there is little published research on optimizing HIVST materials, we found that thorough evaluation of materials through supervised self-testing has been critical to optimizing accuracy. Numerous revisions were required, and evaluation in different settings yielded differing results. Rigorous development and testing of HIVST supportive materials appropriate to country and setting is recommended prior to implementation of HIVST programs.

	Participant -read HIVST	Staff-read HIVST	Confirmatory test	
HIV negative	146	150 (146 + 3 unsure + 1 transcription error*)	156 (149 + 7 invalid HIVST)	• 160/172 = 93% got an accurate HIVST result • 2/172 = 1% got an innacurate HIVST result* • 10/172 = 6% unable to decipher their HIVST result. 7 (4%) of these had performed the test incorrectly, 3 (2%) could not interpret their result
HIV positive	16*	15	16	
HIV unsure	5	0	0	
HIV invalid	5	7	0	

*One was a participant transcription error - she was clear in her post-HIVST interview that she thought she was HIV negative. The second was someone on ART who tested negative via self-test and positive in confirmatory testing

[HIV results among 172 participants in Harare]

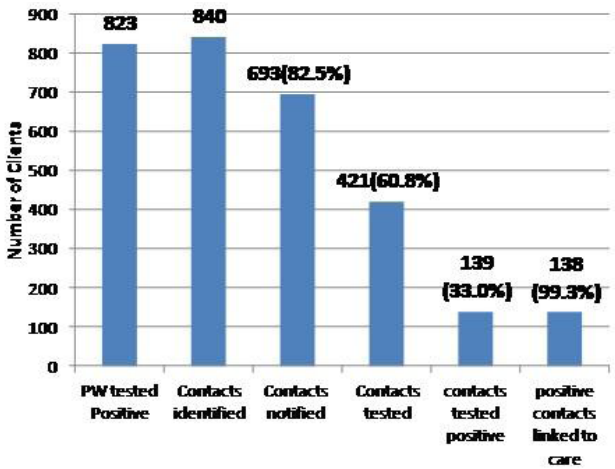
MOPDC0106

Integrating partner notification services into PMTCT (Option B+) services in the northwest and southwest regions of Cameroon

P.T. Muffih[1], E. Mboh[1], E. Fang[1], W. Wainfen[1], H. Fon[1], T. Welty[2], R. Shields[3], M. Golden[4]
[1]Cameroon Baptist Convention Health Services, Bamenda, Cameroon, [2]Cameroon Baptist Convention Health Board, AIDS Care and Prevention Program, McCall, Idaho, United States, [3]Cameroon Baptist Convention Health Services, Bellingham, United States, [4]University of Washington, Seattle, United States
Presenting author email: piustih@cbchealthservices.org

Background: Partner notification (PN) for control of sexually transmitted infections (STIs) is a public health strategy which notifies the partners of infected individuals of their possible exposure to disease. PN has rarely been used in sub-Saharan Africa as an HIV prevention intervention. In Cameroon, patients newly diagnosed with HIV do not usually receive assistance in notifying their sex partners leading to low partner disclosure and poor partner involvement in PMTCT. In 2012, the World Health Organization issued new guidelines in PMTCT including Option B+ which recommends that all HIV positive pregnant women (PW) be placed on antiretroviral treatment for life irrespective of CD4 count. PN was integrated into PMTCT at 22 pilot Option B+ sites as a strategy to increase male partner disclosure, notification, testing and linkage to care.

Methods: Beginning in March 2013, Trained Health Advisors (HA) at the 22 B+ sites interviewed consenting HIV-positive PW about their sexual partners in the last two years and facilitated disclosure or confidentially informed their partners that they had been exposed to HIV. The HAs pre-test counseled the partners and offered HIV testing in the clinic, their home or other location. They then educated both index cases and their partners on HIV prevention and risk reduction and linked all HIV positive partners to care and treatment.



[Figure 1 Uptake of Partner Notification Services at 22 Option B+ sites]

Results: During the 18 months, uptake was monitored monthly and 823 PW tested HIV positive at the 22 option B+ sites (Figure 1). Of the 840 partners they identified, 693(82.5%) were traced and notified of their exposure to HIV. Of the 693 notified, 421(60.8%) did their HIV test and received results. A total of 139(33.0%) of those tested were HIV positive and 138(99.3%) were linked to appropriate C&T services. HIV negative partners (67.0% of those tested) were counseled on risk reduction. Male partner involvement increased greatly at seven of ten sites monitored.

Conclusions: PN is a feasible HIV prevention strategy in resource-limited settings which can identify and test many partners of HIV positive PW. PN can be integrated into Option B+ PMTCT programs to identify HIV positive partners who are placed on treatment alongside the HIV positive PW.

MOPDD01 Implementation Challenges among People Who Inject Drugs

MOPDD0101

The effect of opiate substitution therapy on healthcare utilization and engagement among HIV-infected people who inject drugs in Ukraine

C. Bachireddy[1], J. Izenberg[2], M. Soule[3], S. Dvoryak[4], F. Altice[5]
[1]Harvard Medical School, Brigham and Women's Hospital, Internal Medicine, Boston, United States, [2]University of California, Psychiatry, San Francisco, United States, [3]Harvard Medical School, Massachusetts General Hospital McLean, Psychiatry, Boston, United States, [4]Ukrainian Institute on Public Health Policy, Kyiv, Ukraine, [5]Yale University School of Medicine, Internal Medicine, New Haven, United States
Presenting author email: chet86@gmail.com

Background: Eastern Europe and Central Asia face a rapidly escalating HIV epidemic driven by injection drug use (IDU). We evaluate the role of OST in engaging HIV-infected PWID in care and the effect of OST on utilization of medical services.

Methods: Cross-sectional study of healthcare utilization in the past six months among 296 randomly sampled HIV-infected opioid-dependent PWID conducted in healthcare clinics in 2010 across Ukraine. Participants categorized as therapeutic on OST if on OST for at least three consecutive months prior to the past six months or as not taking OST if not on any OST in the past nine months. Based on this criterion, 24 individuals were excluded.

Results: The 65% on OST (177/272) were less likely to be below the poverty line or live alone and more likely to be married or have gone to prison ($p<0.05$). The two groups did not differ significantly in terms of age, gender, or education. Those on OST had more years of opioid injection but were less likely to have injected in the past 30 days, to have engaged in polysubstance abuse, or to have ever overdosed on drugs ($p<0.01$). In the past 6 months, those on OST were less likely to seek emergency care (72% v 84%, $p<0.05$) and had fewer mean emergency care visits (2.77 v 4.57, $p<0.02$) with no significant differences in mean ambulatory visits (1.78 v 0.59, $p=0.11$) or hospitalizations (0.53 v 0.34, $p=0.36$). Those on OST were more likely to be engaged in HIV care, as evidenced by higher rates of ART (37% v 26%, $p=0.08$), recent CD4 testing (82% v 60%, $p<0.01$), and recent TB testing (95% v 71%, $p<0.01$). Number of self-reported symptoms was higher in the non-OST group compared to those on OST (10.46 v 7.75, $p<0.01$). Limitations include cross-sectional design and potential for recall and social desirability biases.

Conclusions: Despite higher rates of incarceration and more years of opioid injection, those therapeutic on OST were less likely to seek emergency care than those not on OST and more likely to be engaged in HIV care with fewer overall symptoms.

MOPDD0102

The effects of opioid substitution treatment and highly active antiretroviral therapy on the cause-specific risk of mortality among injection drug using people living with HIV/AIDS

B. Nosyk[1,2], J.E. Min[1], E. Evans[3], L. Li[3], L. Liu[4], V. Lima[1,5], E. Wood[1,5], J. Montaner[1,5]
[1]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada, [2]Simon Fraser University, Faculty of Health Sciences, Burnaby, Canada, [3]University of California Los Angeles, UCLA Integrated Substance Abuse Programs, Los Angeles, United States, [4]Northwestern University, Feinberg School of Medicine, Chicago, United States, [5]University of British Columbia, Division of Aids, Faculty of Medicine, Vancouver, Canada
Presenting author email: bnosyk@cfenet.ubc.ca

Background: Prior studies indicate that opioid substitution treatment (OST) reduces the risk of mortality and improves the odds of accessing highly active antiretroviral therapy (HAART), however the relative effects of these treatments for injection drug using people living with HIV/AIDS (PLHIV) are unclear. We aim to determine the independent and joint effects of OST and HAART on mortality, by cause, within a population of injection drug using PLHIV initiating HAART.
Methods: We used a linked population-level administrative database for British Columbia, Canada (1996-2010) to form a cohort of injection drug using PLHIV. We selected all individuals identified as HIV-positive and either having a history of OST at initial HAART receipt, as indicated by methadone or buprenorphine dispensation records in the BC PharmaNet database or having an indication of injection drug use before HIV infection, as indicated in the HIV testing database We employed time-to-event analytic methods, including competing risks models, proportional hazards models with time-varying covariates, and marginal structural models, to identify the independent and joint effects of OST and HAART on all-cause, as well as drug- and HIV-related mortality, controlling for covariates.
Results: Among 1,727 injection drug using PLHIV, 493 (28.5%) died during a median 5.1 years (interquartile range:2.1-9.1) of follow-up: 18.7% due to drug-related causes, 55.8% due to HIV-related causes, and 25.6% due to other causes. Standardized mortality ratios were 12.2 (95%CI:9.8,15.0) during OST, and 30.0(27.1,33.1) during periods out of OST. Both OST (adjusted hazard 0.34; 95%CI:(0.23,0.49)) and HAART (0.39(0.31,0.48)) decreased the hazard of all-cause mortality, however individuals were at lowest risk of death when these medications were used jointly (0.16 (0.10,0.26)). Both OST and HAART independently protected against not only HIV-related death, but also drug-related death and death due to other causes
Conclusions: While both OST and HAART are life-saving treatments, there is an urgency to ensure joint administration to protect against both drug and HIV-related mortality.

MOPDD0103

Assessing the HIV prevention potential of Mexico's "narcomenudeo" drug law reform: implementation challenges among people who inject drugs

L. Beletsky[1,2], P. Gonzalez-Zuniga[2], G. Rangel[3], D. Werb[2], J. Arredondo[2], S.A. Strathdee[2]
[1]Northeastern University, School of Law, Boston, United States, [2]University of California, San Diego, Global Public Health, School of Medicine, La Jolla, United States, [3]United States-Mexico Border Commission, Tijuana, Mexico
Presenting author email: lbeletsky@ucsd.edu

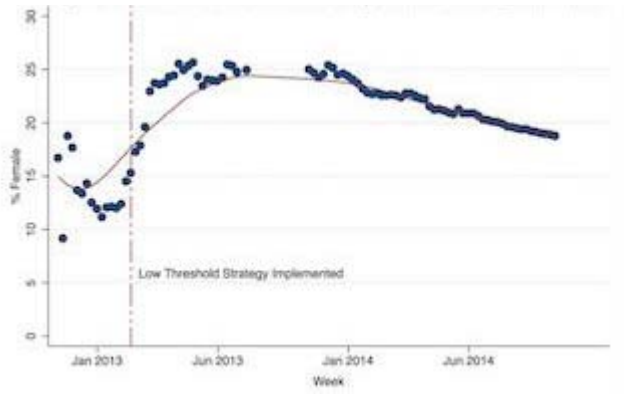
Background: Mexico's innovative 2009 "narcomenudeo" law decriminalized small-scale drug possession, mandating drug treatment diversion in lieu of incarceration and reframing drug policy to facilitate HIV prevention. However, the US-Mexico Border region continues to experience elevated HIV risk related to syringe sharing, while evidence-based addiction treatment and other prevention services targeting people who inject drugs (PWID) remain critically under-resourced.
We designed a longitudinal cohort study to assess the implementation of this structural intervention among at-risk PWID in Tijuana.
Methods: This mixed-methods research program integrated a structured questionnaire and laboratory testing with qualitative interviews assessing legal knowledge, police encounters, drug and sex risk behaviors, and infectious disease status. At baseline, 737 PWID were recruited in Tijuana; 32 participated in qualitative interviews.
Results: Between 2010-2013, only 11% of PWID respondents reported being aware of drug decriminalization; virtually none experienced drug treatment diversion or the law's other operational components. Interviews underscored the law's irrelevance to PWID; 699 (98%) characterized police practices as typically inconsistent with formal law. Instead of diversion to addiction treatment, multivariate modeling suggested that police encounters are independently associated with increased HIV risk behaviors such as syringe sharing (OR=1.26; 95%CI=1.09-1.46) and poly-drug use (OR=2.11; 95%CI=1.38-3.22). Qualitative data underscored the dissonance between the formal legal standards for drug and syringe possession, treatment diversion, and other public health-oriented legal provisions on the one hand, and the lived experience of drug users on the other. Interviews mapped out a number of pathways by which arbitrary police enforcement severely undermine drug users' ability to engage in protective HIV behaviors. Mixed-methods findings reveal that, just as housing instability can aggravate HIV risk, the lack of predictability in one's legal environment—also known as a "weak rule of law"—can compound HIV risk.
Conclusions: Formal drug policy reform may be necessary in many settings to reduce HIV risk among PWID, but appears insufficient as a stand-alone intervention. As policy interventions intended to facilitate HIV prevention gain global momentum, ancillary structural reforms such as police training to improve the rule of law are needed to unlock their public health potential. Operational partnerships with law enforcement are discussed.

MOPDD0104

Low threshold services for females who inject drugs: reducing gender inequities in methadone enrollment

B.H. Lambdin[1,2,3], C. Nyandindi[4], D. Bruce[5], N. Sabuni[4], A. Magimba[4], E. Matiko[6]
[1]Pangaea Global AIDS, Oakland, United States, [2]University of California, Epidemiology and Biostatistics, San Francisco, United States, [3]University of Washington, Global Health, Seattle, United States, [4]Ministry of Health and Social Welfare, Dar es Salaam, Tanzania, United Republic of, [5]Yale University, Medicine, New Haven, United States, [6]Centers for Disease Control and Prevention, Dar es Salaam, Tanzania, United Republic of
Presenting author email: blambdin@pgaf.org

Background: In 2011, the government of Tanzania established methadone assisted therapy (MAT) to combat the dual epidemic of HIV and injection drug use. However, enrollment of females who inject drugs into MAT has lagged behind that of males. To address this inequity, the methadone clinic at Mwananyamala Regional Referral Hospital (MRRH) introduced low threshold services for females in January 2013, allowing women to bypass the historically required attendance at community-based organizations prior to enrollment. Furthermore, existing female clients were encouraged to recruit their peers and one-day of the week was set aside for enrolling female clients only.
Methods: We conducted an interrupted time-series study to evaluate the impact of implementing low threshold services for females enrolling into MAT, using de-identified, routinely collected data from November 2012 to October 2014 at MRRH. Prais-winsten regression models were utilized to estimate the mean change in the proportion of clients that were female and the weekly number of females enrolling, adjusting for male enrollment and a period of MAT enrollment interruption form July-November 2013.
Results: Overall, 759 clients enrolled into the methadone clinic during the study period. Of those enrolling, the mean age was 34 years. The mean number of people enrolling into methadone during the study period was 8 clients (95%CI:7,9) per week. After implementation of low threshold services, the proportion of female clients increased from 14% (95%CI:13,15%) to 24% (95%CI:23,25%;p=0.001), but after the enrollment interruption, the proportion of female methadone clients decreased slightly to 22% (21-22%).



[Figure 1. Lowess Smooth of the Percentage of Female Methadone Clients]

Adjusting for male enrollment, the mean number of females enrolling per week was 2 (95%CI:1-3;p=0.001) people per week higher as compared to before implementation. Following the enrollment stoppage, the average number of female enrollees was comparable to pre-intervention [mean change: 0,95%CI:-1,1;p=0.442].
Conclusions: Implementation of low threshold services improved enrollment into the methadone program among women, thereby increasing the proportion of female methadone clients. However, the gains in enrollment were attenuated after an enrollment interruption, highlighting the importance of program stability with this group of clients.

MOPDD0105

Increasing rates of earlier antiretroviral treatment associated with elevated levels of optimal virologic response among HIV-positive illicit drug users during a treatment-as-prevention-based initiative in a Canadian setting

M.-J. Milloy, T. Kerr, R. Hogg, S. Guillemi, J. Montaner, E. Wood
British Columbia Centre for Excellence in HIV/AIDS, Vancouver, Canada
Presenting author email: uhri-mjsm@cfenet.ubc.ca

Background: Among illicit drug users, renewed efforts to reduce high levels HIV/AIDS-related morbidity and mortality and curb rates of viral transmission rely, in part, on earlier initiation of antiretroviral therapy (ART.) However, there are concerns that starting treatment prior to immunosuppression for members of harder-to-treat groups could contribute to lower levels of treatment adherence and lead to impaired virologic response. Thus, we sought to evaluate trends in CD4 cell count at ART initiation over time and rates of subsequent virologic response among HIV-positive illicit drug users during a community-wide Treatment-as-Prevention campaign in Vancouver, Canada.

Methods: We used data from the ACCESS study, an ongoing longitudinal cohort of HIV-positive illicit drug users linked to comprehensive HIV clinical monitoring and pharmacy dispensation records. In this retrospective study we included all individuals who initiated ART from 2005 onwards. We used multivariable logistic regression to evaluate differences in mean CD4+ cell count at initiation by year of initiation. To estimate time to plasma HIV-1 RNA viral load < 50 copies/mL by CD4 cell count at ART initiation we used Kaplan-Meier and Cox proportional hazards methods.

Results: Between 2005 and 2013, 357 individuals initiated ART. Median CD4 at initiation increased from 130 cells/mL (Inter-Quartile Range [IQR]: 60 - 205) in 2005 to 330 (205 - 430) in 2013. In a linear regression analysis adjusted for age, gender and ancestry, year of initiation was positively associated with CD4 cell count at initiation (b = 30.82 cells per year increase, p < 0.001). Among 357 initiates, 184 (52%) reached non-detectable plasma VL within 360 days. In an adjusted Cox proportional hazards model, CD4 cell count at initiation was positively associated with time to viral suppression (Adjusted Hazard Ratio: 1.21 per 100 cell/mL increase; 95% Confidence Interval: 1.13 - 1.29)

Conclusions: We observed substantial increases in CD4 cell count at initiation over time coincident with a community-wide TasP-based initiative. Individuals initiating ART earlier in the disease course exhibited higher rates of optimal virologic response. These findings support earlier initiation of ART among illicit drug users in order to reduce levels of HIV/AIDS-associated morbidity and mortality and rates of viral transmission.

Monday 20 July

Poster Exhibition

Antibody diversity and function

MOPEA001

Monoclonal antibodies using IgG-V regions from cows vaccinated with HIV gp140 require cysteine and tryptophan for high affinity Env trimer-specific binding

B. Heydarchi[1], R. Center[1], J. Cuthbertson[1], J. Bebbington[1], G. Khoury[1], C. Mackenzie[1], B. Muller[2], C. Gonelli[1], D. Purcell[1]
[1]University of Melbourne, Microbiology and Immunology at the Peter Doherty Institute, Melbourne, Australia, [2]Reef Pharmaceuticals, Melbourne, Australia
Presenting author email: dfjp@unimelb.edu.au

Background: Cows vaccinated with HIV AD8 Env gp140 trimer develop a vast quantity of high titre polyclonal antibody with broad neutralising activity in colostrum. We studied the molecular characteristics of this response by isolating the IgG V-region genes from bovine memory B cells binding HIV-1_{AD8} Env gp140 trimer and constructing monoclonal antibodies (mAbs).
Methods: PBMC from a cow vaccinated over 4 years with HIV-1_{AD8} Env gp140 trimers were stained for CD21$^+$, IgG$^+$ memory B-cells and those binding PE-labelled gp140 were isolated using FACS single-cell sorting. The bovine Ig heavy (H) and light (L) chain variable (V) regions for 33 rearranged immunoglobulin (Ig)-genes were amplified from cDNA by nested PCR, and V regions of H and L were subcloned into expression vectors containing human IgG constant regions. Codons for Cys and aromatic amino acids in CDRH3 were changed to Ala by site-directed mutagenesis. Chimeric bovine-human (BH) IgG mAbs were produced using paired H and L chain plasmid transfection in 293T cells and tested against various Env in ELISA, immunoprecipitation, immunoblotting and pseudotype-reporter neutralisation assays.
Results: HIV-specific memory B cells were found at a frequency of 0.66% of IgG+ CD21+ memory B cells from peripheral blood. From these 33 matched chimeric BH H and L chains binding Env gp140 immunogen were cloned and their CDRH3 size ranged from 12 - 64 amino acids with a high Cys and aromatic-aa frequency. Of these, 2 mAbs, 6A and 8C, displayed strong binding to HIV-1_{AD8} gp140 Env uncleaved trimers, but not monomer, and bound a subset of cleavage-active HIV-1_{AD8} SOS-IP gp140. The VH somatic mutation rate for 6A and 8C was 27% and 25% respectively and their 21 and 14aa CDRH3 domains were 57% and 93% mutated from their DH3 and DH8 germline genes. The HIV-specific binding characteristics of both 6A and 8C mAbs were eliminated when CDRH3 Cys or Trp aa's were changed to Ala. These mAb's didn't have broad neutralising activity.
Conclusions: The 6A and 8C mAbs target conformation-dependent epitopes on uncleaved Env-gp140, but these don't account for the potent neutralising activity of the polyclonal antibody. However, highly evolved Ig-V-regions resulted from vaccination with Env gp140 trimer.

B cells and alterations in subsets

MOPEA002

Early initiation of treatment in primary HIV infection leads to temporary preservation of the B-cell compartment

G. de Bree[1], A. Wheatley[2], R. Lynch[2], M. Grijssen[3], J. Prins[3], J. Lange[4], S. Schmidt[2], A. Mcdermott[2], J. Mascola[2], R. Koup[5], Primo-SHM Cohort
[1]Amsterdam Institute for Global Health and Development, Academic Medical Center Amsterdam, Internal Medicine and Infectious Diseases, Amsterdam, Netherlands, [2]Vaccine Research Center, NIAID, NIH, Bethesda, United States, [3]Academic Medical Center, Amsterdam, Netherlands, [4]Institute for Global Health and Development, Amsterdam, Netherlands, [5]Vaccine Research Center, NIAID, NIH, Bethesda, Netherlands
Presenting author email: g.j.debree@amc.uva.nl

Background: HIV infection induces B cell dysfunction already at the early stage of infection that can be reversed to some extent by combination antiretroviral therapy (cART). It is however unknown if cART initiated during early infection preserves B cell function also after treatment interruption.
Methods: In the present study, a comprehensive analysis of the properties of the HIV-specific B cell response in the Primo-SHM cohort study is performed. In this cohort patients were randomized to no treatment (n=23) or 24 weeks cART (n=24) initiated during primary HIV infection. B cell properties were analyzed at viral setpoint (36 weeks after diagnosis in untreated patients) or 36 weeks after treatment interruption.
Results: At viral setpoint, the B cell compartment in untreated patients showed a significant larger fraction of activated memory B cells (p< 0.001), plasmablasts (p=< 0.001) as well as "tissue-like" B cells (p=0.006) compared to treated patients at viral setpoint. Despite this enrichment of aberrant B cells, untreated patients were able to mount a humoral HIV-specific response as reflected by a significant increase in HIV-specific antibody titers (anti-gp140, anti-RSC3) and development of neutralizing antibodies over time.
Conclusions: These data suggest that early reduction of viral load by cART initiation during early infection may preserve the B cell compartment for a prolonged period after treatment interruption. However, in the untreated patients the aberrant B cell compartment does not prohibit the development of an HIV-specific antibody response. This suggests that the HIV-specific B cell response may benefit from viral exposure and is not impaired by the skewing of the B cell compartment towards a more exhausted profile.

MOPEA003

Numerical and phenotypic B-cell abnormalities and vaccine responses in HIV-exposed uninfected (HEU) children

C. Gravel[1,2], A. Le Campion[1,2], L. Raymond-Marchand[1,2], M. Boucher[3,4], N. Lapointe[4,5], V. Lamarre[4,5], F. Kakkar[4,5], H.C.F. Côté[6,7], H. Soudeyns[1,2,5], CIHR Team on Cellular Aging and HIV Comorbidities in Women and Children (CARMA)
[1]Centre de Recherche du CHU Sainte-Justine, Unité d'Immunopathologie Virale, Montreal, Canada, [2]Université de Montréal, Microbiology, Infectiology & Immunology, Montreal, Canada, [3]Université de Montréal, Obstetrics & Gynecology, Montreal, Canada, [4]CHU Sainte-Justine, Centre Maternel et Infantile sur le SIDA, Montreal, Canada, [5]Université de Montréal, Pediatrics, Montreal, Canada, [6]University of British Columbia, Pathology and Laboratory Medicine, Vancouver, Canada, [7]Women's Health Research Institute, Vancouver, Canada

Background: There is emerging concern about the health of HIV-exposed uninfected (HEU) children, with increased morbidity and mortality from infectious diseases observed among them. Previous work on the Centre maternel et infantile sur le SIDA (CMIS) Mother-Child Cohort (CHU Sainte-Justine, Montreal, Canada; n=705 HEU children) revealed that HEU infants born to mothers with HIV-1 viral load >1,000 copies/ml had significantly higher CD19$^+$ B cell frequencies at 2 months and 6 months of age compared with children born to mothers with undetectable viral load. The objective of this study was to characterize potential immunologic abnormalities in the B cell compartment among HEU infants.
Methods: HIV-infected women were enrolled during pregnancy and they and their children were followed prospectively. Detailed phenotyping of the peripheral B cell compartment was performed by multiparametric flow cytometry (CD3/CD10/CD14/CD16/CD19/CD20/CD21/CD27/IgM) using samples of HEU umbilical cord blood (UCB; n=8) or venous blood (n=4) obtained at 4-6 months of age. The magnitude of the antigen-specific B cell responses elicited by immunization with hexavalent acellular diphtheria-tetanus-polio (DTP) vaccine (administered at 2 and 4 months of age) was estimated by staining with fluorescent tetanus toxoid (TT) oligomers.
Results: Total B cells frequencies doubled between UCB and 4-6 months of age (12.5%±8.6% vs. 28.1%±10.1%). In addition, decreased frequencies of naïve B cells (70.5%±6.1% vs. 64.3%±5.4%) and increased frequencies of activated memory B cells (0.2%±0.03% vs. 2.3%±1.2%) and plasmablasts (0.1%±0.04% vs. 0.7%±0.2%) were observed. Conversely, atypical memory B cell (CD19+CD10-CD27-CD20+CD21-/low) frequencies were unchanged. TT-specific B cells were detected at 4-6 months of age, where they represented 0.075% of class-switched plasmablasts, 0.082% of class-switched classical memory B cells, and 0.106% of class-switched activated memory B cells.
Conclusions: Preliminary results from this ongoing prospective study provide a high-resolution portrait of the global and antigen-specific B cell compartment and are suggestive of the presence of modest vaccine-elicited B cell responses in HEU children. Further studies will be required to validate whether these responses are associated with virologic and/or immunologic parameters in the mother, and to determine the short and long-term clinical impact of these findings.

T-cell immune responses (CD4 and CD8)

MOPEA004

Control of HIV-1 by cytotoxic T cells specific for multiple conserved epitopes

H. Murakoshi[1], T. Akahoshi[1], M. Koyanagi[1], T. Chikata[1], T. Naruto[1], R. Maruyama[1], Y. Tamura[1], H. Gatanaga[1,2], S. Oka[1,2], M. Takiguchi[1]
[1]Kumamoto University, Kumamoto, Japan, [2]National Center for Global Health and Medicine, Tokyo, Japan
Presenting author email: tlmura@kumamoto-u.ac.jp

Background: HIV-1-specific cytotoxic T lymphocytes (CTLs) play a critical role to suppress HIV-1 replication. It is well known that HLA-B*27-restricted and HLA-B*57-restricted CTLs play a key role in the control of HIV-1 in Caucasians and Africans. However, these alleles are very rare in Japan, indicating that HIV-1 is not controlled by these alleles-restricted CTLs in HIV-1-infected Japanese individuals. In the present study, we sought to identify HIV-1-specific CD8$^+$ T cells controlling HIV-1 in HIV-1-infected Japanese individuals by employing exhaustive and comprehensive strategies.
Methods: We analyzed CD8$^+$ T cell responses to 11-mer overlapping HIV-1 Gag, Pol, and Nef peptides in 401 chronically HIV-1-infected Japanese individuals to identify candidates of CD8$^+$ T cell responses controlling HIV-1. Following re-evaluation for the role of the identified specific CTLs in the control of HIV-1, we characterized the cross-reactivity of their escape mutants.
Results: We identified 19 CTL epitope candidates significantly associated with low plasma viral load (pVL) and high CD4 counts in the Japanese individuals. After re-evaluating the correlation between these epitope-specific CTLs and the clinical outcome, we identified 8 Gag and 5 Pol epitope-specific CTLs controlling HIV-1. The breadth of the responses to these 13 epitopes were negatively correlated with pVL ($p = 2.1\times10^{-8}$) and positively with CD4 counts ($p = 5.3\times10^{-8}$), indicating strong synergistic effects of these T cells on HIV-1 control *in vivo*. Nine of these epitopes were conserved among HIV-1 subtype B-infected individuals, whereas three out of 4 non-conserved epitopes were cross-recognized by the specific T cells.
Conclusions: These results suggest that AIDS vaccines inducing CTLs specific for these 12 epitopes would be effective for protection against HIV-1.

Mucosal immunity

MOPEA005

Bacterial vaginosis is associated with loss of gamma delta T cells in the female reproductive tract

M. Alcaide[1], N. Strbo[2], L. Romero[2], D. Jones[3], O. Martinez[4], V. Rodriguez[3], H. Bolivar[1], E. Podack[2], M. Fischl[1]
[1]University of Miami Miller School of Medicine, Medicine, Infectious Diseases, Miami, United States, [2]University of Miami Miller School of Medicine, Microbiology and Immunology, Miami, United States, [3]University of Miami Miller School of Medicine, Psychiatry and Behavioral Sciences, Miami, United States, [4]University of Miami Miller School of Medicine, Miami, United States
Presenting author email: malcaide@med.miami.edu

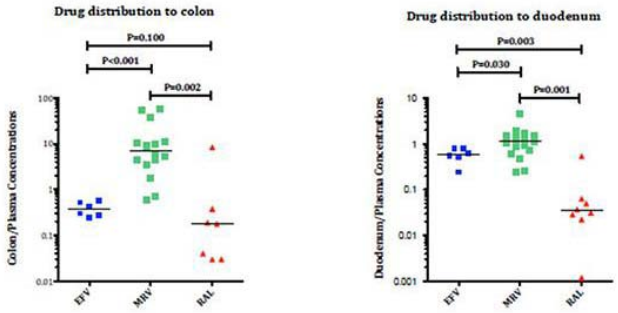
Background: The most common female reproductive tract infection, Bacterial Vaginosis (BV), is characterized by a reduction in vaginal lactobacilli and an increase in gram negative anaerobic bacteria. BV is associated with increased risk of acquiring and transmitting HIV. Gamma delta (GD) Tcells are essential components of the adaptive and innate immune system and play an important role in epithelial barrier protection. The majority of tissue-associated GD cells use the V delta (D1) TCR. GD1 cells have been recently described in the female reproductive tract by this team. We hypothesized that mucosal changes occurring in BV would be associated with diminished regulatory GD1 Tcells, which could account for increased susceptibility to HIV.
Methods: Fourteen HIV-infected (HIV+) and 17 HIV-uninfected (HIV-) at risk, pre-menopausal, women were recruited. Participants underwent vaginal examination with collection of vaginal swabs and endocervical cytobrushes. Gram stains of vaginal secretions were performed and graded using the Nugent score. Frequency of CD3+ T lymphocytes and GD T cells were determined in cervical cytobrush samples by multicolor flow cytometry.
Results: Median Nugent scores were: 5.0 ± 3.3, and 32% of the women had BV. We found no differences in Nugent scores or rates of BV when comparing HIV+ and HIV- women. HIV+ women had lower frequency of cervical GD1 Tcells in comparison with HIV- women (HIV+ = 16.14% ± 19.50;
HIV- = 36.36% ± 27.82; p=0.047). In HIV- women there was a negative correlation between Nugent score and frequency of cervical GD1 Tcells (HIV- r = -0.70, p=0.02; HIV+ r = 0.46, p=0.10; all participants, r = -0.38, p=0.04). HIV- women with BV had lower frequency of GD1 Tcells than those without BV (10.5% vs 44.00%, respectively, p=0.024).
Conclusions: Current knowledge of the immune dynamics at the female reproductive tract is limited and new tools to address mucosal vulnerability to HIV are needed. Changes in the vaginal flora occurring with BV are associated with diminished regulatory GD1 Tcells suggesting disruption of the vaginal mucosa. We propose to use GD Tcell responses as a marker of female genital tract vulnerability to HIV infection. Funded by WIHS (U01 AI103397) and Miami CFAR (P30AI073961).

MOPEA006

Effects of quadruple first-line ART on mucosal immunity and HIV persistence

T. Sainz[1], S. Serrano-Villar[2], S. Mann[3], M.-M. Zhong[4], C. Miller[4], N. Utay[5], B. Siewe[6], T. Wook-Chun[7], P. Troia-Cancio[3], R.B. Pollard[3], D. Asmuth[3]
[1]University Hospital La Paz, Madrid, Spain, [2]University Hospital Ramón y Cajal, Madrid, Spain, [3]University of California Davis, Sacramento, United States, [4]California National Primate Research Center, University of California, Davis, United States, [5]University of Texas Medical Branch, Galveston, United States, [6]Rush University, Chicago, United States, [7]NIAID, Bethesda, United States
Presenting author email: david.asmuth@ucdmc.ucdavis.edu

Background: It is unclear whether initiation of antiretroviral therapy (ART) with regimens aimed at achieving greater concentrations within lymphatic tissues may help to reconstitute mucosal immune abnormalities, decrease inflammatory markers and reduce the viral reservoir.
Methods: We included 12 HIV- controls and 43 ART-naïve HIV patients who were randomized to efavirez, maraviroc (MRV) or MRV+raltegravir (MRV+RAL), each in combination with tenofovir/emtricitabine. Colon and duodenal biopsies were obtained at baseline and at 9 months of ART. We performed a comprehensive assay of T cell subsets by flow cytometry, T cell density in duodenal biopsies, plasma and tissue concentrations of antiretroviral drugs by high-performance liquid chromatography. Plasma interleukin-6 (IL-6), lipoteichoic acid (LTA), soluble CD14 (sCD14) and zonulin-1 were measured by ELISA. Total cell-associated HIV DNA was measured in PBMC and mucosal mononuclear cells. Linear mixed models were computed to estimate the mean change of each parameter in plasma, PBMC colon and duodenum.
Results: Twenty-six HIV-infected patients completed the follow-up. In duodenum, the quadruple regimen resulted in greater CD8$^+$ T cell density decline, greater normalization of mucosal CCR5$^+$CD4$^+$ T cells and increase of the naïve/memory CD8$^+$ T cell ratio, and induced a greater decline of sCD14 levels and duodenal HIV DNA levels (p=0.004 and p=0.067, respectively). MRV showed the highest drug distribution to the gut tissue, and duodenal concentrations correlated well with with a number of markers of the adaptive immunity in duodenum, i.e., %CD4$^+$ and %CD8$^+$ T cells (Rho 0.671, P=0.006 and Rho -0.518, p=0.048, respectively), CD4/CD8 ratio (Rho 0.679, P=0.005), and %CD4$^+$ and %CD8$^+$ HLA-DR$^+$CD38$^+$ T cells (Rho 0.625, p=0.013 and Rho 0.607, p=0.016, respectively). MRV elicited greater activation of the mucosal naïve CD8$^+$ T cell subset, ameliorated the distribution of the CD8$^+$ T maturational subsets and induced higher improvement of zonulin-1 levels.



[Figure 1. Tissue drug distribution. Percentages of colon/plasma and duodenum/plasma drug concentrations. Maraviroc reached the highest distribution to colon and duodenum]

Conclusions: These data suggest that initiating ART with four drugs might more effectively reconstitute duodenal immunity, decrease inflammatory markers and impact on HIV persistence, and show unique effects of MRV in duodenal immunity driven by higher drug tissue penetration and possibly by class-dependent effects.

MOPEA007

Hormonal contraception and cervical immunity before and after HIV acquisition

C. Morrison[1], R. Fichorova[2], P.-L. Chen[3], C. Mauck[4], C. Kwok[3], T. Chipato[5], R. Salata[6], G. Doncel[4]
[1]FHI 360, Clinical and Epidemiological Sciences, Durham, United States, [2]Brigham and Women's Hospital, Harvard Medical School, Boston, United States, [3]FHI 360, Biostatistics, Durham, United States, [4]CONRAD, Washington DC, United States, [5]University of Zimbabwe, Harare, Zimbabwe, [6]Case Western Reserve University, Dept of Medicine, Cleveland, United States
Presenting author email: cmorrison@fhi360.org

Background: We previously reported in a large prospective cohort study - the Hormonal Contraception (HC) and HIV study conducted in Uganda and Zimbabwe - that HIV seroconversion was associated with DMPA use and both were associated with higher cervical RANTES levels 3 months prior to detected seroconversion. Here we evaluate HC use and cervical immunity longitudinally - before and after HIV acquisition.
Methods: We measured levels of inflammatory proteins in 3721 longitudinal cervical samples from 216 HIV seroconverters and 727 matched uninfected women in the HC-HIV study at two quarterly visits prior to HIV seroconversion (t-2, t-1), the seroconversion visit (t0), and two quarterly visits following seroconversion (t+1, t+2) and corresponding visits for HIV-negative women. We used Box-Cox power transformations to normalize protein concentrations and generalized linear models to compare biomarker levels by HIV status and HC use.
Results: Biomarkers remained relatively stable across visits for women remaining HIV-negative. In contrast, among seroconverters, IL-1B, IL-6, IL-8, MIP3a, VEGF, IL-1RA, SLPI and BD-2 declined while RANTES and ICAM-1 increased from t-2 to t+2. While no significant differences were observed at t-2, HIV seroconverters had higher levels of RANTES and lower levels of SLPI by t-1, and these differences continued throughout post-seroconversion visits. Compared with the no HC group, DMPA users had higher levels of RANTES and lower BD-2 levels at both t-2 and t-1 visits. Higher RANTES levels continued at all post-seroconversion visits and lower BD-2 levels continued through t0 for DMPA users.
Conclusions: Changes in the immunoinflammatory environment of the female genital tract possibly related to mucosal susceptibility to HIV occurred within 6 months of, but prior to, seroconversion and continued post-seroconversion. Levels of several immunoinflammatory markers were related to HC use. DMPA, in particular, was consistently associated with higher levels of RANTES, which in turn was associated with subsequent HIV seroconversion.

Virus escape from adaptive immunity

MOPEA008

Reporter assay to measure HIV-1 Nef-mediated evasion from T cells

G. Anmole[1], X.T. Kuang[1], A. Shahid[2], E. Martin[1], Z.L. Brumme[2,3], M.A. Brockman[1,2,3]
[1]Simon Fraser University, Molecular Biology and Biochemistry, Burnaby, Canada, [2]Simon Fraser University, Faculty of Health Sciences, Burnaby, Canada, [3]British Columbia Centre for Excellence in HIV/AIDS, Vancouver, Canada
Presenting author email: gsa26@sfu.ca

Background: HIV-1 Nef promotes persistent infection by downregulating Human Leukocyte Antigen class I (HLA) expression, thus evading recognition by cytotoxic T lymphocytes (CTL). To investigate this activity in greater detail, we have developed a quantitative reporter cell assay to measure the effect of Nef-mediated HLA class I down-regulation on epitope-specific T cell recognition.
Methods: Jurkat "effector" T cells were transfected with a TCRα/β restricted by the HLA-A*02:01 Gag FK10 (FLGKIWPSYK) epitope, CD8α, and NFAT-driven luciferase reporter plasmids. CEM "target" cells stably expressing A*02 were transfected with positive and negative Nef controls (Nef_{SF2}-GFP and Δnef-GFP, respectively) and mutant variants defective for CD4 and HLA class I downregulation ($A_{72}xxA_{75}$-GFP and M20A-GFP, respectively). Transfected target cells were isolated by FACS based on high GFP and low Annexin V expression, pulsed with FK10 peptide and co-cultured with TCR+ effector cells at a 1:1 ratio. To examine endogenous FK10 presentation, CEM-derived GFP-reporter-A*02 "target" cells were infected with HIV-$1_{NL4.3}$ or Nef mutant M20A and co-cultured with TCR+ effector cells. Surface A*02 expression on target cells was analyzed by flow cytometry to assess Nef function. Effector T cell activation was measured by luminescence 6 hours following co-culture.
Results: Effector T cells generated a robust NFAT-mediated luciferase signal following co-culture with FK10-pulsed target cells. Nef-mediated HLA downregulation on target cells resulted in lower luciferase activity, consistent with decreased TCR recognition. As expected, luciferase signal positively correlated with A*02 levels when target cells expressed different Nef mutants (Spearman's R=0.95, P=0.001). Luciferase signal emitted by A*02-FK10-specific effector cells upon co-culture with wild-type HIV-$1_{NL4.3}$ nef was nearly twofold lower than for cells infected with the HIV-$1_{NL4.3NefM20A}$ mutant defective for HLA class I downregulation.
Conclusions: This *in vitro* reporter cell assay provides a new tool to study the immunological interaction between TCR and peptide-HLA on target cells. The assay is quantitative and scalable, which will allow larger studies to more directly assess the impact of patient-derived Nef sequences on antiviral T cell responses in the context of multiple HLA alleles that may contribute to vaccine efforts.

MOPEA009

Nef and Vpu accessory proteins from primary HIV-1 isolates protect infected cells from ADCC

M. Veillette[1], D. Zoubchenok[1], D. Sauter[2], C. Stürzel[2], B. Hahn[3], F. Kirchhoff[2], A. Finzi[4,5]
[1]Université de Montréal, CRCHUM and Department of Microbiology, Infectiology and Immunology, Montreal, Canada, [2]Institute of Molecular Virology, Ulm University Medical Center, Ulm, Germany, [3]University of Pennsylvania, Departments of Medicine and Microbiology, Philadelphia, United States, [4]Université de Montréal, CRCHUM and Department of Microbiology, Infectiology and Immunology, Montreal, Canada, [5]McGill University, Department of Microbiology and Immunology, Montreal, Canada
Presenting author email: andres.finzi@umontreal.ca

Background: Recent studies have linked antibody Fc-mediated effector functions with control of human immunodeficiency type 1 (HIV-1) and simian immunodeficiency (SIV) infections. Interestingly, the presence of antibodies with potent antibody-dependent cellular cytotoxicity (ADCC) activity in the Thai RV144 vaccine trial correlated inversely with HIV-1 acquisition risk. These antibodies were recently found to recognize HIV envelope (Env) epitopes exposed upon Env-CD4 interaction. CD4 downregulation by Nef and Vpu, as well as Vpu-mediated BST-2/tetherin antagonism, were reported to modulate exposure of CD4-induced (CD4i) Env epitopes and were proposed to reduce the susceptibility of infected cells to ADCC mediated by CD4i antibodies or sera from HIV-1-infected individuals.
Methods: In most previous studies, lab-adapted HIV-1 strains were used. Here, we tested if the modulation of ADCC responses by Nef and Vpu accessory proteins is conserved among *primary* HIV-1 isolates. To this end, we evaluated the ability of CD4i antibodies and sera from HIV-1-infected individuals to mediate ADCC on infected primary CD4+ T cells with a panel of patient-derived infectious molecular clones (IMCs) of HIV-1 that contained intact or defective *nef* and/or *vpu genes*, using a FACS-based ADCC assay.
Results: Nef and Vpu accessory proteins from HIV-1 IMCs, including those from group M transmitted/founder viruses and members of the phylogenetically distant group N, prevented exposure of Env CD4i epitopes targeted by ADCC-mediating antibodies and sera from HIV-1-infected individuals.
Conclusions: Our observations highlight the importance of Vpu- and Nef-mediated modulation of Env epitope exposure in preventing the elimination of HIV-1-infected cells by ADCC and help explain the functional and immunological pressure exerted on HIV-1 to downregulate CD4 and BST-2/tetherin.

MOPEA010

Novel approach to identify new ADCC-mediating antibodies targeting the HIV-1 envelope

J. Richard[1], M. Coutu[1], M. Veillette[1], L.-A. Batraville[1], N. Alsahafi[1], J.-P. Chapleau[1], C. Cheng-Mayer[2], X. Wu[2], A. Finzi[1]
[1]The CHUM Research Center, Montreal, Canada, [2]Aaron Diamond AIDS Research Center, New York, Canada

Background: Increased evidence of Fc-mediated effector functions against HIV-1 has led to renewed interest into the role that antibody-dependent cellular cytotoxicity (ADCC) could play in controlling viral transmission and/or the rate of disease progression. Interestingly, the interaction of HIV-1 envelope (Env) glycoproteins with the CD4 receptor was recently reported to be required for efficient exposure of ADCC-mediating Env epitopes at the surface of HIV-1 infected cells. Moreover, potent CD4-induced ADCC-mediating monoclonal antibodies (mAbs) targeting the HIV-1 Env glycoprotein gp120 were isolated from vaccinees of the RV144 trial, which showed modest HIV-1 protection. The focus of this study was to establish a novel approach to allow identification of new ADCC-mediating mAbs targeting the HIV-1 gp120.
Methods: We developed an alternative flow-cytometry-based assay that allows specific measurement of ADCC-mediated elimination of HIV-1 gp120-coated target cells. This assay relies on staining target and effector cells with different dyes, which allows precise gating and permits the calculation of the number of surviving target cells by normalization to flow-cytometry particles. By using small concentrations of recombinant gp120, we generated suitable target cells that recapitulate the ADCC response mediated against HIV-1-infected cells.
Results: This method was successfully applied to screen ADCC activity in plasma from a substantial number of individuals from the Canadian Slow Progressor cohort and also from R5 SHIV-infected macaques. Furthermore, we were able to isolate new ADCC-mediating mAbs both from human and macaque samples. This was achieved by sorting individual B cells after staining with a newly-engineered Env probe, specifically sampling the CD4-bound conformation and presenting higher affinity for ADCC-mediating mAbs.
Conclusions: We developed a novel approach to screen for ADCC activity and isolate new ADCC-mediating mAbs targeting HIV-1 gp120. The identification as well as molecular

characterizations of such mAbs and the sites of vulnerability that they recognize is critical for the design of Env-based immunogens aimed at developing efficient HIV-1 vaccines able to generate strong ADCC-responses.

MOPEA011

Identification of HLA-associated polymorphisms in a cohort of HIV-1 subtype A/E infection

T. Giang[1], T. Chikata[1], Y. Tamura[1], T. Akahoshi[1], H. Murakoshi[1], N. Kuse[1], S. Oka[2], K. Sakai[1], N.V. Kinh[3], M. Takiguchi[1,4]
[1]Center for AIDS Research, Kumamoto University, Kumamoto, Japan, [2]AIDS Clinical Center, National Center for Global Health and Medicine, Tokyo, Japan, [3]National Hospital for Tropical Diseases, Hanoi, Vietnam, [4]International Research Center for Medical Sciences, Kumamoto University, Kumamoto, Japan
Presenting author email: giangminh08@gmail.com

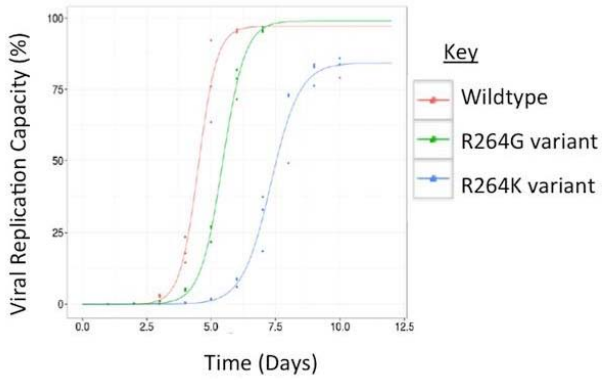
Background: It is well known that HIV-1 specific CTLs select escape mutant viruses during acute and chronic infections. Several population-based studies have indentified a significant association between viral polymorphisms and particular HLA alleles in cohorts of HIV-1 subtype B and C infections. However, these HLA-associated polymorphisms (HLA-APs) in HIV-1 subtype A/E have only partially been studied. In this study, we analyzed HLA-APs in chronically HIV-1 subtype A/E-infected Vietnamese individuals.
Methods: We analyzed HLA-APs in Gag, Pol, and Nef from 400 chronically HIV-1 subtype A/E-infected treatment-naïve individuals. HLA-APs in the three proteins were identified using a phylogenetically corrected logistical-regression model.
Results: We successfully analyzed the sequence of HIV-1 Gag, Pol, and Nef in 370, 359, and 372 individuals, respectively. At a false-discovery rate q≤0.2, we found 220 HLA-APs (50 in Gag, 64 in Pol, and 106 in Nef). Of these, 25% HLA-associated substitutions occurred within CTL epitopes restricted with same HLA alleles previously reported mostly in cohorts of HIV-1 subtype B and C. HLA-APs were more frequently detected in Nef (occurring at 59 of 206 codons [28.6%]) compared to Gag (29 of 498 codons [5.8%]) or Pol (39 of 1003 codons [3.9%]). The numbers of HLA-A-, HLA-B-, HLA-C-APs were 53, 87, and 80, respectively, indicating that a higher number of amino acid mutations restricted by HLA-C alleles compared to that in cohorts of HIV-1 subtype B or C infections.
Conclusions: We here identified 220 HLA-APs in the Vietnamese infected with HIV-1 subtype A/E and found remarkably higher number of HLA-APs in Nef than Gag and Pol as compared to previous studies on HIV-1 subtype B or C infection. The result suggests higher immune responses to Nef in the subtype A/E infection than in the infection of other subtypes.

MOPEA012

Viral clade affects the mechanism of HLA-B27:05-mediated immune control of HIV

J. Brener[1], R. Payne[1], J. Hurst[1], C. Juarez[1], J. Carlson[2], P.C. Matthews[1], P. Goulder[1]
[1]University of Oxford, Oxford, United Kingdom, [2]Microsoft Research, Redmond, United States
Presenting author email: jacqui.brener@wolfson.ox.ac.uk

Background: HLA-B*27:05, expressed most commonly in B Clade infected populations, is strongly associated with viral control and slow disease progression in HIV infection. Immune control hinges largely on the CD8+ T cell response to the HLA-B*27:05-restricted p24 Gag epitope KK10. An escape mutation in this epitope, R264K, is commonly accompanied by an upstream compensatory change, S173A. We hypothesized that clade-specific differences at the 173 residue, specifically T173 in C Clade HIV, may result in differences in the fitness cost and frequency of selection of escape. Clade-specific differences may directly affect the mechanism and potency of HLA-mediated immune control.
Methods: We sequenced the Gag protein in 25 C Clade infected HLA-B*27:05-positive individuals and identified polymorphisms associated with KK10 escape. We assessed the effect of KK10 escape and putative compensatory mutations on viral replicative capacity (VRC) by generating a panel of viral clones expressing escape variants and/or compensatory changes in the context of both the B and C Clade p24 gene, and measuring VRC *in vitro*.
Results: We found that all 15 subjects that had selected an escape mutation at residue R264 had no compensatory change at position 173. R264G was a more common escape variant than is seen in B Clade infection, and was less costly than R264K in VRC assays.
We identified three putative compensatory mutations associated with selection of KK10 escape in C Clade infection; S165N, V168I, and V218M. These mutations partially compensated for the fitness cost of R264K, but less effectively than S173A compensates in B clade infection. In VRC assays, the fitness cost of R264K was greater in the context of C Clade p24 than in B Clade p24.
Conclusions: We show that the most common Gag-KK10 escape mutant in B Clade infection, R264K, has a greater viral fitness cost and less effective compensation in C Clade infection. This is consistent with the increased frequency of the less costly R264G variant in C Clade escape. These results demonstrate that clade-specific differences in viral sequence have a direct effect on critical escape and compensatory mutations, directly implicating the viral sequence in the mechanism of HLA-associated control of HIV.



[Viral Replicative Capacity of C Clade p24 Variants]

HIV-1 controllers (including post-treatment controllers)

MOPEA013

Profound alterations in cholesterol metabolism restrict HIV-1 *trans* infection of CD4 T cells in nonprogressors

G. Rappocciolo, J. Martinson, P. Piazza, P. Gupta, C.R. Rinaldo
University of Pittsburgh, IDM, Pittsburgh, United States
Presenting author email: giovanna@pitt.edu

Background: The small percentage of HIV-infected individuals who control HIV disease progression for many years without cART (NP - nonprogressors) offer a natural model of viral control and clues to curing the infection as well as developing therapeutic and prophylactic vaccines. We have reported that professional antigen-presenting cells (APC), i.e., dendritic cells (DC) and B cells, from HIV-1 infected NP are inefficient in *trans* infection of T cells due to altered cholesterol metabolism, potentially reducing spread of virus and controlling disease progression. Importantly, APC from NP showed impaired *trans* infection both prior to and after primary HIV-1 infection, whereas APC from progressors had this capacity both before and after infection, supporting a host genetic basis for this impairment.
Methods: We conducted a whole genome transcription analysis on DC, B cells and $CD4^+$ T cells from NP and PR to identify differential expression of genes related to cholesterol metabolism. RNA was isolated from APC derived form NP and PR (progressors) and microarray analysis of mRNA transcripts was performed on Illumina HT12.
Results: NP overexpressed genes related to cholesterol metabolism pathways compared to PR. In DCperoxisome proliferator-activated receptor gamma (PPAR-γ) involved in the up-regulation of ABCA1 and CD36 receptor for oxidized LDL, and in B cells, genes related to the endocytosis of LDL and the LDL receptor (LDLR), as well LXRα, which up regulates ABCA1 activity upon *trans* activation by its natural ligands, such as oxysterols. The higher levels of transcripts for these genes were confirmed by RT-PCR.
Conclusions: We have shown that APC from NP completely lack the ability to *trans* infect T cells. This was associated with profoundly enhanced cholesterol metabolism that appears to be an inherited trait, and we have identified gene(s) involved in the uptake, trafficking and metabolism of cholesterol that are associated with the phenotype of defective *trans* infection. These results provide a basis for therapeutic interventions to control of HIV-1 infection through modulation of cholesterol metabolism.

Asymptomatic long term non-progression

MOPEA014

Characterization of anti-gp41 antibodies eliciting viral neutralization and protecting against CD4 depletion in long-term non-progressors

V. Vieillard[1], A. Samri[1], O. Lucar[1,2], J. Crouzet[2], D. Costagliola[3], P. Debré[1], French ALT Study Group
[1]*CIMI-Paris, INSERM U 1135, Paris, France,* [2]*InnaVirVax, Evry, France,* [3]*Institut Pierre Louis d'Epidémiologie et de Santé Publique, Paris, France*
Presenting author email: patrice.debre@psl.aphp.fr

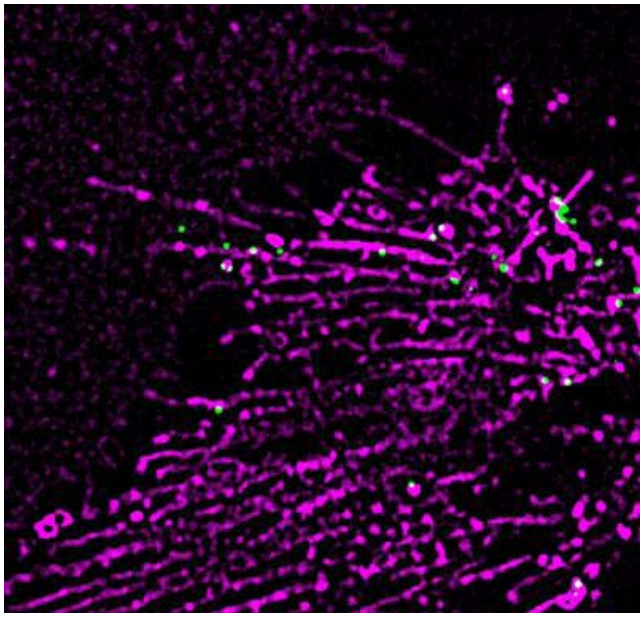
Background: We previously showed that antibodies (Ab), which recognized a highly conserved motif of the gp41, called 3S, are protective against $CD4^+$ T cell depletion. This was analyzed after immunization in a model of SHIV162P3-infected macaques, and naturally in asymptomatic long-term non-progressor (ALT) patients. More recently, we have detected the presence of anti-3S/W614A Ab, which recognized a point-modified form of 3S, in less than 5% of HIV-1 progressor patients. These Ab remain able to protect $CD4^+$ T cells but have also acquired the capacity to elicit viral neutralization. Here, we quantified and characterized these anti-3S W614A Ab in non-treated patients from the French ANRS ALT cohort.
Methods: 64 HIV-1 untreated ALT patients who had enrolled with >600 $CD4^+$ cells /mm^3 (for at least 8 years), were followed-up each year during the first 3 years to evaluate anti-3S-W614A Ab. Ab level was measured by ELISA, and its presence was correlated with different biological parameters (CD4 count, CD4/CD8 ratio, viral DNA, viral load, …). Viral neutralization was performed against a panel of tiers 1 and 2 viruses, using the standard TzM-bl assay.
Results: 25.7 % of patients had detectable anti-3S/W614A Ab at the enrollment period. The presence of these Ab is highly significantly correlated with an increased of the CD4/CD8 T cell ratio (p=0.006), and both decreased of the viral load (p< 0.0001) and viral DNA (p=0.0003). In the same subjects, measured again at 24-36 months following inclusion in the cohort, we observed that subjects with persistently specific Ab still had both significantly lower viral DNA and viral load, as compared to patients without anti-3S/W614A Ab. Importantly; we also report that the efficacy of viral neutralization mediated by anti-3S/W614A Ab, is time-dependent, increasing during the follow-up in term of breadth and potency.
Conclusions: The presence of anti-3S W614A Ab appears to confer crucial advantage in asymptomatic long-term non-progressor HIV-1 patients. These results bring new insights for both pathophysiological research and development of new vaccine strategy.

MOPEA015

CD40L-induced tunneling nanotube networks facilitate proinflammatory dendritic cell-mediated HIV-1 *trans*-infection of $CD4^+$ T cells

C. Zaccard[1], R. Mailliard[1], G. Rappocciolo[1], S. Watkins[2], C. Rinaldo[1]
[1]*University of Pittsburgh, Infectious Diseases and Microbiology, Pittsburgh, United States,* [2]*University of Pittsburgh, Cell Biology and Physiology, Pittsburgh, United States*
Presenting author email: crz14@pitt.edu

Background: We have found that, in addition to their high IL-12p70 producing capacity, dendritic cells (DC) matured in the presence of acute inflammatory mediators are uniquely programmed to form intercellular networks of tunneling nanotubes, or 'reticulate', in response to T helper cell-associated CD40L. We also recently revealed a relationship between HIV-1 disease progression and *trans*-infection when we demonstrated that DC from HIV-1-infected non-progressors (NP) lack the ability to transmit virus to $CD4^+$ T cells due to a paucity of cellular cholesterol. Here we investigate a relationship between inducible nanotube formation, which also requires the presence of cholesterol-rich lipid rafts, DC-mediated *trans*-infection, and HIV-1 disease progression.
Methods: DC were generated using monocytes isolated from HIV-1 seronegative donors or NP from the Multicenter AIDS Cohort Study. NP displayed stable $CD4^+$ T cell counts in the absence of antiretroviral drug therapy over many years of HIV-1 infection. Differential polarization of DC was achieved by exposure to an IFN-g- or PGE_2-containing cocktail to mimic a setting of acute or chronic inflammation, respectively. We treated DC types with CD40L or media, and quantitatively assessed morphological alterations using live-cell confocal microscopy and 3D imaging analysis software. The ability of DC types to transmit virus to $CD4^+$
T cells was determined using our *trans*-infection model, followed by intracellular HIV-1 core antigen staining and flow cytometry.
Results: We determined that CD40L-induced reticulation increases the surface area and spatial reach of proinflammatory DC, facilitating intercellular trafficking of antigens as well as HIV-1 for amplification of virus transmission. Moreover, IFN-g-programmed DC display a superior capacity to mediate HIV-1 *trans*-infection of $CD4^+$ T cells compared to PGE_2-programmed DC, which is further enhanced by the addition of soluble CD40L. Importantly, IFN-g-programmed DC generated from NP display a dramatically reduced ability to reticulate in response to CD40L, which coincides with their failure to effectively mediate HIV-1 *trans*-infection of $CD4^+$ T cells.



[DC nanotubes support cell-to-cell HIV-1 transfer]

Conclusions: The link between inhibited disease progression in HIV-1-infected NP and the inability of their proinflammatory DC to reticulate and *trans*-infect $CD4^+$ T cells provides a rationale for further exploration of therapeutic strategies to target this immune process and potentially control HIV-1 disease progression.

Highly exposed seronegative individuals (HESN)

MOPEA016

Plasma and PBMC miRNA profile in sexually HIV-exposed seronegative individuals

I. Saulle[1], S. Yahyaei[1], M. Biasin[1], M. Garziano[1], M. Masetti[1], A. Berzi[1], D. Trabattoni[1], S. Lo Caputo[2], F. Mazzotta[2], M. Clerici[1,3]
[1]*University of Milan, Biomedical and Clinical Sciences, Milan, Italy,* [2]*S. Mari Annunziata Hospital, Infectious Disease, Florence, Italy,* [3]*Don Gnocchi Foundation, Milan, Italy*
Presenting author email: michela.masetti@unimi.it

Background: MicroRNAs (miRNAs) are small 20- to 24-nt non-coding RNAs involved in the post-transcriptional regulation of gene expression which play important roles in several viral infections. Global expression profiles of cellular miRNAs identified alterations of specific miRNAs post-HIV infection both in vitro and in different patient cohorts; these data suggest a potential role for miRNA in pathogenesis and disease progression. We verified if natural resistance to HIV infection in seronegative individuals repeatedly exposed to HIV (HESN) could be secondary to a peculiar miRNA signature.
Methods: expression levels of 84 miRNAs, selected according to their proven anti-HIV properties were analyzed by a specific miRNA array and results were confirmed by individual RT- qPCR in plasma, unstimulated PBMC and in *in vitro* HIV infected PBMC isolated from 40 HESN, 40 HIV seropositive subjects (HIV+) and 40 healthy controls (HC).
Results: Results showed that:
1) whereas the basal PBMC miRNA profile from HESN was similar to the one observed in HC and was characterized by an increased expression of miR-138, miR-150 and miR-190, mir29a and miR223 expression was significantly upregulated in HESN alone;
2) miR-28, miR-29a, miR-150 and miR223 expression was significantly downregulated in HIV-stimulated PBMC of HESN alone;
3) miR-28, miR-29a, miR-29b, miR-29c, miR125b, miR-146, miR-150, miR-155, miR-190 and miR-382 were increased in plasma of both HESN and HIV+ compared to HC;
4) of miR-138 and miR-223 plasmatic levels are exclusively increased in HESN compared to both HIV-1+ patients and HC.
Conclusions: HIV exposure modifies miRNA expression even in the absence of overt infection. Because the miRNAs that are increased in HESN, i.e. miR-29a, miR-138 and miR-223 were shown to play important role in reducing HIV replication *via* their ability to bind the 3' UTR of viral mRNA, the modulation of these miRNAs could represents a key protection mechanism against HIV infection.

MOPEA017

Immune activation is present in HIV-1 exposed seronegative individuals (HESN) and is indipendent from microbial translocation

M. Garziano[1], I. Saulle[1], F. Gnudi[1], M. Masetti[1], A. Berzi[1], F. Mazzotta[2], S. Lo Caputo[2], D. Trabattoni[1], M. Biasin[1], M. Clerici[1,3]
[1]University of Milan, Biomedical and Clinical Sciences, Milan, Italy, [2]Santa Maria Annunziata Hospital, Infection Disease, Florence, Italy, [3]Don Gnocchi Foundation, Milan, Italy
Presenting author email: micaela.garziano@unimi.it

Background: Analyses on the presence of immune activation in HIV-exposed seronegative individuals (HESN) yielded discrepant results. To clarify this issue we performed an extensive investigation of immune parameters in HESN and, in particular, we analyzed the possible presence in these individuals of microbial translocation, the most widely accepted reason driving immune activation in HIV-infected patients (HIV+).
Methods: Twenty HESN, 20 HIV-unexposed healthy controls (HC) and 20 HIV+ individuals were enrolled to evaluate:
1) T lymphocytes activation markers, maturation pathways and TLR4+CD14+ expression;
2) TLR transduction pathway in response to LPS stimulation;
3) production of proinflammatory cytokines by LPS- stimulated PBMC; and 4) LPS and sCD14 plasma levels.
Results: Results showed that in HESN and HIV+ compared to HC;
1) CD4+CD25+, CD8+CD38+, and memory T lymphocytes were increased whereas naïve T cells were reduced
2) PBMC were more responsive to LPS stimulation and were characterized by increased mRNA levels of effector mediators; and
3) IL6, TNFa and IFNg production was augmented. In contrast with these results, LPS and sCD14 levels were significantly reduced in HESN and HC compared to HIV+; these discrepancies were not secondary to differences in TLR4 expression.
Conclusions: Immune activation and increased responsiveness to LPS characterize the HESN phenotype; this is not driven by alterations of the gastrointestinal barrier and microbial translocation. The activation state seen in HESN may influence the induction of stronger adaptive antiviral immune responses and may represent a virus exposure-induced innate immune protective phenotype against HIV.

Correlates of immune protection

MOPEA018

Association of the presence of HIV-1 broadly neutralizing antibodies during pregnancy and prevention of mother to child transmission at delivery

T. Mduluza[1,2], S. Dzoro[2,3], K. Bedi[3], S. Mpoloka[3], S. Gaseitsiwe[2], R. Musonda[2]
[1]University of Zimbabwe, Biochemistry, Harare, Zimbabwe, [2]Botswana AIDS Institute, Research Laboratory, Gaborone, Botswana, [3]University of Botswana, Biological Sciences, Gaborone, Botswana
Presenting author email: mduluza@medic.uz.ac.zw

Background: Neutralizing antibody assays are now being widely employed in different laboratories in search for correlates of protective immunity. There are strong arguments in favor of a beneficial role of some broadly neutralizing antibodies in prevention of HIV infection if these antibodies exist prior to exposure. Further, correlates of broadly neutralizing antibodies may provide essential pointers to HIV vaccine development.
Methods: Archived plasma samples at the Botswana-Harvard HIV Institute, were assayed for presence of neutralizing antibodies using TZM-bl cells with a *tat* regulated luciferase reporter gene. A panel of well characterized HIV-1 strains was used, and results were expressed as fifty percent or ninety percent inhibitory dose (ID50/ ID90), defined as the plasma dilution causing fifty percent or ninety percent reduction in relative luminescence (RLU) compared to virus control wells after subtraction of background RLU. The plasma samples used were collected during pregnancy and at delivery.
Results: There were no statistically significant differences in the distribution of ID50 neutralizing antibody titres or neutralization breadth among transmitters and non-transmitters, observed at enrolment at ID50 and throughout. However, non-transmitters had significantly higher neutralization potency at ID90 against the HIV-1 laboratory strains. Similarly, a high neutralization of all the panel viruses was observed by the plasma samples collected at delivery by the non-transmitters.
Conclusions: HIV-1 broadly neutralizing antibodies were observed to be present in infected pregnant women with an ability to give above 50% viral neutralization at all time points. While highly potent neutralizing antibodies showing ID90 was associated with reduced mother to child transmission of HIV *in utero* and at delivery. However this relationship demand further investigation as giving pointers to the important components essential for vaccine development. There is need to understand further the components that exhibit HIV-1 neutralizing effects, the immunologic environments that support viral neutralization and reduced mother to child HIV transmission, as well as their dominant effect.

MOPEA019

Neutralizing antibody response in chronically HIV-1 infected ART naïve children from India: a follow-up study

M.A. Makhdoomi[1], A. Nair[1], S. Kumar[1], H. Aggarwal[1], S. Sharma[1], R. Lodha[2], R. Singh[2], M. Singla[2], N. Shah[2], S.K. Kabra[2], K. Luthra[1]
[1]All India Institute of Medical Sciences, Biochemistry, New Delhi, India, [2]All India Institute of Medical Sciences, Pediatrics, New Delhi, India
Presenting author email: muzamilbiochem@gmail.com

Background: Broadly cross neutralizing antibodies develop only in a subset of individuals after primary infection. There is paucity of data on antibody response elicited by HIV-1 infected children. In this study, we assessed the neutralizing antibody specificity, over time, in HIV-1 infected children from India.
Methods: A cohort of thirty one ART naïve HIV-1 chronically infected children were enrolled. Plasma neutralization activity at two time points was assessed against a panel of six subtype B and C tier 2 using TZM-bl cell line. Max50 binding titres were determined by ELISA using consensus V3B, V3C, IDR, MPER-B and MPER-C peptides. CD4bs specificity of plasma antibodies was evaluated using CD4bs-selective probe RSC3 and its mutant RSC3Δ371I.
Results: This is the first longitudinal study to profile neutralizing antibody activity in HIV-1 infected children from India. All HIV-1 infected children (21 male and 10 female; age range: 5-17 years) were ART naïve, asymptomatic and had mother to child transmission. Twenty (64.5%) baseline and twenty two (71%) follow up samples neutralized ≥50% of the viruses tested. Four baseline (12.5%) and seven (22.5%) follow up plasma samples neutralized all six viruses tested. A modest improvement in neutralization breadth (P=0.035) and potency (P=0.0335) was observed with time. Subtype C specific neutralization predominated in baseline plasma samples (P=0.016); interestingly, follow up samples exhibited cross neutralizing activity (P=0.095). Heatmap analysis revealed that Du156.12 and Du172.17 (clade-C viruses) were most sensitive while ZM53M.PB12 (clade-C) followed by SC422661.8 (clade-B) isolates were most resistant to antibody neutralization. Epitope mapping revealed relative abundance of V3C reactive antibodies with a positive trend (P=0.043) in follow up samples. No correlation was observed between neutralization activity and Max50 binding titres of anti-V3C plasma antibodies in the baseline (P=0.468) or follow up (P=0.435) samples. None of the plasma showed MPER specific antibodies. CD4bs specific antibodies were found in four plasma sample AIIMS_353, AIIMS_513, AIIMS_524 and AIIMS_525 with significantly higher Max50 binding titres (P=0.032) in respective follow up samples.
Conclusions: Improvement in plasma cross neutralizing activity with time, suggests the evolution of broadly neutralizing antibodies in the infected children. CD4bs antibodies could be important neutralizing determinants and need to be characterized further.

MOPEA020

Identification of the structural determinants for the selective anti-HIV-1 activity of the all-β alternative conformer of the γ-chemokine XCL1/lymphotactin

C. Guzzo[1], J.C. Fox[2], H. Miao[1], B.F. Volkman[3], P. Lusso[1]
[1]National Institute of Allergy and Infectious Disease, NIH, Bethesda, United States, [2]Medical College of Wisconsin, Department of Biochemistry, Milwaukee, United States, [3]Medical College of Wisconsin, Biochemistry, Milwaukee, United States
Presenting author email: christina.guzzo@nih.gov

Background: HIV-1 replication is regulated *in vivo* by a complex network of cytokines and chemokines. XCL1/lymphotactin, a unique metamorphic chemokine, was recently identified by our group as a broad-spectrum HIV-1 inhibitor that blocks viral entry via direct interaction with the gp120 envelope glycoprotein. Strikingly, only one of the two conformations that XCL1 can adopt is associated with antiviral activity. Indeed, HIV-1 inhibition by XCL1 requires access to the alternative all-β conformation, which interacts with glycosaminoglycans (GAG) but not with the specific XCL1 receptor, XCR1.
Methods: We investigated the structure-function correlations in XCL1 and specifically compared the determinants responsible for HIV-1 inhibition with those involved in GAG interaction. A panel of mutants of the stabilized all-β variant, XCL1 W55D, bearing individual alanine substitution of all basic amino acids in the structured core of XCL1 (aa. 1-54), as well as three residues within the C-terminal tail, was assayed for inhibition of HIV-1 infection. Virion capture assays were performed to assess the impact of alanine substitutions on the ability of XCL1 to directly bind HIV-1 virions.
Results: The results obtained by alanine scanning mutagenesis in both infection and virion-capture assays identified 5 basic residues as key determinants of the antiviral activity of XCL1.

Strikingly, four of these five residues cluster to form a large positively-charged surface in the all-β XCL1 conformation, while they are dissociated in the classic chemokine fold, which is inactive against HIV-1, thereby providing a structural basis for the selective antiviral activity of alternatively-folded, all-β conformer of XCL1. Furthermore, we observed that changes to the N-terminal domain, which is proximal to the cluster of putative HIV-1 gp120-interacting residues, also affect the antiviral activity of XCL1. Interestingly, the complement of residues involved in HIV-1 blockade is partially overlapping, but distinct from those involved in the GAG-binding function of XCL1.

Conclusions: Here, we identify the interactive surface of XCL1 that is implicated in binding to the HIV-1 envelope and HIV-1 inhibition, providing a structural basis to explain why only the all-β XCL1 conformer is effective against HIV-1. Our findings may be useful in guiding the rational design of new inhibitors of HIV-1 entry.

Mucosal transmission

MOPEA021

Effect of rectal gonorrhea and chlamydia on cytokine expression and HIV viral load in the rectum

O. Davies, J. Tiraboschi, S. Costelloe, J. White, S. O'Shea, J. Fox
Guy's & St Thomas' Hospitals NHS Trust, London, United Kingdom
Presenting author email: julie.fox@kcl.ac.uk

Background: The effect of rectal gonorrhea (GC) and chlamydia (CT) on HIV viral load in the rectum, and its potential significance on the onward transmission of HIV is unclear. We developed a standardised method for quantifying rectal HIV viral load (VL) and investigated the effect of rectal GC and CT on rectal and plasma HIV VL and cytokine expression in HIV-1 infected MSM.

Methods: 42 HIV infected MSM on (n=21) and off ART (n=21) were recruited. Results of those with and without rectal gonorrhoea and chlamydia were compared. Those with rectal GC/CT were re-sampled ≥2 weeks after receiving treatment for the STI. Four rectal swabs were taken via proctoscopy and analysed for HIV VL, STI, and cytokines. Rectal HIV VL was quantified using the Roche Cobas TaqMan 48 analyzer and HIV-1 High Pure Extraction System. Total swab RNA was quantified and HIV VL expressed as copies/µg RNA. Plasma HIV VL was measured using the Roche AmpliPrep/Cobas Taqman system. Quantitative detection of 10 cytokines was carried out using cytokine array. Independent t-tests were used for comparative analysis.

Results: Of the 21 MSM on ART, 7 had rectal GC/CT and 14 did not. All plasma and rectal HIV viral loads were < 100 copies. There was no significant difference in rectal VL (p=0.38), IL6 (p=0.41), IFNγ (p=0.42), and TNFα (p=0.26) levels between individuals with and without GC/CT.

Of 21 ART naïve MSM, 7 had rectal GC/CT and 14 did not. There was no significant difference in rectal VL (p=0.50) or major cytokines between those with and without rectal GC/CT. Following treatment of rectal CT/GC there was a non-significant drop in rectal HIV VL (median 0.6, range 0.3-1.4log; p=0.52) and no change in plasma VL (p=0.37).

Conclusions: A standardized method for quantifying rectal HIV VL has been established. Rectal GC/CT do not impact on rectal or plasma HIV VL in those on ART, and the impact in ART naïve individuals was not significant. This suggests minimal impact of GC/CT on onward transmission of HIV.

MOPEA022

CD161-expression on CD4+ T cells is enriched in the female genital tract and identifies a subset of activated cells rather than Th17 commitment as in blood

G. Boily-Larouche[1], J. Lajoie[1], K. Odiwuor Omollo[2], J. Cheruiyot[3], J. Njoki[3], M. Kimani[3], J. Oyugi[2,3], J. Kimani[3], K.R. Fowke[1,2,4]
[1]University of Manitoba, Medical Microbiology, Winnipeg, Canada, [2]University of Nairobi, Medical Microbiology, Nairobi, Kenya, [3]Kenyan AIDS Control Program, Nairobi, Kenya, [4]University of Manitoba, Community Health Science, Winnipeg, Canada
Presenting author email: genevieve.boily.larouche@gmail.com

Background: In blood the C-type lectin CD161 identifies a subset of proinflammatory tissue-homing CD4$^+$ T cells committed to the Th17 lineage. Preferential depletion of circulating CD161$^+$CD4$^+$ T cells has been observed among HIV-infected individuals and this subset is permissible to HIV. In the female genital tract (FGT), a portal of entry for HIV, the pattern of CD161 expression on CD4+ cells remains elusive and its relevance to identifying Th17 commitment and HIV targets cells remain unknown. In this study, we characterized CD161 expression in the FGT.

Methods: The study groups included female sex workers (FSW) chronically infected by HIV (n=16), HIV-negative women new to sex work (n=36), HIV-exposed seronegative (HESN) (n=33) and HIV-negative non-FSW (low-risk) (n=30) from Nairobi, Kenya. Blood and cervical cytobrushes were collected from women enrolled in the Pumwani sex worker cohort in Nairobi, Kenya. CD161$^+$ and CD161$^-$ subsets were characterized by flow cytometry. Age, menstrual cycle phase, behavioural and clinical factors were collected for all participants.

Results: CD161$^+$CD4$^+$ T cells were enriched in the FGT of HIV-negatives and not preferentially depleted in HIV-infected FSW relative to low-risk controls. CD161$^+$ cells harboured a more activated phenotype and expressed higher frequencies of tissue-homing markers and HIV co-receptor CCR5. PMA/Ionomycin stimulation confirmed the Th17 commitment of circulating CD161$^+$ CD4$^+$ T cells. Stimulation of cervical cells induced only IFN-gamma in both subsets. IL-17 and IL-22 levels were high at baseline in both subsets of cervical cells and could not be induced. CD161$^+$ cell activation phenotype was altered in FSW compared to non-FSW. FSW had higher frequency of cervical CD69$^+$CCR5$^+$ CD161$^+$ CD4$^+$ T cells. The increased frequency of CD161$^+$ HIV targets was counterbalanced in HESN by a reduction of CCR5 on CD161$^+$ cells.

Conclusions: In the FGT, CD161 expression did not characterize Th17 committed cells. The unique FGT environment may promote Th17 differentiation independently of CD161 expression. However, CD161 expression in the FGT identified a subset of CD4$^+$ cells that was highly activated and thus potential HIV targets. This subset may represent memory tissue-resident T cells that respond to exposure to sex-work derived antigens including antigens from sex, HIV or other sexually transmitted infections.

MOPEA023

HIV-1 Nef controls cellular invasion through differential modulation of host proteins

R. Saxena[1], K. Singh[2], K. Mitra[2], A.K. Tripathi[3], A.K. Tripathi[4], J.K. Ghosh[4], R. Tripathi[1]
[1]CSIR-Central Drug Research Institute, Toxicology Division, Lucknow, India, [2]CSIR-Central Drug Research Institute, Electron Microscopy Lab, Sophisticated Analytical Instrument Facility, Lucknow, India, [3]King George's Medical University, Department of Medicine, Lucknow, India, [4]CSIR-Central Drug Research Institute, Molecular and Structural Biology, Lucknow, India
Presenting author email: res1618@gmail.com

Background: HIV-1 infection involves significant host-virus interaction. At mucosal membranes, HIV-1 gets access to infect activated immune cells and establishes itself. Characterization of target cells and the pathways of viral dissemination is essential to better understand HIV-1 spread. Nef is an accessory viral protein that facilitates alterations in cellular pathways via sequence specific protein-protein interactions and is known to regulate host invasion. We aimed to explore how Nef variants affects Nef mediated invasion of HIV-1 targeted immune cells.

Methods: Through proteomics approach, two Nef variants RP14 and RP01 sequenced from HIV-1 patients were investigated for their implications in different HIV-1 targeted cells. 2D-Gel Electrophoresis in SupT1 cells by Nef, demonstrated several differentially expressed proteins identified through LC-MS/MS and further analyzed by qPCR, Western blotting and Immunofluorescence studies with Nef variants in SupT1 and THP-1 cells. Enzymatic assays, Cell migration and invasion studies were employed to determine biological function affected by Nef mediated regulation of host proteins. Based upon sequence variation a specific Nef domain was targeted for regulating the invasiveness of target cells. Site-directed mutagenesis and inhibitor confirmed the Nef mediated regulation of host invasion.

Results: Nef modulated host proteins were identified as Cyclophilin A, EIF5A-1 Rho GDI 1, VDAC1, OTUB1 and ENO1. Both ENO1 and VDAC1 were downmodulated by RP01 but remained unaffected by RP14. Interestingly, effects of Nef on ENO1 and VDAC1 regulation were found to be cell lineage-specific, being inhibitory in T cells, stimulatory in monocytes. ENO1 and VDAC1 being involved in cellular invasion, invasiveness was found to be enhanced in THP-1 cells but was inhibited in SupT1 cells by RP01. Both the Nef mutant and inhibitor led to reduction of enhanced expression of targeted host proteins and increased invasiveness in THP-1 cells, whereas the effect was reversed in T cells. A specific Nef domain regulating spread of HIV-1 infected immune cells was thus determined.

Conclusions: The study suggest a possible mechanism of host invasion by HIV-1 through Nef mediated regulation of host proteins. Identification of physiologically relevant host targets involved in cellular invasion leading to viral infection at mucosal barriers would contribute for building effective therapeutic strategies.

Founder viruses/transmission bottleneck

MOPEA024

Galectin-3 promotes HIV-1 cell-to-cell transmission via up-regulating GM1 ganglioside in lipid raft of CD4+ T cells

S.-F. Wang[1,2,3], C.-H. Tsao[3], S.W. Huang[2], Y.-W. Hong[1,2], C.S. Yeh[1,2], M.-L. Chiang[3], D. Hsu[3,4], Y.-M. Chen[2,5], H.-Y. Chen[3,4], F.-T. Liu[3,4]
[1]Kaohsiung Medical University, Department of Medical Laboratory Science and Biotechnology, Kaohsiung, Taiwan, Province of China, [2]Kaohsiung Medical University, Center for Infectious Disease and Cancer Research, Kaohsiung, Taiwan, Province of China, [3]Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan, Province of China, [4]University of California, Department of Dermatology, Davis, United States, [5]Faculty of Medicine, College of Medicine, Medical University, Department of Microbiology, Kaohsiung, Taiwan, Province of China
Presenting author email: wasf1234@gmail.com

Background: We previously reported that galectin-3 translocates to the cytosolic face of the immunological synapse (IS) in T cells following T cell receptor engagement and galectin-3 associates with Alix. We demonstrated that galectin-3 is dependent on Alix to promote HIV-1 budding. We also reported that endogenous galectin-3 localizes in membrane lipid rafts and regulates dendritic cell migration. Lipid raft integrity is essential for HIV-1 virological synapse (VS) formation and cell-to-cell transmission. We hypothesized that galectin-3 plays a role in HIV-1 cell-to-cell transmission.
Methods: Lipid raft extraction and immunoblotting were used to know galectin-3 expression level in membrane lipid raft. Cell-to-cell transmission assay was conducted to evaluate the effect of galectin-3 on HIV-1 cell-to-cell transmission. Immunofluorescence staining and live imaging observation were used to trace galectin-3 dissemination via VS and galectin-3 colocalization with Alix, Gag and GM1 on VS. FACS was used to address the effect of galectin-3 knockdown or overexpression on GM1 expressing level in CD4+ T cells.
Results: Immunoblotting results indicate that galectin-3 expresses in membrane lipid rafts in T cells. Results from immunofluorescence staining showed that galectin-3 and Alix coloclaized with Gag in lipid rafts of VS between HIV-1 infected and uninfected CD4+ T cells. Live video-microscope imaging observation showed that EGFP-galectin-3 or EGFP-Alix co-transmission with iCherry-Gag from HIV-1 effector cells to the target cells. Cell-to-cell transmission assay found that the efficiency of HIV-1 transmission is significantly increased by galectin-3 overexpression but attenuated in galectin-3 knockdown CD4+ T cells. Similar results were found in Alix knockdown CD4+ T cells. Moreover, galectin-3-promoted HIV-1 cell-to-cell transmission efficacy is positively correlated with the expression level of galectin-3 in the effector cells. Cholera toxin B(CTB) staining results showed that GM1 ganglioside expression was regulated by galetcin-3 and Alix. We found that galectin-3 compensated the effect of Alix-knockdown on HIV-1 cell-to-cell transmission via up-regulating GM1 ganglioside expression. We also observed that ectopic expression of galectin-3 N-terminal domain inhibit HIV-1 cell-to-cell transmission in CD4+ T cells.
Conclusions: We conclude that endogenous galectin-3 facilitates HIV-1 cell-to-cell transmission by up-regulating GM1 ganglioside expression and galectin-3 may be a potential target for HIV-1 therapy.

Acute and early infection

MOPEA025

Early antiretroviral treatment (ART) fails to achieve sustained HIV viral remission but limits viral diversity

P. Zangari[1], P. Palma[2], H.K. Tchidjou[2], G. Liuzzi[3], C. Alteri[4], A. Bertoli[4], C.F. Perno[4], P. Rossi[2], S. Bernardi[2]
[1]Tor Vergata University, Pediatrics, Rome, Italy, [2]Bambino Gesù Children's Hospital, University Department of Pediatrics, DPUO, Unit of Immune and Infectious Diseases, Rome, Italy, [3]National Institute for Infectious Diseases 'L. Spallanzani', Clinical Department, Rome, Italy, [4]Tor Vergata University, Department of Experimental Medicine and Surgery, Rome, Italy
Presenting author email: paolazangari@hotmail.com

Background: As reported by recent evidences and despite the previous excitement generated by the case of Mississippi baby, early ART alone may not be sufficient for sustained HIV remission. Major benefits of early ART include a more limited viral diversity. Few cases supported this data due to the difficulty of performing amplification and sequencing analysis during viral suppression. Here, we reported a case of limited HIV-1 viral evolution in an early treated child for which plasma samples were available at different time points.
Methods: The child was monitored for HIV-1 viral load (VL), CD4 and genotypic resistance test. The HIV-1 genetic evolution was evaluated on pol gene. A neighbor joining (NJ) tree was constructed to define the HIV-1 subtype and the sequence inter-relationships between the mother/child pair. Once the HIV-1 subtype was assigned, the statistical robustness of the monophyletic clade was confirmed also by the ML tree.
Results: A perinatally HIV-1 infected infant was treated within 7 weeks of age with zidovudine, lamivudine, nevirapine and lopinavir/ritonavir. At HAART initiation HIV-1 VL and CD4 percentage were >500.000 copies/ml and 35%, respectively. Plasma genotypic resistance test revealed a wild-type virus. The child reached VL undetectability after 33 weeks of HAART and maintained it until 177 weeks of HAART, when a low level viremia replication was detected (VL< 40 copies/ml, ABBOTT). At this time CD4 percentage was 40%. Again the genotypic resistance test revealed a wild-type virus. The phylogenetic analysis performed on the HIV-1 pol sequences of the mother and the child revealed that sequences clustered with C subtype reference strains and formed a monophyletic cluster distinct from the other C sequences included in the analysis (bootstrap value >90%). A minimal evolutionary divergence between the two plasma sequences of the child was also detected (mean±SE:0.000090±000087) and it was sustained by a single nucleotide substitution at position 231 of RT (C to T [F77F]).
Conclusions: Early ART limits the viral evolution avoiding the emergence of new viral variants. This result may have important implications in host immune control and may sustain the challenge of new personalized immunotherapeutic approaches to achieve a prolonged viral remission.

T cell-based vaccines

MOPEA026

Strong functional constraint at residues in HIV-1 Gag are predicted by measures of evolutionary rather than population-level genetic conservation

M. John[1,2], S. Gaudieri[2,3], A. Chopra[2], S. Leary[2], J. Jorritsma[2], S. Mallal[2,4], B. Baraki[5], M. Brockman[5,6], Z. Brumme[5,6]
[1]Royal Perth Hospital, Department of Clinical Immunology, Perth, Australia, [2]Institute for Immunology and Infectious Diseases, Murdoch University, Murdoch, Australia, [3]University of Western Australia, School of Anatomy, Physiology and Human Biology, Nedlands, Australia, [4]Vanderbilt University, Division of Infectious Diseases and Department of Pathology, Microbiology and Immunology, Nashville, United States, [5]Simon Fraser University, Burnaby, Canada, [6]British Columbia Centre for Excellence in HIV/AIDS, Vancouver, Canada
Presenting author email: silvana.gaudieri@uwa.edu.au

Background: Previous genetic studies have identified evolutionary conservation (EvC) in HIV-1 proteins relative to SIV orthologues. We hypothesized that such "high EvC" residues are likely to reflect inherent constraint rather than lack of immune targeting and will demonstrate high replicative cost when mutated. In contrast, residues that are conserved among HIV-1 population isolates but not conserved among phylogenetically-related lentiviruses ("low EvC/high PopC") may represent sites of early population-level fixation of HLA- or other human-driven mutations in HIV. This latter type of site may not be substantially mutationally constrained; furthermore, population-level HLA adaptation at these sites may render them poorly immunogenic in vivo. We would predict that HIV epitopes spanning "high EvC" sites will have greater immunogenicity than full-length autologous virus or constructs designed to capture population-level HIV-1 sequence conservation only.
Methods: Mutations at a "high EvC" site in $p24^{Gag}$ (L188I/D) and "low EvC/high PopC" site in $p17^{Gag}$ (E106L) were selected based on structure information and modeling methods and engineered into an HIV-1 NL4-3 reference strain backbone. VsVg-pseudotyped HIV-1 stocks were generated in HEK-293 cells and their $p24^{Gag}$ levels assessed by ELISA. Infectivity and replication capacity of wild-type NL4.3 and mutant viruses were assessed using an established GFP-reporter T-cell assay.
Results: The "low EvC/high PopC" mutant E106L showed similar viral particle production, infectivity and viral spread to wild-type NL4-3. In contrast, the "high EvC" mutant L188D showed no evidence of viral particle production, infectivity or viral spread, suggesting a viral egress defect. Interestingly, the "high EvC" mutant L188I, where the conserved residue was replaced with a structurally similar amino acid, showed viral particle production comparable to that of NL4-3, but poor infectivity and viral spread; suggesting a viral entry defect.
Conclusions: The initial sites tested support the hypothesis that EvC can be used as a probe to identify virological constraint and/or potential host adaptation early in the pandemic. In this case, E106L falls within an area that is poorly covered by known T-cell epitopes and may represent a site of HIV adaptation to HLA at the population-level. These data may be applied in the development of HIV immunogens as well as in rational drug design.

MOPEA027

Effect of losartan on lymphoid tissue fibrosis and inflammation in virologically suppressed HIV patients after 48 weeks

B. Torres Murillo[1], A.C. Guardo[2], M. Caballero[3], A. Fabra[4], L. Leal[1], C. Lucero[1], A. Leon[1], J.M. Gatell[1], M. Plana[2], F. Garcia[1]
[1]Hospital Clinic, Infectious Diseases, Barcelona, Spain, [2]Hospital Clinic, IDIBAPS, Barcelona, Spain, [3]Hospital Clínic, ICEMEQ, Barcelona, Spain, [4]Hospital Clinic, Barcelona, Spain
Presenting author email: fgarcia@clinic.ub.es

Background: Virologically suppressed HIV patients present a higher level of residual inflammation and chronic immune activation than non-infected population. It has been related to higher fibrosis on lymphoid tissue and end-organ diseases. No therapies have been developed to effectively target these inflammatory mediators. Anti-fibrotic and anti-inflammatory properties of the angiotensin receptor antagonist losartan have been described. The objective was to investigate the effect of losartan on lymphoid tissue fibrosis and inflammatory mediators in treated HIV patients.
Methods: 22 chronic HIV-patients, virologically supressed for at least 48 weeks, in treatment with Tenofovir/Emtricitabine/Efavirenz (200/245/600 mg) QD were randomized either to continue with the same antiretroviral therapy (cART) (n=12) or to add losartan (n=10) for 48 weeks. Tonsil biopsy was performed at baseline and at week 48. Markers of inflammation and coagulation (hsPCR, TNF alpha, IL-6 and D-dimer), markers of CD4 and CD8 lymphocytes activation (38+DR+) and senescence (28-57+), markers of monocyte differentiation (CD14+, CD16+) and monocyte activation (soluble CD163) were analyzed. The difference of these parameters between week 48 and baseline was analyzed between groups.
Results: Median age was 40 years. Median (IQR) time since HIV diagnosis was 8.5 (5.3-14.8) years and the median (IQR) time on cART before enrolment was 5.5 (3.2-13) years. All participants were with viral load < 37 copies at baseline. 11 tonsil biopsies were suitable for analysis (six in the losartan group). All biopsies except one showed no fibrosis at baseline. At week 48 five patients had an increased proportion of fibrosis compared to baseline with no difference between groups (p=1). There were very minimum changes in hsPCR, TNF alpha, IL-6 and D-dimer between baseline and week 48 with no differences between groups. Similarly, no differences were observed during this time period between both groups in markers of CD4 and CD8 lymphocytes activation [CD4+38+DR+ (p=1); CD8+38+DR+ (p=0.67);], senescence [CD4+28-57+ (p=0.67); CD8+28-57+ (p=0.67)], monocyte differentiation CD14++16- (p=0.67); CD14+16+ (p=0.19)] neither in markers of monocyte activation [soluble CD163 (p=0.39)].
Conclusions: Angiotensin receptor antagonist losartan did not have an impact on lymphoid tissue fibrosis or markers of inflammation, coagulation, T cell activation, senescence, monocyte differentiation and monocyte activation in HIV infected patients on cART.

Adjuvants

MOPEA028

Modulation of binding antibody responses to trimeric gp145 and gp41 HIV-1 envelope proteins by utilizing different adjuvants and delivery platforms as a prime-boost strategy

K. Peachman[1], G. Gao[2], O. Jobe[1], C. Alving[3], V. Rao[2], M. Rao[3]
[1]Henry M. Jackson Foundation / USMHRP, Adjuvant and Antigen, Silver Spring, United States, [2]Cathloic University of America, Biology, Washington, United States, [3]Walter Reed Army Institute of Research / USMHRP, Adjuvant and Antigen Research, Silver Spring, United States
Presenting author email: kpeachman@hivresearch.org

Background: The potential importance of binding antibodies in preventing HIV-1 acquisition was recently demonstrated by the RV144 phase III HIV-1 vaccine trial. The importance of adjuvants and delivery platforms for the generation of the desired immune response has generally been underestimated in the vaccine field. We examined if immunization with HIV-1 envelope proteins in the absence of any priming vector could induce binding and functional antibodies including V2-specific antibodies by utilizing a prime-boost strategy involving different adjuvants (monophosphoryl lipid A and *E. coli* heat labile enterotoxin [HLT]) and delivery platforms (liposomes and transcutaneous).
Methods: JR-FL HIV-1 gp145 protein trimerized with foldon and consisting of gp120, gp41 ectodomain, and MPER, and gp41-Soc (ecto and cytoplasmic domains without the transmembrane region fused to small outer capsid protein of bacteriophage T4) were expressed individually in 293F cells and purified. New Zealand White Rabbits were immunized at weeks 0, 4, and 8 with trimeric gp145 or gp41-Soc. The proteins were encapsulated in liposomes containing monophosphoryl lipid A and injected intramuscularly for all 3 immunizations (IM) or the boost at week 4 was a transcutaneous immunization (TCI) administered by applying the protein mixed with HLT on the surface of the skin (IM/TCI/IM). Serum samples were analyzed for 18 weeks post-immunization for antibodies by ELISA. Purified IgG from immune sera was assessed for neutralization of primary HIV-1 in a macrophage system before and after depletion of V2 antibodies.
Results: Rabbits immunized IM/TCI/IM with trimeric gp145 or with gp41-Soc had significantly higher gp140, gp120, or gp41-specific IgG endpoint titers (4-fold, 3.2-fold, and 4.7-fold, respectively) than IM immunized rabbits. Similarly, V2-specific antibodies were approximately 16-fold higher in the IM/TCI/IM group. Purified IgG from IM/TCI/IM rabbits were more potent in neutralizing primary HIV-1 in the macrophage system than the IM rabbits. Depletion of V2-specific antibodies resulted in reduced neutralization; however, antibodies to other regions of the envelope protein may have also contributed to the neutralization.
Conclusions: This study highlights the importance of the adjuvants and the delivery platforms and provides a novel means for inducing high titer binding and functional antibodies, which should be considered for future HIV-1 vaccines.

Novel vectors and strategies

MOPEA029

pVLP: a new DNA vaccine strategy for HIV

A. Calazans[1], R. Lindsay[2], G. Morrow[2], C. Parks[2]
[1]Fiocruz, CDTS, Rio de Janeiro, Brazil, [2]IAVI, Design and Development Lab, Brooklyn, United States
Presenting author email: acalazans@cdts.fiocruz.br

Background: We created a new DNA vaccine strategy for HIV. We developed a DNA vaccine that induces the formation of a VLP *in vivo*. This VLP has unique features as: the envelope is the sequence of EnvBG505, a good binder of the neutralizing antibodies PG9, PG16 and PGT145; the Gag protein is processed; the genomic RNA of Gag is encapsulated. So, this VLP was designed to elicit neutralizing antibodies, to induce better T-cell response against Gag and to active the innate immune system through the ligation of the viral RNA to RIG-I receptors.
Methods: 5 groups of 10 mice were electroporated, on week 0 and week 3, with the following constructs: pVLP-LTRGagPro (the full construction), pVLPGagpro (VLP without RNA), pVLPLTR-Gag (VLP immature), pVLPGag and pVLP-ENvBG505 (as a regular DNA vaccine) and mock. We initially make an *in vitro* test to check the building of the VLP. We transfected the DNA of pVLP-LTRGagPro to 293-T cells and treated the sup with biotynilated neutralizing antibodies linked to magnetic beads. We performed intracellular staining from the mice spleen, and realized ELISA for Env antibodies and Luminex assay for inflammatory cytokines from the serum.
Results: We separated the VLP with p24 HIV ELISA kit. It showed a good binding of the VLP to the neutralizing antibodies PG9, PG16, PGT145 and VRC04. . The percentage of CD4 cells producing cytokines was 01% (IFNG), 0,15% (IL-2) and 0,2% (TNFa) for the construct pVLP-LTR-GagPro- much higher than the others constructs. The percentage of CD8 cells producing cytokines was 0,3 %(IFNg), 0,2%(IL-2) and 0,25%(TNFa), also much higher than the others constructs. All pVLP constructs induced more antibodies to EnvBG505 than the Env as a regular DNA vaccine. The pVLP-LTRGagPro, the one containing RNA, induces more IL-1B than the others constructs 24 hours post vaccination.
Conclusions: This vaccine induced both cellular and humoral responses. The pVLP-LTRGagPro induced better T-cells responses. Env as pVLP induced greater antibodies levels than Env as a regular DNA vaccine. The pVLP-LTRGagPro was able to trigger innate responses, as can be seen by the incresead levels of secreted IL-1B.

MOPEA030

Deletion of immunomodulatory A44L, A46R and C12L viral genes from Modified Vaccinia Ankara (MVA) genome: effect on its immunogenicity

M.P. Holgado[1], C. Maeto[1], J. Falivene[1], M.P. del Medico-Zajac[2], G. Calamante[2], M.M. Gherardi[1]
[1]Instituto de Investigaciones Biomedicas en Retrovirus y SIDA - UBA - CONICET, Ciudad Autonoma de Buenos Aires, Argentina, [2]Instituto de Biotecnologia, CICVyA - INTA Castelar, Buenos Aires, Argentina
Presenting author email: piaholgado@gmail.com

Background: MVA still retains genes involved in host immune response evasion. Previously,we reported the optimization of its vaccine potential after removing the C12L gene, coding an IL-18 binding-protein. Here we analyze the immunogenicity of MVA vectors harboring the simultaneous deletion of two viral genes:A44L, implicated in synthesis of steroid hormones and A46R, which inhibits transduction signals from Toll-like receptors (MVAΔA44L-A46R:MVAd);or including C12L deletion also (MVAΔC12L/ΔA44L-A46R:MVAt).
Methods: C57Bl/6 mice were intramuscularly immunized with wild-type (MVAwt) or deleted MVAs (ΔMVAs).We evaluated the adaptive T-cell response to VACV (Vaccinia-Virus) epitopes at acute and memory phases (7 and 45 days post-immunization (dpi) respectively) in spleen

and inguinal lymph-nodes. The proportion of IFNg and IL-2 producing cells was measured by ELISPOT. We analyzed the percentage of specific cytotoxic CD8 T-cells by flow-cytometry through CD107a/b surface-marker, and the response of memory T-cells by CD44 and CD62L expressions among specific proliferating CD8 T-cells ($CFSE_{low}$).To study the innate response, we immunized mice with MVAwt or MVAt and pattern of cytokines produced were evaluated between 0-30 hours post-immunization (hpi).

Results: At 7dpi, both ΔMVAs induced significant increases in IFNg anti-VACV CD8 and CD4-T cells versus MVAwt (up to 1.5 to two-fold higher,p< 0.01),and also in IL-2 anti-VACV CD8 and CD4 T-cells (five-fold higher,p< 0.01; two-fold higher p< 0.05,respectively). Importantly, ΔMVAs still elicited higher IFNg and IL-2 CD8 and CD4 T-cell responses than MVAwt at 45dpi (p< 0.05).Proliferating anti-VACV T-cells were augmented from 3%(MVAwt) to 6% (MVAt) for CD8 T-cells, and 1% to 7% for CD4 T-cells. Moreover, MVAt elicited a higher proportion of specific central-memory (T_{CM}:37%) and effector-memory CD8 T-cells (T_{EM}:25%) compared to MVAwt (T_{CM}:20%,T_{EM}:11%) as well as for CD4 T-cells (T_{CM}:37%,T_{EM}:16% and T_{CM}:8%,T_{EM}:2%,respectively).

Furthermore, ΔMVAs induced a higher percentage of specific cytotoxic$^+$/IFNg$^+$ CD8 T-cells than MVAwt. The innate response analysis showed that MVAt yield higher levels of IFNg and IL-12 at 20 and 30hpi compared to MVAwt.

Conclusions: Simultaneous deletion of specific viral genes from MVA genome with inter-related functions like A46R and C12L is an adequate strategy to improve its vaccine-potential. This might be especially important for the development of vaccines against HIV, where the improvement of vectors is urgently needed.

MOPEA031

Generating an anti-HIV vaccine using lipid nanoparticle-encapsulated nucleoside-modified mRNA encoding envelope

N. Pardi, M. Hogan, J.A. Hoxie, D. Weissman
University of Pennsylvania, Perelman School of Medicine, Division of Infectious Diseases, Philadelphia, United States
Presenting author email: pnorbert@mail.med.upenn.edu

Background: In recent years a great body of knowledge has been accumulated on the molecular mechanisms of HIV-1 infection but no highly effective vaccine has been developed to date. mRNA has emerged as a new promising therapeutic agent, and we demonstrate is an effective method for generating potent vaccine responses.

Methods: To create a vaccine with maximal potency, *in vitro* transcribed mRNAs were optimized for higher levels and extended translation by introducing 5' cap, selected 5'- and 3'-UTRs, coding sequence and poly(A)-tail modifications and were HPLC-purified. mRNAs were encapsulated into lipid nanoparticles (LNPs) that have recently proved to be efficient tools for *in vivo* nucleic acid delivery. To achieve both strong T cell and B cell responses, heterologous mRNA prime - protein boost vaccination regimens were used. For priming, LNP-encapsulated mRNA encoding HIV envelope gp160 was administered intradermally into mice. Cell surface Env was used to increase exposure of neutralizing epitopes. Four weeks after the second mRNA prime, Env protein with alum was injected intramuscularly as a boost. mRNA encoding adjuvants were studied for their ability to increase responsiveness. Flow cytometry, ELISAs, and neutralizing assays were used to evaluate T cell and B cell responses.

Results: Elevated levels of IFN-χ, TNF-α, IL-2 and CD107a in antigen-specific CD4$^+$ and CD8$^+$ T cells and high gp120 antibody titers could be measured following two rounds of mRNA prime - protein boost vaccination.

Conclusions: Our results demonstrate that antigen-encoding nucleoside modified mRNA induces effective HIV-specific immune responses and has great potential for vaccination against infectious diseases.

MOPEA032

Immunological characterization of an HIV vaccine comprised of Gag and dgp41 virus-like particles produced both in plants and by live Vaccinia virus vectors

L. Meador[1], S. Kessans[2], J. Kilbourne[1], K. Kibler[1], T. Mor[1], B. Jacobs[1]
[1]Arizona State University, Tempe, United States, [2]University of Canterbury, Christchurch, New Zealand
Presenting author email: lydia.meador@asu.edu

Background: While antiretroviral therapy has greatly slowed progression to AIDS, the majority of infected people live in poor or impoverished countries without access to treatment making the lack of a preventative vaccine candidate more apparent than ever. The RV144 clinical trial produced the most promising results to-date using a non-replicating canarypox viral vector and boosting with proteins, but the modest 31% efficacy left room for improvement. Our project builds upon this system via a novel combination of a replicating but highly attenuated strain of Vaccinia virus and plant-produced HIV virus-like particles (VLPs), making a cost-effective, scalable vaccine production platform.

Methods: We are targeting CD8 T cell responses to Gag known to be associated with viral control. VLPs generated in *Nicotiana benthamiana* expose the membrane proximal region of gp41 important for broadly neutralizing antibodies. We tested combinations of virus and VLP prime-boost systems in C57BL/6 mice to analyze CD8 T cell responses in addition to monitoring serum, vaginal, and fecal antibodies and an anti-vector response. We further characterize the interaction of VLPs with the innate immune system and cellular activation of human PBMCs and mouse splenocytes.

Results: Initial characterization shows VLPs induce cellular activation of critical cell types, such as DCs, and activation of toll-like receptor pathways. Electron microscopy shows the potential for VLP production in Vaccinia infected cells *in vivo* to further boost responses. Additionally, mouse experiments reveal that priming with a Vaccinia followed by boosting with both virus and VLPs induces the most robust response. The viral vector largely contributes to the CD8 T cell response while VLPs are critical for high antibody titers. Multiple boosts with vaccinia do induce anti-vector responses in serum. Mucosal IgA responses were low, but significant in fecal samples.

Conclusions: Our plant-produced VLPs appear to contain unique adjuvant-like properties, likely due to the method of production which involves *Agrobacterium*, thus potentially enhancing the immune response. Vaccinia showed promising T cell responses and we are attempting to increase immunogenicity by using a mouse-adapted strain. We plan to test alternate immunization routes in order to boost mucosal responses.

Therapeutic vaccines

MOPEA033

Monocyte-derived DC electroporated with mRNAs encoding both specific HIV antigens and DC adjuvants are able to improve T cell functionality

A.C. Crespo[1], L. Miralles[1], J. Aerts[2], K. Thielemans[2,3], B. Mothe[4], J. Martínez-Picado[4], C. Brander[4], F. García[5], M. Plana[1], iHIVARNA Consortium
[1]Hospital Clinic, IDIBAPS, University of Barcelona, Retrovirology and Viral Immunopathology Laboratory, Barcelona, Spain, [2]Medical School of the Vrije Universiteit Brussel, Laboratory of Molecular and Cellular Therapy, Department of Physiology-Immunology, Brussels, Belgium, [3]EtheRNA, Brussels, Belgium, [4]AIDS Research Institute IrsiCaixa, Institut d'Investigació en Ciències de la Salut Germans Trias i Pujol, Universitat Autònoma de Barcelona, Badalona, Spain, [5]Hospital Clinic, IDIBAPS, University of Barcelona, Infectious Diseases Department, Barcelona, Spain
Presenting author email: fgarcia@clinic.ub.es

Background: In the context of therapeutic vaccination of HIV-infected patients, we have tested *in vitro* a combination of mRNA sequences that fulfil two main objectives. On the one hand, a specific T cell activation immunogen mRNA that focuses the response onto the most vulnerable targets in the HIV viral proteome and on the other hand, a previously tested stimulus (TriMix: a mixture of CD70+CD40L+caTLR4 mRNAs) for appropriate activation of antigen presenting cells (DCs).

Methods: DCs were generated from peripheral blood monocytes (MDDC) from chronically HIV infected patients by incubation with GM-CSF and IL-4. These cells were electroporated with TriMix (15 µg) and/or HIVACAT (20 µg) mRNA, with their respective controls. After that, DCs were cocultured with autologous PBMCs for up to 6 days. In addition, the maturation profile of MDDCs (CD80, CD83, CD86, CCR7) was analyzed by FACS 24h after electroporation. Functional analysis was performed using different techniques: 25-multiplex Luminex assay, T cell proliferation by CFSE and IFN-γ ELISPOT at different time points.

Results: Increased expression of CD80, CD83 and CCR7 was observed on MDDCs upon electroporation with TriMix mRNA. Functionally, mRNA electroporated MDDCs were able to stimulate T cells from HIV-infected individuals on cART *in vitro*. In fact, MDDCs electroporated with both HIV antigens and TriMix, induced higher T-cell activation than their respective separated components or whole AT2-inactivated virus in terms of both IFNγ secretion and proliferation. Other Th1, Th2 and proinflammatory cytokines showed a similar profile secretion pattern. Finally, a higher proportion of stimulated CD8$^+$ T cells, than of CD4$^+$ T cells, was detected.

Conclusions: mRNA electroporation of MDDCs improved their maturation status and was able to enhance HIV specific T cells responses. Our results suggest that this mRNA combination could be considered for a HIV therapeutic vaccination approach.

MOPEA034

Therapeutic conserved elements (CE) DNA vaccine increases T cell responses against highly conserved viral sequences in the setting of pre-existing immunodominant responses induced by chronic viral infection

P. Munson[1], D. Bratt[2], M. Koday[2], M. Treants[1,2], J. Fuller[1], M. Agy[2], B. Agricola[2], X. Hu[3], V. Kulkarni[3], B. Felber[3], G. Pavlakis[4], Y. Liu[1], J. Mullins[1], D. Fuller[1]
[1]University of Washington, Microbiology, Seattle, United States, [2]University of Washington National Primate Research Center, Seattle, United States, [3]National Cancer Institute, Human Retrovirus Pathogenesis Section, Frederick, United States, [4]National Cancer Institute, Human Retrovirus Section Vaccine Branch, Frederick, United States
Presenting author email: munsop@uw.edu

Background: We have previously shown that in SIV-infected rhesus macaques undergoing antiretroviral therapy (ART), therapeutic DNA immunization protected ~50% of animals from viral rebound after discontinuing ART. To improve this approach, we are investigating a novel conserved elements (CE) therapeutic DNA vaccine which consists exclusively of CE sequences. We hypothesize that a CE DNA vaccine will achieve a more profound functional cure by forcing immune escape mutations in regions of the virus that would have the greatest impact on viral fitness. A question that must first be addressed is whether immunization with a vaccine expressing conserved, but generally subdominant epitopes, can induce responses against CE in the setting of an immunodominant response induced by infection. To investigate this question, we compared immunogenicity of a CE DNA vaccine to a DNA vaccine expressing whole SIV Gag in rhesus macaques chronically infected with SHIV, as well as the role of CE specific responses in long term viral control.
Methods: Two groups of rhesus macaques chronically infected with SHIV89.6P were immunized with either a traditional DNA vaccine expressing whole SIV Gag or an SIV CE DNA vaccine. An IFN-γ ELISpot assay was employed to map T cell responses induced in the blood and gut against the full SHIV proteome and the CE sequences. Intracellular cytokine staining was also used to assess functional quality of T cell responses directed against CE.
Results: Prior to immunization, both groups had similar responses to variable and immunodominant regions of Gag with little to no detectable responses to CE. Animals immunized with whole Gag exhibited no significant increase in responses against CE. In contrast, CE vaccinated animals developed a nearly ten-fold increase in IFNg and cytolytic T cell responses against CE.
Conclusions: These results illustrate that a CE DNA vaccine was able to overcome immunodominant responses associated with a viral infection and re-direct the cellular response toward increased targeting of the subdominant conserved viral sequences when compared to a traditional full length Gag DNA vaccine. These results support the feasibility of developing a therapeutic CE DNA vaccine to induce a functional cure against AIDS.

MOPEA035

Immune response to sequences surrounding the 12 protease cleavage sites generated during ARV treatment improved CD4 counts of SIVmac251 infected rhesus monkeys

M. Luo[1,2], D. Tang[1], J. Pinto[3], M. Nykoluk[1], P. Lacap[1], C. Czarnecki[1], J. Tuff[1], R. Capina[1], J. Whitney[4], M. Alonso[3], T. Ball[2,5], G. Kobinger[2,6], P. Sandstrom[5], F. Plummer[2,7]
[1]National Microbiology Laboratory, HIV Host Genetics/NHRL, Winnipeg, Canada, [2]University of Manitoba, Medical Microbiology, Winnipeg, Canada, [3]University of Santiago de Compostela, Santiago de Compostela, Spain, [4]Harvard Medical School, Beth Israel Deconess Medical Center, Boston, United States, [5]National Microbiology Laboratory, NHRL, Winnipeg, Canada, [6]National Microbiology Laboratory, Special Pathogens, Winnipeg, Canada, [7]National Microbiology Laboratory, Winnipeg, Canada
Presenting author email: ma.luo@phac-aspc.gc.ca

Background: Effective therapeutic vaccines used in combination of ARV to treat HIV infected patients can reduce drug induced toxicity, help to re-constitute immune system and achieve a functional cure. We conducted a pilot study to test the therapeutic effect of a novel HIV vaccine targeting the 12 protease cleavage sites in combination of ARV.
Methods: SIVmac251 infected rhesus monkeys were treated with a combination of FTC, PMPA and raltegravir for 49 days. Seven days after ARV initiation the monkeys in the treatment group received rVSVpcs (i.m.). Three additional therapeutic treatment with rVSVpcs (i.m.)/NANOpcs(i.n.), NANOpcs(i.n), and NANOpcs(i.n.) were carried out with 2-week intervals. ARV treatment was stopped after 49 days and viral load, CD4/CD8 counts, antibody and T cell response to PCS peptides and pooled Gag and Env peptide were analyzed.
Results: ARV treatment suppressed viral load of all macaques, but only the viral load of 6 out of 11 macaques was suppressed to non-detectable level during the treatment/ARV period. However, even with the short duration of ARV treatment and incomplete viral load suppression, the immune responses to PCS peptides were generated after 4 therapeutic treatments. The CD4 counts of PCS vaccine treated macaques were significantly improved after 35 days and 49 days of ARV treatment(p=0.027 and 0.044), whereas there is no significant improvement in CD4 counts of monkeys only received ARV treatment despite the viral load suppression.
Conclusions: Our study showed that new immune response to PCS peptides can be generated even with incomplete viral load suppression after a short period ARV treatment. The combination of PCS vaccine treatment and ARV generated new immune response to PCS peptides, improved CD4 counts of SIVmac251 infected monkeys and can be used to improve patient care to achieve a functional cure.

MOPEA036

Safety and immunogenicity of ChAd.HIVconsv and MVA.HIVconsv therapeutic vaccines in a cohort of early treated HIV-1 infected individuals

B. Mothe[1,2,3], C. Manzardo[4], P. Coll[1,2], P. Cobarsi[2], A. Sanchez-Bernabeu[1], R. Escrig[2], N. Perez-Alvarez[2,5], J.M. Miró[4], L. Dorrell[6], B. Clotet[1,2,3], T. Hanke[7], C. Brander[1,3,8], BCN01 Study Group
[1]IrsiCaixa AIDS Research Institute - HIVACAT, Badalona, Spain, [2]Fundació Lluita contra la Sida, Hospital Germans Trias i Pujol, Badalona, Spain, [3]UVic-UCC, Vic, Spain, [4]Hospital Clínic-IDIBAPS, Barcelona, Spain, [5]Technical University of Catalonia, Barcelona, Spain, [6]John Radcliffe Hospital, Oxford, United Kingdom, [7]The Jenner Institute, Oxford, United Kingdom, [8]ICREA, Barcelona, Spain
Presenting author email: bmothe@flsida.org

Background: T-cell vaccines targeting the most conserved regions of the HIV-1 proteome may be required for the elimination of the latent viral reservoir. HIVconsv vaccines vectored by chimpanzee adenovirus (ChAdV63) and modified vaccinia virus Ankara (MVA) have shown to induce high levels of effector T cells in healthy individuals (HIVCORE02 trial). BCN01 (NCT01712425) is a phase I study to evaluate the safety and immunogenicity of ChAdV63 and MVA.HIV-consv vaccines in early-treated HIV-1 infected individuals
Methods: 24 individuals identified with recent HIV infection (< 6m from acquisition) who initiated Tenofovir/Emtricitabine/Raltegravir within 1 week after diagnosis, received an intramuscular ChAdV63.HIVconsv ($5x10^{10}$vp) vaccination after 6 months under cART. Participants were given an MVA.HIVconsv booster immunization ($2x10^8$pfu) 24 or 8 weeks afterwards and were followed for 6 months. Local and systemic events were recorded for a minimum of 7 days following each immunization. Immunogenicity to the vaccine insert and the rest of the HIV-1 proteome was assessed by IFNg ELISPOT.
Results: Local and systemic events after vaccination occurred in 22/24 individuals, mostly severity grade 1-2 and transiently (48 hours). Local pain was more often reported with MVA than ChAdV63 vaccination. Responses to conserved regions before cART initiation were only observed in 4 individuals and diminished significantly after achieving viral supression. All participants significantly increased T-cell responses that targeted the vaccine insert, with a peak 1-4 weeks after MVA vaccination (median of 1,015 SFC/10^6 PBMC, range 140-6,805, p=0.0003, Wilcoxon t-test compared to baseline). Over vaccination period, no unspecific expansion of T cells targeting HIV-1 regions outside HIVconsv insert or CEF was noted, allowing for an optimal focusing of T-cell responses on conserved regions (48% of total HIV immune response being HIVconsv-specific 4 weeks after MVA vaccination). Among vaccinees, no significant differences in peak immunogenicity was observed between short and long prime/boost regimen.
Conclusions: ChAd.HIVconsv and MVA.HIVconsv was a safe strategy to shift pre-existing immune response towards conserved, vaccine-encoded regions of HIV in a cohort of early-treated individuals and may set the stage for successful subsequent of cure strategies.

MOPEA037

Development of a latency reversing activator vaccine (ACT-VEC) platform for HIV-1 cure therapy

J.F.S. Mann[1], T. Biru[2], P.T. Wille[2], K. Klein[1], E.J. Arts[1]
[1]University of Western Ontario, Microbiology and Immunology, London, Canada, [2]Case Western Reserve University, Medicine, Cleveland, United States
Presenting author email: jmann62@uwo.ca

Background: HIV-1 persists within cellular reservoirs as a transcriptionally silent provirus, creating a significant roadblock to cure research. Numerous promising therapeutic and pharmacological interventions are currently being evaluated; however to date none have resulted in reservoir eradication. We have designed an activator vaccine (ACT-VEC), using autologous derived VLPs, which target the resting CD4 T cell reservoir, inducing latency reversal. We describe the safeguards incorporated into our VLPs as well as preliminary data from our *in vitro* latency reversal studies.
Methods: Plasmids used in these studies were derived from the laboratory strain NL4-3, envC3 1086 and patient derived HIV-1 inserted into the pRECΔgag-U3 VLP-vector. ACT-VEC were generated with deleted (Δ) 5'LTR, AAH>RRK integrase mutation and deletions within the RNA packaging element (ΔSL3). VLPs were then created by HEK293T transfection. Resulting VLPs were assessed by RT-PCR for RNA content and for the presence of viral proteins by western blot. VLPs were co-cultured with autologous patient derived DCs and then used to ac-

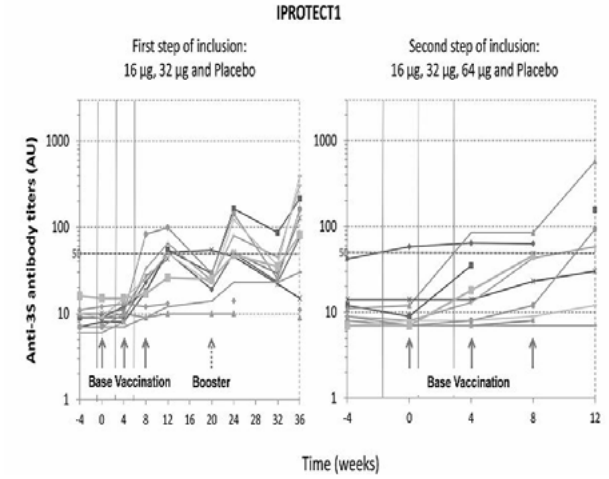
tivate autologous CD4 T cells from PBMC. An IFN-γ ELISpot was used to quantify virus specific T cells, p24 ELISA to measure viral latency reversal, and 454 deep sequencing to characterize HIV resulting from latency reversal and compare to viral DNA isolated from PBMC.
Results: Here we show our ACT-VEC VLPs have reduced HIV-1 RNA packaging (up to 221-fold), while having no impact on viral protein production. This along with mutations in Integrase and Δ5'LTR rendered our ACT-VEC incapable of reverse transcription, integration, or RNA packaging. Preliminary studies involving deep sequence analysis revealed ACT-VEC are genetically diverse and identical to virus generated by our latency reversal assays. Significantly, autologous ACT-VEC were able to stimulate 30-fold more HIV RNA from infected T cells than Flu/Tet/CMV recall antigens and more than NL4-3 controls. Our latency reversal studies showed ACT-VEC outperform clinically relevant compounds such as Rhomidepsin and Vorinostat.
Conclusions: Here we clearly demonstrate that our novel ACT-VEC formulations represent a safe vaccine platform for use as a therapeutic intervention and that ACT-VEC may signify a promising strategy to purge the latent viral reservoir and facilitate cure.

MOPEA038

VAC-3S immunotherapeutic HIV vaccine combined with ART is immunogenic and safe. Phase II initial analysis of the IPROTECT1 multicenter European study

C. Katlama[1], J.K. Rockstroh[2], J.M. Gatell[3], R. Ho Tsong Fang[4], P.M. Girard[5], L. Slama[6], A. Simon[7], O. Launay[8], L. Cotte[9], J. Reynes[10], S. Gharakhanian[11]
[1]AP-HP Pitie Salperiere Hospital & INSERM, Paris, France, [2]University of Bonn, Bonn, Germany, [3]Hospital Clinic, Barcelona, Spain, [4]InnaVirVax, Genopole Evry, France, [5]AP-HP St Antoine Hospital, Paris, France, [6]AP-HP Tenon Hospital, Paris, France, [7]AP-HP Pitie-Salpetriere Hospital, Paris, France, [8]AP-HP Cochin-Pasteur & INSERM CIC, Paris, France, [9]Croix Rousse Hospital, Lyon, France, [10]University Hospital, Montpellier, France, [11]Cambridge Innovation Center, InnaVirVax, Cambridge, United States

Background: VAC-3S is a novel vaccine directed to the highly conserved gp41, 3S motif of HIV-1. Anti-3S antibodies (Abs) block 3S binding to gC1qR, prevents CD4 surface expression of NKp44L, the natural ligand of NKp44 expressed on activated Natural Killer cells. Anti-3S Abs have anti-CD4 apoptotic effects, *in vitro*. High 3S Abs are associated with low inflammation biomarkers in SHIV-infected macaques. Anti-3S Abs have been shown to be negatively correlated with HIV DNA. We hypothesize that VAC-3S enables re-establishment of CD4/CD8 homeostasis hence can comprise the immunological component of an HIV functional cure approach.
Methods: Prospective, randomized, placebo-controlled, double-blind, 3-step study in Europe, assessing immunotherapeutic properties of VAC-3S at 16, 32, 64 mg with 3 IM base immunizations at 4 wk intervals and 3 maintenance boosters in the 16, 32 mg arms. Ninety HIV ART suppressed pts with 200-350 & 350-500 CD4 c/mm^3 planned. Endpoints include: anti-3S Abs (ELISA), T lymphocyte activation/differentiation, HIV DNA, inflammatory biomarkers. Planned analysis after 50% inclusions in first 2-steps.
Results: In these first two steps, 56 pts (47 male / 9 female), randomized, and completed vaccinations. Pts are 62% Caucasian, 30% African heritage. Median age 46 years (23-59); BMI 23 kg/m^2 (16-33), HIV duration 60 months (1-346); baseline CD4 count 365 cells/mm^3 (200-596); nadir CD4 167 cells/mm^3 (31-410). One serious Adverse Event (AE) prior to vaccination, one viral rebound post-ART non-adherence. One hundred twenty AEs reported after a total 182 vaccinations, were local (erythema, induration, sensitivity, pain), or systemic (headache, myalgia, vertigo). AEs were mild in 53% pts, moderate in 39% pts, severe in 6% pts. Figure 1 shows immunogenicity. Median CD4/CD8 ratios, at baseline, were 0.48 (0.20-1.46) and 0.66 (0.23-2.90) in the low and high CD4 strata, respectively. At the 12-weeks post-vaccination point CD4/CD8 ratio was 0.49 (0.21-1.120) in the low and 0.57 (0.34-2.82) in the high CD4 strata.



[Figure 1 VAC-3S Immunogenicity Results]

Conclusions: VAC-3S is a novel mechanism immunotherapeutic HIV vaccine. Phase II preliminary results, confirms phase I safety, as well as, immunogenicity for all new dose levels assessed. Scheduled long term evaluation includes CD4/CD8 homeostasis, HIV DNA and biomarkers of chronic inflammation.

MOPEA039

Broadly specific, cytolytic T cell responses and lower inflammatory responses correlate with durable viral remission following therapuetic DNA vaccination in SIV-infected macaques

D. Fuller[1,2], A. Narendran[3], P. Rajakumar[4], J. Che[4], E. Yager[3], C. Stagmar[3], M. Murphey-Corb[4]
[1]Deborah L Fuller, University of Washington, Seattle, United States, [2]Washington National Primate Research Center, AIDS Division, Seattle, United States, [3]Albany Medical College, Albany, United States, [4]University of Pittsburgh, Pittsburgh, United States
Presenting author email: fullerdh@wanprc.org

Background: We previously reported (DOI: 10.1371/journal.pone.0033715) that an adjuvanted DNA vaccine that stimulated mucosal CD8+ T cell responses in the gut of SIV-infected macauqes during antiretroviral drug therapy (ART) induced 3 different virological outcomes: Viral rebound within 6 months after stopping ART (5/14 vaccinated animals and 6 controls), protection from viral rebound for 12-18 months after withdrawing drugs (5/14 animals) or no detectable virus (4/14 animals) for over 30 months (duration of the study) after stopping ART.
Methods: At study end, macaques were necropsied to determine the impact of vaccination on residual virus in the gut and lymphoid tissues. To define what immune responses contributed to long-term viral control, lymphocytes were isolated from blood and gut tissues and T cell responses and inflammatory cytokines in the blood and gut were measured by ICS, ELISPOT and cytometric bead array. Results in macaques that had no detectable virus or exhibited a significant delay in viral rebound after stopping ART were compared to macaques that exhibited immediate viral rebound within 6 months after stopping ART.
Results: The 4 macaques with no detectable virus in the blood had detectable viral RNA and/or DNA in at least one lymph node or in gut tissues demonstrating the vaccines substantially reduced residual virus but did not clear the virus. Animals that exhibited delayed viral rebound or no viral rebound had a higher frequency of CD8+ T cells with cytolytic effector function, higher CD4+ T cell proliferation, and broadly specific mucosal SIV-specific CD8+ T cell response targeting more conserved viral sequences in Gag when compared to animals that rebounded within 6 months after stopping ART. In addition, lymphocytes isolated from macaques that exhibited delayed or no viral rebound post-ART expressed lower levels of the inflammatory cyotkines (TNF-α, IL-6) prior to stopping ART when compared to macaques that exhibited immediate viral rebound within 6 months post-ART.
Conclusions: These results show that immunotherapuetics that can broaden virus-specific T cell responses against more conserved viral seequences and at the same time, reduce inflammation during HAART may be an effective approach to achieve durable viral remission.

HIV-1 super-infection/inter/intra subtype co-infection

MOPEA040

Prevalence and clinical impacts of HIV-1 intersubtype recombinants in Uganda

G.Q. Lee[1], D.R. Bangsberg[2,3,4], C. Lachowski[1], C.J. Brumme[1], Y. Boum[2], A.R. Mocello[5], S.H. Kigozi[2], P.W. Hunt[5], J.N. Martin[5], P.R. Harrigan[1]
[1]BC Centre for Excellence in HIV/AIDS, Laboratory Program, Vancouver, Canada, [2]Mbarara University of Science of Technology, Mbarara, Uganda, [3]Massachusetts General Hospital, Boston, United States, [4]Harvard Medical School, Boston, United States, [5]University of California, San Francisco, San Francisco, United States
Presenting author email: glee@cfenet.ubc.ca

Background: Few epidemiological and clinical outcome data exist for HIV-1 intersubtype recombinants in rural African communities. The objective of this study is to estimate prevalence, examine time trends, and test for clinical correlates and outcomes associated with HIV-1 intersubtype recombination in Mbarara, Uganda, where HIV-1 subtypes A1 and D co-circulate.
Methods: Near-full-genome HIV-1 RNA population sequence data was collected using nested PCR targeting *gag* to *nef* as five amplicons followed by Sanger sequencing from n=504 treatment-naïve individuals enrolled between 2005-2010 in the Mbarara-based UARTO cohort, who then received PI or NNRTI-containing regimens and were monitored until 2013. HIV-1 subtypes were inferred by Los Alamos RIP 3.0 (window size 400). Statistical significance was defined as p=0.003 after Bonferroni correction.
Results: When each genomic region was individually examined, intersubtype recombinants were detected most frequently in the *vif-vpu* region (24%), followed by GP41 (18%), *gag*

(15%), *prrt* (10%), *int* (8%), *nef* (4%). Of the 200 patients that had sequence data for all seven genomic regions examined, prevalence of intersubtype recombination was 46%. The most frequently observed recombinant was A1-D (25%). Other combinations were A1-C, A1-G, C-A1, C-D, D-A1, D-C, D-G (one breakpoint) and A1-C-D, A1-D-C, A1-D-G, D-A1-C, D-A1-G (two breakpoints). Phylogenetic analysis by maximum-likelihood tree of the 200 near-full-genome sequences showed that A1-D recombinants did not share a common ancestor and suggested multiple recombination events. Stratification by year shows no temporal trend (all p>0.1). Subjects infected with non-recombinants versus recombinants were not significantly different in baseline viral load (p=0.7), baseline CD4 count (p=0.2), time to suppression < =400 copies/mL (p=0.03), time to post-suppression virologic rebound (p=0.1), and time to CD4 recovery defined as baseline+200 or above 350 cells/µL (p=0.6).

Conclusions: Intersubtype recombination is common in Uganda but it was not associated with baseline viral load nor CD4 count and did not impact treatment outcomes. HIV-subtyping for clinical records and/or association studies should be annotated with the name of the gene used for subtyping.

HCV

MOPEA041

Stability of the NS3 Q80K polymorphism over time within HCV genotype 1a infected patients

J. Joy, W. Dong, C. Chui, C. Brumme, A. Poon, P.R. Harrigan
BC Centre for Excellence in HIV/AIDS, Vancouver, Canada
Presenting author email: prharrigan@cfenet.ubc.ca

Background: HCV genotype 1a (GT1a) infections harbouring a baseline Q80K polymorphism in the NS3 gene display reduced virologic response to IFN-based HCV treatments containing simeprevir. In the context of individual infections, the stability of this clinically important polymorphism over time is unknown.

Methods: Using plasma samples serially collected over a 10-year period (mean 4.5 years between samples) from 121 HCV treatment naïve GT1a infected injection drug seroconverting users, we sought to investigate gain or loss of the Q80K polymorphism over time. RNA was extracted using a NucliSens easyMag. HCV NS3 was amplified by nested RT-PCR and a 1200- or 564-bp fragment was sequenced by Sanger methods. Sanger chromatograms were interpreted automatically using in-house software (RECall). Each sample was HLA typed to confirm database annotations on source individuals. HCV sequences were multiply aligned using MAFFT v7.154b. Phylogenetic trees were inferred using an approximate maximum likelihood method (FastTree2) and rooted under a molecular clock model using Path-O-Gen.

Results: In no case did patients whose first and last samples formed a monophyletic group alter their Q80K status. Nine patients changed genotypes (6 GT3a to GT1a, 2 GT1a to GT3a, and 1 GT1b to GT1a). Furthermore, in 10 patients, GT1a infections did not form a monophyletic group. Both between genotype and within genotype changes in viral lineage between collection dates suggest either
(1) clearance followed by reinfection with a new variant or
(2) a mixed infection.
In sum, we observed 9 changes in Q80K in 121 patients, but in every case this resulted from patients switching HCV lineages rather than a mutation in their original HCV lineage.

Conclusions: These results suggest that, in the absence of therapy, Q80K is highly stable within HCV lineages and does not evolve in response to immune or other host specific effects. Future work will employ deep sequencing to evaluate the importance of mixed infections relative to clearance and reinfection by a different HCV lineage. The observed changes in infection status amongst these patients supports genotypic and resistance testing of patients prior to starting therapy, particularly amongst those at high risk of exposure to new variants of HCV such as intravenous drug users.

MOPEA042

Discovery of a novel class of naturally occurring indirect-acting antiviral agents against both HIV-1 and hepatitis C virus infection

J. Cheng[1], P. Cheung[2], A. Olmstead[1], S. Mc Arthur[1], J. John[1], V. Svinti[1], L. Foster[3], R. Harrigan[2], F. Jean[1]
[1]University of British Columbia, Microbiology and Immunology, Vancouver, Canada, [2]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada, [3]University of British Columbia, Biochemistry and Molecular Biology, Vancouver, Canada
Presenting author email: fjean@mail.ubc.ca

Background: Due to similar routes of infection for HIV-1 and hepatitis C virus (HCV), it is estimated that up to one-third of people with HIV-1 are co-infected with HCV. Concurrent treatment of HIV-1 and HCV is feasible but may be complicated by pill burden, drug-drug interactions, and toxicities. In this context, access to new broad-spectrum antivirals that can treat both HIV-1 and HCV concurrently would be a tremendous advantage for dually infected individuals. Here, we report the discovery of a novel class of naturally occurring antiviral peptides against both HIV-1 and HCV infection.

Methods: In this study, the antiviral activities of our peptides were tested in physiologically relevant cell-based systems of viral infection against both HCV [JFH-1 strain; human hepatoma cells
(Huh7.5.1 cells)] and HIV-1 [NL4-3 strain; human T-cells (GXR cells of CEM origin)]. We identified the critical amino acid residues necessary for the broad-spectrum antiviral activities using alanine scanning and positional scanning. Using circular dichroism spectroscopy and nuclear magnetic resonance spectroscopy, we demonstrated a structure-activities relationship between membrane-induced peptide folding and antiviral activity. Furthermore, by applying peptide biotin/avidin pull-down assays coupled with high throughput mass spectrometry (MS), we identified the molecular targets of our antiviral peptides.

Results: Our peptide-based therapeutics with submicromolar antiviral activity acted extracellularly, reducing challenges associated with intracellular delivery of drug candidates. Pretreatment of the host cells with our peptide antivirals is not required to block HIV-1 and HCV viral infection. Using MS, we identified host-cell tetraspanin-enriched microdomains (TEMs) - ubiquitous specialized membrane platforms - as the main targets of our antiviral peptides. Taken together, the results of our virological, chemical, and biological studies reveal a novel class of indirect-acting antivirals (IAAs) that specifically interact with the host's TEMs and interfering with the virus lifecycle.

Conclusions: Given the limited number of anti-HIV/HCV drugs in clinical trials, our discovery of a novel class of IAAs against HIV-1 and HCV infection is timely and important. With the increasing number of human viruses hijacking the TEM platforms, our novel class of TEM-directed antivirals represent powerful molecular tools for dissecting the emerging role of TEMs in viral infections and their therapeutic potential.

Novel assays of immune responses

MOPEA043

Changes in concentrations of circulating calprotectin and S100A9 in successfully treated HIV-1 patients over time

C. Gilbert[1], C. Subra[1], A. Posvandzic[1], P. Tessier[1], S. Trottier[1], J.-P. Routy[2], C. Tremblay[3], M.-A. Jenabian[4]
[1]Université Laval, Microbiology-Infectiology-Immunology, Québec, Canada, [2]McGill University, Montréal, Canada, [3]Université de Montréal, CHUM, Montréal, Canada, [4]Université du Québec à Montréal, Montréal, Canada
Presenting author email: caroline.gilbert@crchudequebec.ulaval.ca

Background: Sustained levels of inflammatory markers such as IL-6 and the coagulation marker in the plasma are hallmarks of aging-related diseases associated with chronic HIV-1 infection. S100A8 and S100A9 proteins and their heterodimer called calprotectin are also considered as biomarkers of inflammatory disorders and cardiovascular diseases. Principally released by myeloid cells, these proteins have been shown to enhance transcription of viral RNA and production of new HIV-1 particles. In this study, we examined if the secretion of calprotectin by stimulated macrophages in the context of HIV-1 infection and can be increased in the plasma of HIV-1 patients.

Methods: Calprotectin, S100A8 and S100A9 were quantified in the stimulated macrophages or in the plasma of healthy subjects, ART-naive, ART successfully treated, and elite-controller HIV-1 infected patients, by using specific ELISAs.

Results: In vitro HIV-1 infection, as well as stimulation by TLR7/8 agonists and interferon-b, enhanced calprotectin secretion from macrophages. However, plasma calprotectin was only slightly enhanced in HIV-1 patients and was increased in patients receiving ART, successfully treated less than ten years following diagnosis. Surprisingly, plasma calprotectin and S100A9 concentrations were negatively correlated with the duration of HIV-1 infection.

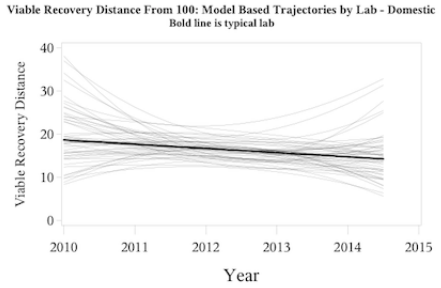
Conclusions: Further investigations are needed to determine if there is a link between plasma calprotectin amount and cardiovascular diseases in HIV-1 patients as it might help classify long term risks of HIV-1 patient to develop cardiovascular disease.

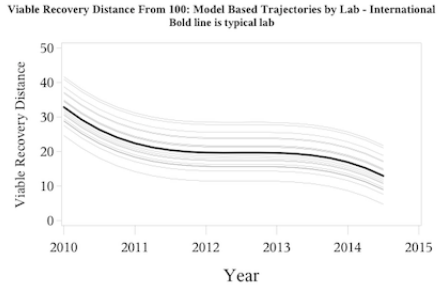
MOPEA044

External quality assurance improves both domestic and international laboratory performance for peripheral blood mononuclear cell cryopreservation

R. Coombs[1], J. Bainbridge[2], M. Cooper[3], R. Louzao[2], W. Rountree[2], J. Darden[4], A. Weinberg[5], C. Rinaldo[6], R. Bosch[7], J. Ward Jr[8], T. Denny[2]
[1]University of Washington, Laboratory Medicine, Seattle, United States, [2]Duke University, Immunology Quality Assurance Program, Durham, United States, [3]Frontier Science and Technology Research Foundation, Buffalo, United States, [4]Social & Scientific Systems, Inc., Silver Spring, United States, [5]University of Colorado, Pediatrics, Medicine and Pathology, Aurora, United States, [6]University of Pittsburgh, Infectious Diseases and Microbiology, Pittsburgh, United States, [7]Harvard School of Public Health, Statistical Data Analysis Center, Cambridge, United States, [8]Biomedical Research Institute Repository, Rockville, United States
Presenting author email: bcoombs@u.washington.edu

Background: The research quality of HIV-1-infected peripheral blood mononuclear cell (PBMC) specimens collected for storage depends on the processing steps before specimens arrive at a biorepository. Our objective was to evaluate whether an ongoing external quality assurance (EQA) program improved PBMC cryopreservation.
Methods: Four PBMC proficiency-testing panels per year were evaluated from the first quarter (Q1) of 2010 to Q2 of 2014. Fresh PBMC were collected from two donors at each participating site, processed and counted, viability determined and aliquots containing 5-million cells each were prepared and stored at -80° Celsius before shipping on dry-ice to the Immunology Quality Assurance (IQA) program for temporary storage in liquid nitrogen. These PBMC were assessed for percent viability and viable recovery. Mixed-effects or linear regression model trajectories were used to determine trends in laboratory performance over the study period. Among the participating 82-96 domestic (DPL) and 28-36 international processing laboratories (IPL), a subset of 26-35 AIDS Clinical Trial Group laboratories (ACTGL) contributed additional data for analysis.
Results: The overall median (IQR; range) PBMC viability and viable recovery for 1,602 PBMC proficiency-testing specimens from DPLs was 98% (97-99; 72-100) and 91% (78-104; 1.5-220); for the 583 PBMC specimens from IPLs, the median was 98% (96-99; 40-100) and 90% (74-105; 1.3-197). The trend in DPL mean PBMC viability increased from 97% in 2010 to 98% in 2012; the IPL viability response was biphasic and increased rapidly from 94% in 2010 to 98% in 2014.





The mean viable recovery steadily converged upon 100% from an absolute distance of 19% to a distance of 15% for domestic laboratories and from 33% to 15% for international laboratories. All lines represent individual laboratories and the linear trends were in direction of improvement, p<.01; the bold line represents a 'typical' lab and is the centroid of the distribution about which the individual laboratory trajectories vary. The improvement in PBMC viable recovery was most pronounced for the international laboratories.

[Figure 1. Trends in PBMC viable recovery]

The trend in viable recovery steadily approached 100% for both groups; all linear trends were in direction of improvement (p<0.01), which likely reflected improved PMBC processing practices. For the ACTGL, 127,678 protocol-related HIV-1-infected PBMC specimens were shipped to the BRI specimen biorepository. The median (IQR) processing time remained unchanged at 120 minutes (150-96) but the median freeze time declined from 250 minutes (335-180) to 220 minutes (300-170) and compliance with prompt shipping criteria increased from a mean of 89% (Q1 2010) to 97% (Q2 2014) of laboratories (both comparisons p<0.01).
Conclusions: Participation in a PBMC cryopreservation EQA program was associated with significant trends toward improved PBMC viability and viable recovery.

Novel assays for assessment of ARV resistance/tropism

MOPEA045

Applying TRIP technology to visualise latent HIV-1 integrations on chromosome landscapes

H.-C. Chen[1], A. Jordan[2], G. Filion[1]
[1]Centre for Genomic Regulation, Gene Regulation, Stem Cells and Cancer, Barcelona, Spain, [2]Molecular Biology Institute of Barcelona, Barcelona, Spain
Presenting author email: hengchang.chen@crg.eu

Background: HIV-1 latency is currently the main challenge for antiretroviral therapy. As of today, there has been no systematic study of latent HIV integrations for lack of high throughput technologies to discover them. In this study, we used TRIP (Thousands of Reporters Integrated in Parallel) to map HIV-1 provirus integration and measure their individual transcription. Briefly, the principle of TRIP is to tag proviruses with random barcodes in order to quantify their individual expression.
Methods: Transgenic barcoded viruses infected Jurkat T cells with M.O.I. 0.5. Infected cells were separated into two populations (high- and low expression) based on expression of transducing GFP on the HIV-based vector. DNA of each cell population was digested by the restriction enzyme. Fragments containing provirus insertion points were self-ligated and amplified by nested PCR. Paired-end high throughput sequencing allows us to map the insertion point, determine where proviruses integrate. Meanwhile, RT-PCR was applied on mRNA extracted from the same cell population to quantify barcode expression.
Results: We divided infected Jurkat T cells in high and low HIV expression and mapped 102 and 109 unique integrations containing detectable provirus expression, respectively. 72.5% (respectively 70.5%) of the integration sites were located inside genes. The majority of the integrations were found in introns and gene-rich chromosomes. We used PHA and vorinostat to reactivate latent HIV infections. Surprisingly, integrations had different tropism towards antiretroviral drugs, meaning that PHA and vorinostat had very different action on the latency landscape of HIV. Interestingly, many integrations were reactivated by none of the drugs.
Conclusions: Latency is the main roadblock to the development of a cure for HIV-1. In this study, we illustrate the use of dual maps to visualise HIV-1 provirus integrations and expression. Our results implied that certain new antiretroviral drugs, like vorinostat can not globally reactivate latent HIV. In the future, such dual maps will be applied as novel diagnostic guidelines on validating the spectrum of antiretroviral drugs towards latent proviruses.

MOPEA046

Determination of integrase inhibitor resistance using a novel HIV phenotype assay

M. Robbins[1], P. Cheung[1], W. Zhang[1], M. Sidhu[1], K. Logue[2], G. Taylor[3], Z. Brumme[4], M. Brockman[5], P.R. Harrigan[1,6]
[1]BC Centre for Excellence in HIV/AIDS, Laboratory Program, Vancouver, Canada, [2]St. Clair Medical Association, Toronto, Canada, [3]University of Alberta, Department of Medicine, Edmonton, Canada, [4]Simon Fraser University, Health Sciences, Burnaby, Canada, [5]Simon Fraser University, Molecular Biology and Biochemistry, Burnaby, Canada, [6]University of British Columbia, Medicine, Vancouver, Canada
Presenting author email: mrobbins@cfenet.ubc.ca

Background: Although the integrase inhibitor dolutegravir (DTG) can overcome prior raltegravir (RAL) and elvitegravir (EVG) resistance, resistance to DTG sometimes emerges, leading to treatment failure. We developed a HIV integrase inhibitor phenotype assay to test patient recombinant viruses for resistance with the objective of producing a more predictive resistance report for physicians. Here we report integrase inhibitor phenotype results for viruses from two patients on DTG with previous RAL failure.
Methods: Genotypic (Sanger) and phenotypic integrase inhibitor (RAL, EVG and DTG) analyses were done on longitudinal samples prior to RAL treatment, at the time of RAL failure, at initiation of DTG treatment and at DTG failure, if applicable. Recombinant viruses were produced by co-transfection of polymerase chain reaction (PCR) amplicons with linearized pNL4-3 integrase-deleted plasmid into a reporter T-cell line (CEM-GXR) that produces green fluorescent protein (GFP) when infected with HIV. Matching genotypes were generated for PCR amplicons. To phenotype patient viruses, 1 percent of virus-infected (GFP positive) cells were plated with 10-fold dilutions of RAL, EVG or DTG drugs and inhibitory concentration 50 percent (IC50) and fold change (FC) were determined on days 3 to 6. Predicted integrase inhibitor resistance was generated using the Stanford database (HIVdb).

Results: Fold change generated by our HIV integrase inhibitor phenotype assay matched HIVdb resistance predictions for these two patients with one exception, a sample for patient #4 from Nov., 2010 at the time of RAL resistance (Table 1). Genotypes for this virus sample predicted high level resistance to RAL and EVG (HIVdb=5; not shown) which correlated with phenotypic resistance (FC>100; not shown). HIVdb predicted moderate resistance to DTG for this sample (HIVdb=4) (Table 1) while our phenotype assay showed it was susceptible to DTG (Table 1; FC=1.8).

Patient#2	pNL4-3	Pre-RAL (2008)	On RAL (2012)	On DTG (2013)	On DTG (2014)
Fold change relative to pNL4-3	1.0	1.1	N/A	>100	>100
Predicted resistance level (HIVdB)	1	1	4	5	5
Major integrase mutations	none	none	Q148H, G140S	Q148H, T97A, G140S	Q148H, L74M, T97A, G140S
Viral Load (copies/mL)	N/A	1959	1353	832	4433
Patient#4	pNL4-3	Pre-RAL (Oct. 2006)	On RAL (Aug.2010)	On RAL (Nov.2010)	On DTG (Oct.2014)
Fold change relative to pNL4-3	1.0	2.2	1.4	1.8	N/A
Predicted resistance level (HIVdB)	1	1	2	4	N/A
Major integrase mutations	none	none	N155H	Q148H, G140S	N/A
Viral Load (copies/mL)	N/A	53000			43

[Table 1. INI phenotype data for dolutegravir (DTG)]

Conclusions: Matched genotype and phenotype data is required to produce predictive resistance reports to prevent treatment failure. For the new class of integrase inhibitors, our phenotype assay can be used to determine resistance of patient viruses. This phenotype data can be combined with genotypic results and virological outcomes to determine and monitor integrase inhibitor susceptibility.

Animal models of transmission, disease resistance and progression

MOPEA047

SIVagm from vervet African green monkeys can utilize non-CCR5 entry pathways *in vitro* and *ex vivo*

N. Riddick, S. Whitted, R.M. Goeken, J.M. Brenchley, V.M. Hirsch
Laboratory of Molecular Microbiology, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Rockville, United States
Presenting author email: nadeene.riddick@nih.gov

Background: CCR5 has been described as a primary coreceptor for SIV. A recent study identified SIV-infected sooty mangabeys that were genetically CCR5-deficient. This finding suggests that the use of non-CCR5 entry pathways *in vivo* may be a feature of SIV strains found in natural hosts. We sought to further examine the role of CCR5 as an entry coreceptor for SIV derived from another natural host species, the vervet African green monkey. We also examined the ability of AGM-derived alternative coreceptors to serve as potential entry coreceptors for SIVagm.
Methods: PHA-stimulated AGM PBMC were infected with SIVagm in the absence or presence of CCR5 antagonist, maraviroc. Viral replication kinetics were determined by measuring reverse transcriptase activity in culture supernatant. *In vitro* infections with pseudotype reporter viruses were conducted in target cells expressing CD4 and various coreceptors. AGM PBMC were sorted into multiple subsets using a FACSAria cell sorter. cDNA synthesized from extracted RNA was used in qPCR assays to determine coreceptor mRNA levels.
Results: SIVagmVer90 efficiently replicated in AGM PBMC in the absence and presence of maraviroc, which suggests the use of non-CCR5 entry pathways. *In vitro* infections revealed that reporter viruses carrying various SIVagm envelopes, including transmitted/founder (T/F) envelopes, utilized AGM-derived GPR15 and CXCR6, in addition to CCR5, for entry into target cells. AGM PBMC were sorted into various cell subsets to determine if GPR15 and/or CXCR6 are expressed on CD4 lymphocytes. CCR5, GPR15 and CXCR6 mRNA were detected in the CD4 memory subset, while CXCR6 mRNA was also detected in the CD4 naïve subset. Messenger RNA from all three coreceptors was also detected in the CD8 cell subsets.
Conclusions: These results indicate that SIVagm viruses can utilize non-CCR5 entry pathways *ex vivo*, and various SIVagm envelopes, including T/F envelopes, utilized GPR15 and CXCR6 for entry into target cells. Detection of GPR15 and CXCR6 mRNA in AGM CD4 lymphocytes supports the notion that these alternative coreceptors may serve as potential SIV entry coreceptors. These data suggest that the use of non-CCR5 entry pathways may be a common feature to SIV derived from natural hosts, and may contribute to the non-pathogenicity seen in these animals.

Novel animal/virus models for vaccine, cure research, and inhibitor development

MOPEA048

Probing and characterizing resistance to integrase inhibitors using simian immunodeficiency virus 239

S.A. Hassounah[1], Y. Liu[2], T. Mesplède[2], M. Oliveira[3], P.K. Quashie[1], D. Moisi[3], P.A. Sandstrom[4], B. Brenner[2], M.A. Wainberg[2]
[1]McGill AIDS Centre, Lady Davis Institute, Jewish General Hospital, McGill University, Experimental Medicine, Montréal, Canada, [2]McGill AIDS Centre, Jewish General Hospital, McGill University, Montréal, Canada, [3]McGill AIDS Centre, Jewish General Hospital, Montréal, Canada, [4]National HIV and Retrovirology Laboratory, National Microbiology Laboratory, Public Health Agency of Canada, Ottawa, Canada
Presenting author email: said.hassounah@gmail.com

Background: We previously showed that SIVmac239 is susceptible to raltegravir (RAL), elvitegravir (EVG) and dolutegravir (DTG) with IC50s in the nanomolar range, and integrase (IN) mutant SIV displayed similar resistance profiles to HIV. A long-acting form of a new IN strand transfer inhibitor (INSTI) termed S/GSK-1265744, a DTG analogue, was shown to protect macaques against repeated vaginal and rectal exposures of SHIV. These studies show that nonhuman primates can be utilized to investigate the potential role of INSTIs in HIV therapy, pathogenesis and transmission. Our objectives were to observe whether HIV and SIV share similar resistance pathways under INSTI pressure in selections and cell-free assays and to test the effects of HIV-1 IN resistance mutations on SIV IN activity.
Methods: Tissue culture selections were performed in rhesus macaque peripheral blood mononuclear cells infected with SIVmac239 in the presence of INSTIs. The SIVmac239 IN gene was cloned into a pET15b vector. Purified recombinant SIVmac239 WT, E92Q, T97A, G118R, Y143R, Q148R, N155H, R263K, E92Q/T97A, E92Q/Y143R, R263K/H51Y and G140S/Q148R IN enzymes were generated and strand transfer activities and INSTI inhibitory constants were assessed using cell-free assays.
Results: Genotypic analysis of the IN coding region of SIVmac239 in tissue culture selections under EVG pressure yielded the E92Q mutation after 30 weeks, and a mixture including the 263R/K mutation after 22 weeks of DTG pressure. The G118R and G140S/Q148R substitutions diminished target DNA affinity (~5.5 and 2-fold) and enzyme efficiency by 80% and 60%, respectively. G140S/Q148R negatively impacted strand transfer activity (70% of WT levels). RAL and EVG showed reduced activity against the Q148R, E92Q/Y143R and G140S/Q148R variant enzymes. The Q148R and G140S/Q148R enzymes showed moderate resistance to DTG.
Conclusions: SIVmac239 viruses treated with DTG led to the emergence of a R263R/K mixture, and the detection of the E92Q mutation in SIVmac239 viruses treated with EVG. This study further confirms that the same mutations associated with drug resistance in HIV display similar profiles in SIV. This study provides support for a DTG monotherapy study that should be conducted in SIV-infected rhesus macaques and for studies aimed at SIV eradication in the macaque model.

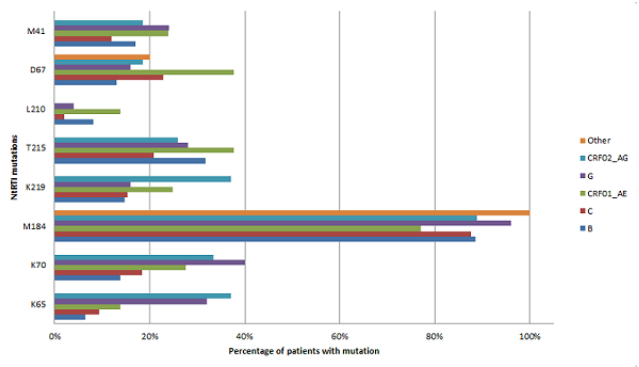
Impact of co-factors / viral clade / tropism / genetic factors / age on disease progression

MOPEB148

Antiretroviral resistance following first-line antiretroviral therapy failure across diverse middle-income settings in the SECOND-LINE study

E.P. Lam[1], C.L. Moore[1], C. Seas[2], C. Nwizu[3], A. Kamarulzaman[4], P. Chetchotisakd[5], J. van Wyk[6], H. Teppler[7], N. Kumarasamy[8], J.-M. Molina[9], D.A. Cooper[1], M.A. Boyd[1], SECOND-LINE Study Group
[1]The Kirby Institute UNSW Australia, Sydney, Australia, [2]Instituto de Medicina Tropical Alexander von Humboldt, Universidad Peruana Cayetano Heredia, Lima, Peru, [3]Center for Clinical Care and Clinical Research in Nigeria, Abuja, Nigeria, [4]Clinical Investigations Centre, University of Malaya, Kuala Lumpur, Malaysia, [5]Infectious Diseases Unit, Srinagarind Hospital, Khon Kaen University, Thailand, [6]AbbVie Inc., Chicago, United States, [7]Merck & Co, Whitehouse Station, New Jersey, United States, [8]YRG Care, Chennai, India, [9]Department of Clinical Infectious Diseases, Hôpital Saint-Louis, Paris, France
Presenting author email: z3373215@zmail.unsw.edu.au

Background: Antiretroviral therapy (ART) resistance data is predominantly derived from understanding of HIV subtype B. This study describes mutations and correlates after first-line ART virological failure in participants in the SECOND-LINE study with diverse HIV subtypes. We expect to find the rates, types and predictors of mutations will be similar between B and non-B subtype viruses.
Methods: Parent study participants were assessed at baseline for demographics, HIV history, ART exposure, viral load (VL), CD4+ count (CD4+) and genotypic ART resistance testing (GART). We used backwards stepwise multivariate regression (MVA) to assess the association of baseline variables with presence of ≥3 nucleoside/nucleotide reverse transcriptase inhibitor (NtRTI) mutations, ≥1 non-nucleoside/nucleotide reverse transcriptase inhibitor (NNRTI) mutation, ≥3 thymidine-analogue NtRTI (ta-NtRTI) mutations (TAMs), the K65/K70 mutation, and etravirine/rilpivirine activity (ETR/RPV) at entry to study (first line failure of a NNRTI+2NtRTIs regimen).
Results: Of 541 modified intention-to-treat SECOND-LINE participants, 491(91%) had a successfully characterised baseline viral isolate. Subtype distribution: B (n=123,25%), C (n=202,41%), AE (n=109,22%), G (n=25,5%) and AG (n=27,5%). In multiple MVAs, higher CD4+ and lower VL at baseline were associated with fewer mutations. Higher VL was significantly associated with ≥3 NtRTI mutations (OR=1.39;95%CI 1.07-1.78;p=0.013) and ≥3 TAMs (OR=1.62;95%CI 1.15-2.29;p=0.006). CD4+ 200-394 cells/mm^3 was significantly associated with < 3 NtRTI mutations (OR=0.47;95%CI 0.29-0.77;p=0.003), not having K65/K70 mutations (OR=0.43;95%CI 0.26-0.73;p=0.002) and higher ETR sensitivity (OR=0.52;95%CI 0.35-0.78;p=0.002). Recent TDF-use was associated with K65/K70 mutations (OR=8.91;95%CI 5.00-15.85;p< 0.001).MVA also showed novel mutation predictors by clade; subtype CRF01_AE was significantly associated with ≥3 NtRTI mutations (OR=2.34;95%CI 1.31-4.17;p=0.004) and higher RPV resistance (OR=2.13;95%CI 1.30-3.49;p=0.003), subtype C with < 3 TAMs (OR=0.45;95%CI 0.21-0.99;p=0.015). Subtypes CRF01_AE (OR=2.46;95%CI1.26-4.78;p=0.008) and G (OR=4.77;95%CI 1.44-15.76;p=0.01) were both associated with K65/K70 mutations.



[NtRTI mutation frequency by subtype]

Conclusions: The associations of first-line resistance across HIV subtypes in this study are consistent with knowledge derived from subtype B, with some exceptions. Our results support WHO recommendations of earlier ART initiation and ta-NtRTI use after first-line TDF-containing NNRTI+2NtRTI. They also stress the importance of VL testing and its priority over genotypic resistance testing in low/middle-income countries.

MOPEB149

Factors associated with incomplete immunologic recovery in HIV-infected patients with clinical and virologic success after 10 years of antiretroviral therapy: a prospective cohort study

F. Raffi[1], A. Perrier[2], V. Le Moing[3], A. Assuied[2], B. Spire[4], C. Michelet[5], R. Verdon[6], C. Jadand[7], G. Chêne[2], C. Leport[7], and the ANRS CO8 APROCO-COPILOTE Study Group
[1]Université de Nantes, ID, Nantes, France, [2]INSERM U897 Epidemiologie-Biostatistiques, Bordeaux, France, [3]Université de Montpellier, Infectious Diseases, Montpellier, France, [4]INSERM U912, Marseille, France, [5]Université de Rennes, Infectious Diseases, Rennes, France, [6]Université de Caen, Infectious Diseases, Caen, France, [7]INSERM, UMR 1137, site Bichat, Paris, France
Presenting author email: francois.raffi@wanadoo.fr

Background: HIV infected patients with virologic suppression and absence of recent clinical events after 10 years of antiretroviral therapy might have incomplete immune recovery.
Methods: Prospective APROCO-COPILOTE cohort of patients started on protease inhibitor (PI)-containing regimen in 1997-1999. Evaluation of patients with 10 year follow-up and clinico-virological success. Impact of antiretroviral treatment history on the immunologic response measured at 10 years was assessed by multivariate logistic regression models. Outcome variables were CD4 response (CD4 cell counts > 500/ µl) and complete immunologic response (CD4 cell counts > 500/ µl and CD4:CD8 ratio > 1).
Results: Among the 610 patients (median follow-up on antiretroviral therapy: 120.3 months (IQR 119.5-121.5), 399 had no clinical progression and sustained virologic suppression during the last year. Median baseline values were : age 38.5 years, CD4 254/ µl, HIV RNA 4.6 $\log_{10}$ c/mL. Initial PI was unboosted indinavir or nelfinavir (77%). Of the 399 patients, 67% had CD4 response and 20% complete immunologic response. In multivariate analyses, factors associated with incomplete CD4 response were older age at baseline (OR 2.62, 95% CI 1.56-4.40), absence of CD4 recovery > 500/µl at month (M)8 (OR 2.39, 95% CI 1.11-5.12) or M12 (OR 4.57, 95% CI 2.23-9.36), not being antiretroviral-naïve at time of PI-containing HAART initiation (OR 1.89, 95% CI 1.12-3.22) and a higher number of treatment sequences (OR 2.16, 95% CI 1.27-3.67). Factors associated with incomplete immunologic response were non-African origin (OR 0.29, 95% CI 0.11-0.76), low CD4:CD8 ratio at M4 (OR 9.37, 95% CI 1.55-56.6) or M12 (OR 3.72, 95% CI 1.08-12.8), and longer duration of antiretroviral treatment interruption (OR 7.75, 95% CI 1.84-32.7), while baseline CD4 and CD4:CD8 ratio were not predictors of 10 year immunologic outcomes.
Conclusions: In this population having started antiretroviral therapy with first generation PI, long-term immunologic recovery was rarely complete after 10 years of antiretroviral therapy despite clinical and virological success. Failure to achieve long-term immunologic response was not associated with baseline immunological parameters but with immunologic response during the first year of treatment, as well as with less complex therapeutic history and shorter duration of treatment interruptions.

MOPEB150

Rate of CD4 decline and factors associated with rapid CD4 decline in asymptomatic HIV-infected patients

N. Chaiyasin, S. Sungkanuparph
Faculty of Medicine Ramathibodi Hospital, Mahidol University, Department of Medicine, Bangkok, Thailand
Presenting author email: ssungkanuparph@yahoo.com

Background: CD4 cell count decline to <200 cells/mm^3 prompts HIV-infected patients to have risk of opportunistic infections. Currently, data of CD4 decline and factors associated with rapid CD4 decline among asymptomatic HIV-infected patients in resource-limited settings is still limited and the threshold to initiate antiretroviral therapy (ART) varies among different developing countries.
Methods: A retrospective cohort study was carried out in asymptomatic HIV-infected patients who were antiretroviral-naïve, having CD4>200 cell/mm^3, and following-up for at least a year in a medical-school hospital in Bangkok. Time to CD4<200 cells/mm^3 was estimated using Kaplan-Meier analysis. Factors associated with rapid CD4 decline were determined using Cox proportional hazard model.
Results: Eighty patients were included. Mean(SD) age was 36.4(9.1) years and 58.8% were females. Twenty-one(26.2%) patients had comorbid diseases. Mean(SD) baseline CD4 was 423(119) cells/mm^3. During a median(IQR) follow-up time of 29.0(14.1-49.6) months, 21(26.3%) patients had CD4 decline to <200 cells/mm^3. From Kaplan-Meier analysis, median time to CD4< 200 cell/mm^3 was >60 months. Probabilities of CD4 decline to <200 cells/mm^3 at 1, 2, 3, 4, and 5 years were 8.1%, 14.5%, 20.1%, 29%, and 38.8% respectively. Estimated time to 25% of patients having CD4 decline to < 200 cells/mm^3 between patients with baseline CD4 ≥350 vs <350 cells/mm^3 was 48.4 vs 14.0 months (log-rank test, p=0.008). From univariate analysis, baseline CD4 <350 cells/mm^3 was significantly associated with rapid CD4 decline [hazard ratio(HR) 3.281; 95% confidence interval(CI) 1.298-8.292; p=0.012] and age<30 years

had a trend toward being associated with rapid CD4 decline [HR 2.381; 95%CI 0.994-5.703; *p*=0.052]. Gender, comorbid disease, risk of HIV infection, duration of HIV diagnosis, and body weight were not associated with rapid CD4 decline (*p*>0.1). From multivariate analysis, only baseline CD4 <350 cells/mm^3 was significantly associated with rapid CD4 decline [HR 4.208; 95%CI 1.428-12.397; *p*=0.009].

Conclusions: One fourth of asymptomatic HIV-infected patients had CD4 decline to <200 cells/mm^3 within 5 years. Baseline CD4 <350 cells/mm^3 was independently associated with rapid CD4 decline in asymptomatic HIV-infected patients. This finding indicates that asymptomatic HIV-infected patients with CD4 <350 cells/mm^3 in resource-limited settings are a priority for ART.

MOPEB151

Children and adolescents infected with HIV-1 subtype F or BF recombinants failing ARV therapy shows a more extensive resistance profile to protease inhibitors

P.M. Guimarães[1], J. Cavalcanti[1], A. Campeas[2], J.L. Ferreira[1], F. Cabral[1], R. Palasio[1], F. Almeida[3], L. Brigido[1]
[1]Adolfo Lutz Institute, Virology Center, São Paulo, Brazil, [2]Institute of Infectious Diseases Emilio Ribas, São Paulo, Brazil, [3]Santa Casa Hospital, São Paulo, Brazil
Presenting author email: lubrigido@gmail.com

Background: Treatment of children and adolescents is specially challenging due to age related issues as ARV availability and treatment adherence. Genotypic resistance test may favor salvage therapy and is performed at our service to subsidize clinical care in Sao Paulo, Brazil.

Methods: We evaluated all HIV-1 *pol* sequences available at our laboratory from patients under 19 yo failing ARV therapy (2010 to 2014). Stanford HIVdb was used to determine HIV susceptibility to ARV. Intermediate or high level resistance were considered as GSS=0. Sequences were considered with Triple Class Resistance (TCR) when presented a GSS=0 to at least one drug at each classical class (NNRTI, NRTI and PI). Yates corrected or Fisher, two-tailed, was used to determine level of significance.

Results: Sequences from 174 patients were analyzed. 44% of patients were male, with median age 14 (IQR 12-16), 489 CD4 cells/mm^3 and 3.74 $\log_{10}$. Of total sequences, 157 showed some degree of resistance. Proportion of sequences with GSS=0 was 96% (151/157) to NRTI, 69% (109/157) to NNRTI and 44% (69/157) to PI. TCR was observed in 28% (47/157). Subtype B was found in 69% of 174 sequences, F in 12%, BF in 16% and C in 3%. When B and non-B were compared, median treatment time was 11 years (IQR 6-13), and median number of regimens was 3 (IQR 2-4). Regarding ARV use, all patients were exposed to NRTI, 76% to PI and 74% to NNRTI. No differences in exposure to drug classes among subtypes B and non-B were observed. However, PI drugs showed more frequently a GSS=0 among non-B subtypes, especially BF recombinants, with significant differences to Atazanavir (p< 0.035), Fosamprenavir (p< 0.044), Saquinavir (p< 0.022), and marginally to Lopinavir (p=0.051). These differences were not observed for drugs of the NRTI and NNRTI classes.

Conclusions: Subtype F and BF harbor polymorphisms that may favor resistance evolution. Closer monitoring of children living with non-B variants may be warranted to improve virological suppression. The high prevalence of TCR reinforces the need for strategies to improve viral suppression and the availability of newer treatment options for children and adolescents.

Long-term non-progressors and elite controllers

MOPEB152

Hospitalizations among HIV controllers versus persons with medically-controlled HIV

T. Crowell[1,2], A. Ganesan[2,3,4], S. Berry[5], R. Deiss[2,3,6], B. Agan[3,4], J. Okulicz[3,7], Infectious Disease Clinical Research Program (IDCRP) HIV Working Group
[1]U.S. Military HIV Research Program, Silver Spring, United States, [2]Henry M. Jackson Foundation for the Advancement of Military Medicine, Bethesda, United States, [3]Infectious Disease Clinical Research Program, Bethesda, United States, [4]Walter Reed National Military Medical Center, Infectious Disease Service, Bethesda, United States, [5]Johns Hopkins University School of Medicine, Division of Infectious Diseases, Baltimore, United States, [6]Naval Medical Center, Infectious Disease Clinic, San Diego, United States, [7]San Antonio Military Medical Center, Infectious Disease Service, San Antonio, United States
Presenting author email: tcrowell@hivresearch.org

Background: HIV controllers (HIC) spontaneously maintain low HIV viral load (VL) without antiretroviral therapy (ART) and have a lower risk of AIDS or death than other HIV-infected persons. Previous data suggest HIC may be hospitalized more frequently than persons who achieve medical control (MC) with ART. We evaluated rates and reasons for hospitalization among HIC and MC participants in the US Military HIV Natural History Study.

Methods: The HIC group (n=221) was composed of elite (n=33) and viremic (n=188) controllers defined by VL control below the limit of detection or ≤2000 copies/mL, respectively, for ≥12 months without ART. HIC were censored upon ART initiation. MC participants (n=870) were defined by VL < 400 copies/mL for ≥12 months on continuous ART. Person-time was accumulated only during periods of VL control. Hospitalizations were tallied annually from 2000-2013 and assigned a diagnostic category. Negative binomial regression with GEE was used to calculate incidence rate ratios (IRRs) for factors associated with hospitalization.

Results: The median age at the start of VL control for the HIC and MC groups was 32.2 and 33.8 years, respectively (p=0.025). Compared with the MC group, a higher proportion of HIC were female (11% vs. 5%; p=0.003) and African American (54% vs. 40%; p< 0.001). There were 483 hospitalizations during 5,098 person-years (PY).

Mean hospitalization rates were 9.4/100 PY among HIC and 8.8/100 PY among MC participants. Non-AIDS-defining infections were the most common reason for hospitalization (31% of admissions in each group).

In multivariable analysis, independent risk factors for hospitalization included age >60 years (IRR 2.16 [1.01-4.63], as compared with <30 years) and CD4 <200 cells/uL (IRR 2.58 [1.46-4.57], as compared with >750 cells/uL).

There was no significant difference in hospitalization rate for HIC compared with MC (IRR 1.15 [0.80-1.65]) after adjusting for age, race, sex, CD4, year, and duration of HIV infection.

Conclusions: Hospitalization rates were similarly low for both HIC and MC participants, with infectious causes being the most common reason for admission. Differences in rates and reasons for hospitalization may have been difficult to detect due to the young age of our cohort and continued long-term follow-up is warranted.

Disease burden: morbidity / mortality / life expectancy

MOPEB153

Advancing in age: what effect on mortality and loss to follow-up in the course of ART? The IeDEA West Africa cohort collaboration

N. de Rekeneire[1], E. Balestre[2], P. Coffie[3], S. Eholié[4], E. Messou[5], V. Kwaghe[6], O. Benson[7], A. Sadawago[8], Y. Abo[9], F. Dabis[2]
[1]University of Bordeaux, ISPED - INSERM U 897, Bordeaux, France, [2]University of Bordeaux, ISPED, Bordeaux, France, [3]PAC-CI, Abidjan, Cote D'Ivoire, [4]Medical School of University Félix Houphouet-Boigny, Abidjan, Cote D'Ivoire, [5]CEPREF, Abidjan, Cote D'Ivoire, [6]University of Abuja Teaching Hospital, Abuja, Nigeria, [7]University of Benin City Teaching Hospital, Benin City, Nigeria, [8]CHU Souro Sano, Bobo-Dioulasso, Burkina Faso, [9]CMSDS/CNTS, Abidjan, Cote D'Ivoire
Presenting author email: nathalie.de-rekeneire@isped.u-bordeaux2.fr

Background: A growing number of people aged 50 years and older are living with HIV in low- and middle-income countries. With the increase of antiretroviral therapy (ART) use in these countries, HIV-related mortality is dropping including in the WHO African region. Studying the effect of age on mortality and loss to follow-up (LTFU) is essential as older HIV positive patients are at greater risk of adverse ART outcomes.

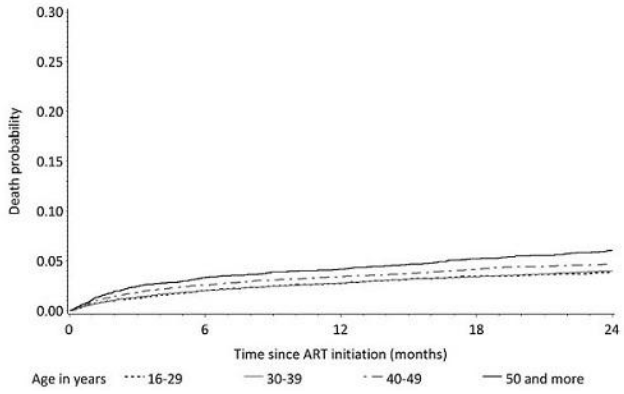
Methods: We analyzed data collected within the International epidemiological Databases to Evaluate AIDS (IeDEA) West Africa collaboration. Eligible patients were ART-naïve HIV-1 infected adults aged 16 years or older who initiated ART, and attended ≥2 clinic visits during their first 24 months of follow-up. Age was divided in 4 age groups: 16-29, 30-39, 40-49, ≥50 years. LTFU was defined as no contact within 6 months before the cohort closure date. Kaplan-Meier curves and multivariable Cox proportional hazard regression analyses were performed to study the effect of age on mortality, and LTFU.

Results: Among the 50,459 eligible patients, 65.6% were women, with a median age of 36.3 years [IQR: 30.5-43.2] at ART initiation: 5,325 (10.6%) were aged ≥50 years, and 1,033 (2%) aged ≥60 years. The median follow-up time was 31.1 months [IQR: 11.4- 57.4].

At month 24, 1,855 (3.7%) of the patients had died, and 11,178 (22.2%) were LTFU. In multivariable Cox analyses, those aged ≥50 had an increased risk of death (hazard ratio [HR]= 1.54; 95% CI: 1.31-1.82; ref. 16-29 age group). Male gender, a WHO clinical stage III or IV, an initial CD4 cell count < 350 cells/mm^3, an initial hemoglobin < 12g/dl, or a BMI < 18 were also all associated with an increased risk of death (all p < .0001).

Those in the older group were less likely to be LTFU after ART initiation than those in the 16-29 age group (HR=0.86; 95% CI: 0.80-0.93).

Conclusions: Being older at ART initiation was associated with an increased risk of mortality and a lower risk of being LTFU. Tailored programs focused on improving the outcomes of older HIV patients in sub-Saharan Africa are needed.



[Kaplan-Meier estimates of mortality by age]

MOPEB154

Cause of death comparison in a US HIV-infected patient cohort and the National Death Index

F. Palella[1], R. Hart[2], C. Armon[2], C. Akridge[2], J. Chmiel[3], T. Subramanian[2], K. Wood[2], K. Buchacz[4]
[1]Northwestern University, Infectious Diseases, Chicago, United States, [2]Cerner Corporation, North Kansas City, United States, [3]Northwestern University, Chicago, United States, [4]Centers for Disease Control and Prevention, Atlanta, United States
Presenting author email: f-palella@northwestern.edu

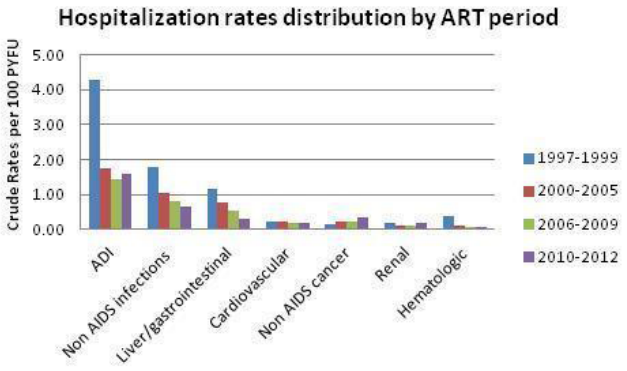
Background: Complete cause of death (COD) information for HIV-infected persons is important epidemiologically but difficult to obtain. Whether National Death Index (NDI) supplements and corroborates COD provided by medical records and research-collected data is unclear.
Methods: Records for HIV Outpatient Study (HOPS) decedents at 8 U.S. HIV clinics who died during 2001-2010 were matched to the NDI database. We assessed primary and contributing COD from HOPS data and NDI (entity-axis codes) including extent of COD concordance, discordance and missing data.
Results: Of 569 deaths, HOPS and NDI COD data were fully concordant for 62 (11%) and partially concordant for 138 (24%) decedents. HOPS lacked COD data for 279 (49%) decedents and NDI for 77 (14%), p=0.10; no COD was available for 45 (8%) in either database. Among 290 persons with COD listed, imprecise COD terms like "AIDS", "HIV", or "cardiac arrest" were listed in HOPS for 155 (53%) decedents and for 187 (64%) in NDI, p< 0.001. Only imprecise COD were listed in HOPS for 37 (6%) decedents vs. 82 (14%) in the NDI, p< 0.001. After excluding imprecise COD, ≥ 1 COD was available for 205 (45%) decedents in NDI but not HOPS, for 48 (10%) decedents in HOPS but not NDI (p< 0.001), and for 205 (45%) in both datasets. Having no or only imprecise HOPS COD was less common for the 324 who died ≤ 6 months after HOPS contact (119, 37%) than the 245 who died > 6 months after last HOPS contact (197, 80%), p< 0.001, and less common for the 343 decedents in 2001-2005 (165, 48%) than the 226 decedents in 2006-2010 (151, 67%), p< 0.001. After incorporating NDI data, the percentage of decedents with specific COD increased from 51% to 86%, particularly if they died > 6 months after last HOPS contact (from 24% to 82%). In the NDI, we found no differences in COD completeness by calendar year.
Conclusions: Matching with NDI data enhanced COD ascertainment for HIV-infected persons, particularly persons who died >6 months after last HOPS contact. Our findings support use of NDI to improve the quality of COD capture among contemporary HIV-infected persons.

MOPEB155

Trend and causes of hospitalizations among patients with HIV entering care in Italy: a 15 years study from the ICONA cohort

A. Mammone[1], R. Cauda[2], V. Vullo[3], C. Viscoli[4,5], P. Caramello[6], F. Baldello[7], P. Bonfanti[8], G. Angarano[9], A. Antinori[10], M. Puoti[11], A. D'Arminio Monforte[12], E. Girardi[1], ICONA Foundation Study Group
[1]National Institute for Infectious Diseases IRCCS 'L. Spallanzani', Department of Epidemiology and Preclinical Research, Rome, Italy, [2]Catholic University, Institute of Clinical Infectious Diseases, Rome, Italy, [3]University of Rome La Sapienza, Department of Infectious Diseases, Rome, Italy, [4]IRCCS San Martino University Hospital, Infectious Diseases Unit, Genoa, Italy, [5]University of Genoa, Genoa, Italy, [6]Amedeo di Savoia Hospital, Department of Infectious Diseases, Turin, Italy, [7]University of Perugia, Section of Infectious Diseases, Department of Experimental Medicine and Biochemical Sciences, Perugia, Italy, [8]Azienda Ospedaliera Lecco, Department of Infectious Diseases, Lecco, Italy, [9]University of Bari, Clinic of Infectious Diseases, Bari, Italy, [10]National Institute for Infectious Diseases 'L. Spallanzani', Clinical Department, Rome, Italy, [11]Niguarda Hospital, Infectious Diseases Department, Milan, Italy, [12]University of Milan, Clinic of Infectious and Tropical Diseases, Department of Health Sciences, Milan, Italy
Presenting author email: antonella.darminio@unimi.it

Background: Declining rates of hospitalizations occurred shortly after the availability of combination antiretroviral therapy (cART). However, trends in the late cART era are less defined, and data on the impact of cART use on different causes of hospitalization are needed.
Methods: We included HIV-infected persons enrolled in 1997-2012 in the Icona Foundation Study cohort; a hospitalization was considered if occurred at least 30 days after the enrollment. Participants' follow-up accrued from the date of enrollment (baseline) to a hospitalization or their last visit. Participants could be included in multiple periods and could contribute to more than 1 hospitalization per period.
Incidence of hospitalizations (per 100PYFU) were calculated for the overall study period, for the following study periods characterized by different availability of ART: 1997-1999 (early cART); 2000-2005 (cART); 2006-2009 (late cART); 2010-2012 (new classes cART) and by current CD4 count (grouped as 0-350, 351-500, and >500).
Causes of hospitalization were grouped in AIDS defining illness (ADI), non-AIDS infections (i.e. pneumonia, endocarditis, meningitis), liver/gastrointestinal, cardiovascular, psychiatric, hematological and renal diseases and non-AIDS cancer.
Results: Of the 10,527 participants (25.3% females, 38.2% heterosexuals, 26.6% with HCV; median age 36 years (IQR 31-42)), for a total of 51,281 PYFU, 1562 (15%) were hospitalized at least once with 2822 separate hospital admissions, resulting in a rate of hospitalization of 5.5 per 100 PYFU. The rate decreased from 9.9 in 1997-1990 to 4.2 in 2010-2012.
Overall, hospitalization were due mostly to ADI and to non-AIDS infections; a steady decrease by study period was observed in all diagnostic categories except non-AIDS cancers for which we observed an increase, while cardiovascular disease remains unchanged (Figure 1).



[Figure 1]

In a multivariate model, cART use, absence of HCV coinfection, study period and higher current CD4-count were associated with a significant reduction of the risk of hospitalization (Table 1).

		Relative Rates RR	95% CI
CD4 count (ref <350)	350-499	0.41	0.37-0.45
	>=500	0.28	0.25-0.30
On ART (ref No)	Yes	0.24	0.20-0.27
HCV coinfection (ref No)	Yes	2.01	1.90-2.26
ART period (ref 1997-1999)	2000-2005	0.79	0.72-0.88
	2006-2009	0.77	0.69-0.87
	2010-2012	0.72	0.65-0.82

[Table 1. Poisson regression analysis]

Conclusions: Our findings show that hospitalization rates decrease during time in ICONA patients, and is approaching the rate of the Italian general population. This decrease is striking during the period 2000-2005 and for ADI and non-AIDS infections, which however are responsible for more than 50% of hospitalization even in the more recent time period.

MOPEB156

Reductions in mortality rates among HIV-positive people who inject drugs in Vancouver, Canada, during a treatment-as-prevention-based HAART scale up initiative: a gender-based analysis

K. Hayashi[1,2], T. Kerr[1,2], H. Dong[1], S. Dobrer[1], S. Guillemi[1], R. Hogg[1,3], J. Montaner[1,2], E. Wood[1,2], M.-J. Milloy[1,2]
[1]British Columbia Centre for Excellence in HIV/AIDS, Vancouver, Canada, [2]University of British Columbia, Department of Medicine, Vancouver, Canada, [3]Simon Fraser University, Faculty of Health Sciences, Burnaby, Canada
Presenting author email: khayashi@cfenet.ubc.ca

Background: HIV/AIDS remains a major cause of death among people who inject drugs (PWID). However, little is known about the impact of recent efforts to expand access to antiretroviral therapy (ART) on mortality in this population, including how such impacts might vary by gender. We conducted a gender-based analysis to identify rates and predictors of death among HIV-positive PWID in Vancouver, Canada.
Methods: Longitudinal cohort data on HIV-positive PWID were linked to a provincial vital statistics database to ascertain rates and causes of death between May 1996 and May 2013. Age-adjusted Poisson regression was used to examine changes in HIV-related mortality rates before and after the implementation of a Treatment-as-Prevention initiative in 2010. Multivariable Cox proportional hazards regression was used to identify predictors of all-cause mortality. Analyses were stratified by gender.
Results: Among 961 participants, including 353 (36.7%) women, there were 264 deaths during the study period, resulting in a mortality rate among men of 4.64 (95% confidence interval [CI]: 3.98 - 5.40) and 4.41 (95% CI: 3.65 - 5.32) deaths per 100 person-years among women. In both genders, HIV-related mortality rates have declined since 2010 ($p < 0.01$). In multivariable survival analyses, those who initiated ART at a CD4 cell count ≥200 cells/mm^3 and had ≥95% adherence to ART in the first year of treatment had a significantly lower hazard of death compared to those who never accessed ART among both men (adjusted hazard ratio [AHR]: 0.17; 95% CI: 0.09 - 0.33) and women (AHR: 0.35; 95% CI: 0.17 - 0.72). Daily illicit prescription opioid use was independently and positively associated with mortality among men only (AHR: 2.06; 95% CI: 1.35 - 3.14).
Conclusions: In this 18-year cohort study of community-recruited HIV-positive PWID, mortality rates were similar between male and female participants. High-intensity prescription opioid misuse predicted mortality among men, indicating a need to identify factors shaping harms from illicit prescription opioid use among this population. HIV-related mortality rates have significantly declined since the beginning of efforts to expand access and adherence to ART, suggesting that Treatment-as-Prevention-based efforts to scale-up ART among PWID are associated with declines in HIV/AIDS-related mortality among this population.

MOPEB157

Comorbidities of patients with newly diagnosed human immunodeficiency virus (HIV) in the USA: a longitudinal analysis of incident HIV patients

N. Meyer, X. Song
Truven Health Analytics, Cambridge, United States
Presenting author email: nicole.fulcher@truvenhealth.com

Background: Patients with HIV infection can present with multiple comorbidities prior to starting antiretroviral therapy (ART). Some of these comorbidities are potential risk factors for future diseases such as cardiovascular (CV) and renal impairment. Furthermore, choice of ART may hasten the process of future disease development. The prevalence of these comorbidities has not been well-defined over the course of the HAART era. This study examined comorbidities that may impact risk of developing CV and renal conditions in incident HIV populations and compared the prevalence of these comorbidities between 2003 and 2013.
Methods: Patients newly diagnosed with HIV (ICD-9 diagnosis code: 042.xx, 795.71, V08) were selected from MarketScan Commercial and Medicare Databases (2002-2014) and Medicaid database (2002-2013). MarketScan databases are longitudinal and patients' risk factors and treatment patterns can be observed over multiple years. In this analysis, index date was the first HIV diagnosis date. All patients had 6 months of data prior to index date and were followed until end of data. Patients with baseline evidence of HIV or ART were excluded. Baseline comorbid conditions, including diabetes, hypertension, CV conditions, and renal impairment were examined using ICD-9 diagnosis codes.
Results: A total of 35,997 newly diagnosed HIV patients (mean age: 39.2, male: 74.0%) were selected from the Commercial database, 2,279 (mean age: 73.0, male: 56.5%) from Medicare, and 19,609 (mean age: 36.0, male: 45.1%) from Medicaid. Among all Commercial patients in 2003-2013, mean Charlson comorbidity index (CCI) was 0.2; 5.2% patients had diabetes, 12.0% hypertension, 6.6% dyslipidemia, 1.7% CVD, and 2.4% renal impairment. Medicare patients had a mean CCI of 0.7, 30.4% patients had diabetes, 48.0% hypertension, 24.4% dyslipidemia, 15.9% CVD, and 17.62% renal impairment. Medicaid patients had a mean CCI of 0.2, 8.4% patients had diabetes, 15.9% hypertension, 5.1% dyslipidemia, 2.3% CVD, and 3.2% renal impairment. Patients diagnosed with HIV in 2013 had higher prevalence of comorbidities than those newly diagnosed in 2003 (Table 1).

Baseline Measures	Commercial 2003	Commercial 2013	Medicare 2003	Medicare 2013	Medicaid 2003	Medicaid 2013
Patients (N)	1,390	3,303	177	436	3,008	1,632
Age (mean,SD)	39.4(11.6)	38.8(12.9)	72.2(8.0)	72.9(7.2)	34.7(15.3)	39.2(14.1)
CCI (mean,SD)	0.15(0.36)	0.15(0.36)	0.66(0.48)	0.71(0.45)	0.20(0.40)	0.19(0.40)
CV Events(any)	1.1%	2.0%	13.0%	20.4%	1.5%	2.3%
Mycardial Infraction	0.1%	0.3%	1.1%	2.1%	0.5%	0.5%
Peripheral Vascular Diseases	0.1%	0.5%	5.6%	7.3%	0.5%	1.0%
Essential Hypertension	9.0%	14.2%	31.6%	62.6%	9.2%	15.8%
Diabetes Mellitus	4.5%	6.1%	18.1%	49.5%	6.1%	7.7%
Renal Impairment	2.8%	3.1%	10.7%	29.4%	2.4%	3.6%

[Table 1]

Conclusions: Patients with new HIV infection present with multiple comorbidities including renal and CV prior to ART initiation and the trend in these comorbidities has risen since 2003. Understanding these risk factors will help optimize HIV treatment.

Opportunistic infections (excluding TB)

MOPEB158

Clinical presentation and management of parvovirus B19 associated red cell aplasia: experience at the tertiary care institute in Durban, South Africa

M.-A. John[1], T. Manzini[1,2], C. Du Plessis[1,2], B. Gosnell[1,2], Y. Moosa[1,2]
[1]University of Kwa Zulu Natal, Infectious Diseases, Durban, South Africa, [2]King Edward V111 Hospital, Durban, South Africa

Background: In HIV infected individuals persistent anaemia and immune reconstitution anaemia are manifestations of parvovirus B19 (PBV19) disease. Up to 25% of severe chronic anaemia in AIDS has been ascribed to PVB19. Diagnosis in HIV/AIDS is made on serum DNA PCR and treatment includes immunoglobulins, HAART and supportive blood transfusion. However, relapse is common.
We describe the presentation, management and response to treatment of HIV related severe PB19 associated anemia at a resource limited public hospital.
Methods: A retrospective audit of cases managed by our infectious diseases unit. Clinical and laboratory data were anonymously collected using a standard data collection worksheet and entered on IBBM Statistical Package for the Social Sciences (SPSS) version 22. Adults with anaemia were eligible if they were PVB19 positive on serum PCR and HIV co-infected.
Results: Eleven patients, representing 18 admission episodes were identified from 2011 to 2014. The majority were female (7) with a mean age of 30yrs. The median CD4 count was 100 cells/mm^3 (range: 4-230). Nine were on HAART for a median of 198 days(range 36-851) prior to anaemia admission and 7 had undetectable viral load on presentation.
All but 3 had a pyrexia of >37.5 ^{0}C. Severe anaemia with a median haemoglobin of 5.1 g/dl(range:2.3-10.8) was observed.
Serum IgM was positive in 6 of 15 (40%) and serum IgG positive in 2 of 14 (14.3%) admission episodes. Qualitative DNA PCR was positive in all patients and 9 bone marrow trephine revealed giant pronormoblasts.
All patients received red cell transfusion. A mean of 6 units was transfused before referral to our unit and 7 patients received addition transfusions (mean 3, range:1-5).
Nine patients received a 6.13 days (range:1-11) of intravenous immunoglobulin(IVIG) at 0.4mg/kg/day and 6 relapsed. The 7th patient had 3 episodes of relapse before receiving IVIG. One patient died of MDR tuberculosis and the remainder continue to be monitored. Mean hospital stay was 16 days.

Conclusions: PVB19 is an uncommon opportunistic infection but resource intensive. Serology is misleading as 40% had positive IgM whilst two had confirmed PVB19 in the presence of IgG.
Current treatment is suboptimal as six patients on HAART and IVIG relapsed.

Tuberculosis and other mycobacteria

MOPEB159

CYP2B6 genotype based efavirenz dose recommendations during rifampicin based anti tuberculosis co-treatment for a sub-Saharan Africa population

J.K. Mukonzo[1], R.K. Bisaso[1], J. Ogwal-Okeng[1], L. L-Gurstafsson[2], E. Aklillu[2]
[1]*Makerere University College of Health Sciences, Pharmacology & Therapeutics, Kampala, Uganda,* [2]*Karolinska Institute, Laboratory Medicine, Stockholm, Sweden*
Presenting author email: mukojack@yahoo.co.uk

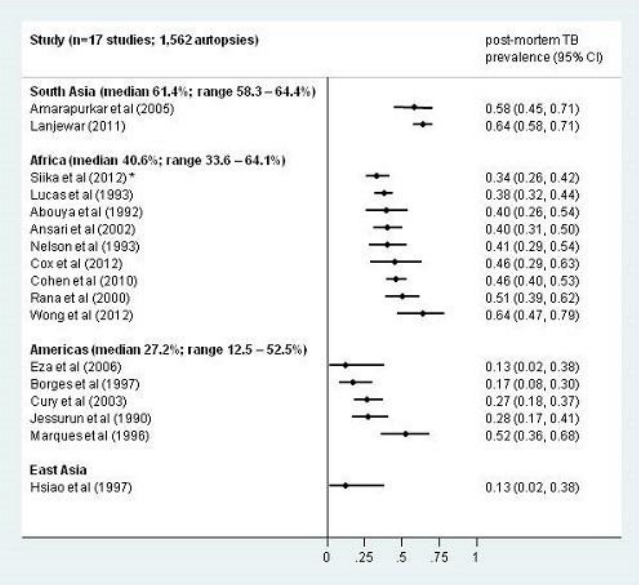
Background: Pharmacogenetics is a major determinant of the efavirenz-rifampicin interaction during HIV-TB co-treatment, leading to variations in both efavirenz plasma exposure and dose requirements. The purpose of this study was to assess the effect of genetic factors on EFV pharmacokinetics, treatment outcomes and provide genotype based EFV doses recommendations for adult TB-HIV-1 co-infected Ugandans receiving rifampicin based anti-tuberculosis co-treatment.
Methods: Steady state plasma EFV concentrations (n=1216) from 158 HIV-TB co-infected patients (76 females) treated with efavirenz/lamivudine/zidovidine and rifampicin based anti-TB treatment were analyzed. Patient genotypes for *CYP2B6* (**6* & **11*), *CYP3A5* (**3*,**6* & **7*) and *ABCB1 c.4046A>G*, baseline biochemistries and CD4 and viral load change from baseline were determined. A one-compartment population PK model with first-order absorption (NONMEM™) was used to estimate genotype effects on EFV pharmacokinetics. PK simulations were performed based upon population genotype frequencies. Predicted AUCs and trough concentrations were compared between the product label / known reference values and simulations for the different doses (200mg, 250mg, 300mg, 450mg, 600mg).
Results: EFV post-induction CL/F was 2.5 and 1.7 fold higher in *CYP2B6*6/*6* and *CYP2B6*1*/6* compared *CYP2B6*1/*1*, while a 23% increase in F1 was observed for the variant ABCB1 c.4046A>G. EFV mean AUC was significantly higher in *CYP2B6*6/*6* genotypes compared to *CYP2B6 *1/*1* (p< 0.0001). Simulation based AUCs for a 600 mg EFV dose were 1.25 and 2.10 times greater than the product label mean AUC for the Ugandan population in general and *CYP2B6*6/*6* genotypes respectively. Simulated exposures for EFV daily doses of 450mg and 250mg for the general population and *CYP2B6*6/*6* genotypes respectively were comparable to the product label. Viral load fell precipitously on treatment with only fourteen (8.9%) patients having HIV RNA > 40 copies/mL after 84 days of treatment. No trend with exposure was noted for these fourteen patients.
Conclusions: During rifampicin co-treatment, daily doses of 450mg and 250mg might meet the EFV dosing needs of HIV-TB infected Ugandans in general and individuals homozygous for CYP2B6*6 variant allele, respectively.

MOPEB160

Prevalence of tuberculosis in post-mortem studies of HIV-infected adults and children in resource-limited settings: a systematic review

R.K. Gupta[1], S.B. Lucas[2], S.D. Lawn[3,4]
[1]*Division of Medicine, University College London, London, United Kingdom,* [2]*Department of Histopathology, Guy's & St Thomas' NHS Foundation Trust, London, United Kingdom,* [3]*Department of Clinical Research, Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, United Kingdom,* [4]*Desmond Tutu HIV Centre, Institute of Infectious Disease and Molecular Medicine, University of Cape Town, Cape Town, South Africa*
Presenting author email: rishgupta@gmail.com

Background: Tuberculosis (TB) is a major cause of HIV-related deaths worldwide. However, since TB frequently remains unascertained in HIV-infected people, data from autopsy studies are needed to assess the true burden of TB at death.
Methods: We systemically searched Medline and Embase databases and conference abstracts for literature reporting on autopsy studies of HIV-infected adults and children in low- or middle-income countries. We summarized the prevalence of TB found at autopsy and explored how this varied with age and geographic region, using forest plots, and with national TB prevalence, using linear regression. Statistical heterogeneity was assessed using the I-squared statistic.
Results: A total of 36 studies (reporting on 3,237 autopsies) were included, of which 20 studies were from sub-Saharan Africa. The overall median TB prevalence at autopsy was 27.7% but was extremely heterogeneous (range, 0-64.4%). Prevalence was markedly higher in adults (median, 40.4%; range, 12.5%-64.4%) than in children (median, 3.2%; range, 0-17.8%). Post-mortem TB prevalence varied by world region: the median prevalence in adults was 61.4% (range, 58.3%-64.4%) in South Asia (n=2 studies); 40.6% (range, 33.6%-64.1%) in sub-Saharan Africa (n=9 studies); and 27.2% (range, 12.5%-52.5%) in the Americas (n=5 studies).



*[Figure 1: Forest plots showing post-mortem prevalence of tuberculosis (TB) stratified by world region in studies that included adults only (n=17). Data presented represents a total of 1,562 autopsies. CI = confidence interval. *Studies that presented % of subjects with TB at autopsy as cause of death only]*

Autopsy prevalence correlated with national TB prevalence (R^2=0.24; P=0.045). The vast majority of TB cases (median, 85%) had disseminated, multi-organ disease. The organs most frequently involved were the lungs (median, 79%), spleen (median, 82%), liver (median, 79%) and lymph nodes (median, 59%). A median of 44% (range, 14%-67%) of TB cases remained undiagnosed before death. In studies done in Africa in adults over a 20-year period (1992-2012), there was no reduction in post-mortem TB prevalence over time. TB was the primary cause of death in a median of 95.1% (range, 50-100%) of those with prevalent TB found at autopsy.
Conclusions: TB accounts for approximately 40% of HIV/AIDS-related deaths in adults in resource-limited settings. The vast majority of this TB disease is widely disseminated, but half of the disease burden remains undiagnosed at the time of death. This highlights the critical need to improve the prevention, diagnosis and treatment of HIV-associated TB globally.

MOPEB162

Population-based, active TB case finding during large-scale, mobile HIV testing campaigns in rural Uganda

E. Ssemmondo[1], F. Mwangwa[1], J. Kironde[1], D. Kwarisiima[1], T. Clark[2], E. Charlebois[3], M. Kamya[4], D. Havlir[2], G. Chamie[2]
[1]*Makerere University-University of California, San Francisco (MU-UCSF) Research Collaboration, Kampala, Uganda,* [2]*University of California, Division of HIV/AIDS, San Francisco, United States,* [3]*University of California, Center for AIDS Prevention Studies, San Francisco, United States,* [4]*Makerere University College of Health Sciences, Department of Medicine, Kampala, Uganda*
Presenting author email: essemmondo@idrc-uganda.org

Background: Shifting TB screening out of health facilities and into communities may reduce delays in TB diagnosis and undiagnosed disease. Population-based surveys from sub-Saharan Africa have found a large range (29-5000) in the number needed to screen to identify one new case of TB; data from rural settings are lacking. We sought to determine the yield of TB screening during population-based, mobile HIV testing campaigns in rural Uganda.
Methods: We performed 2-week mobile, multi-disease community health campaigns (CHC) in seven communities of 10,000 persons each in eastern Uganda, within an ongoing community cluster randomized trial of universal HIV testing and treatment in Uganda and Kenya (SEARCH, NCT:01864603). At each CHC, staff attempted to obtain two spot sputum samples from adults (≥15 years) reporting prolonged cough (>2 weeks). We performed same-day fluorescence microscopy (FM) on sputum, and referred participants with acid-fast bacilli (AFB)-positive sputa for TB treatment at local clinics. We determined the number of persons needed to screen to identify one TB case, and the number of cases identified that linked to clinic and initiated TB treatment.

Results: Of 36,691 census-enumerated adults in seven communities, 27,113 (74%) attended CHCs. 5,765 (21%) adults reported cough, and 2,860 (11%) reported cough >2 weeks. Staff obtained sputum in 2,112/2,860 (74%) participants with prolonged cough, and identified 7 adults with AFB-positive sputum; 6 new diagnoses, and one known case already on treatment. The yield of symptom and sputum screening was 7/27,113 (0.026%) among all adults, and 7/2,860 (0.24%) among adults with prolonged cough. All six newly diagnosed AFB+ participants linked to TB care within 2 weeks; five patients initiated TB treatment. CHC-based HIV testing uptake was >99%, with 878 (3.2%) HIV-infected adults identified; all seven TB cases were HIV-uninfected.
Conclusions: In a rural Ugandan setting, the number of adults needed to screen to detect one new TB case was 477 among adults with cough >2 weeks. TB screening as an adjunct to large-scale, mobile HIV testing campaigns provides an opportunity to increase TB case detection.

MOPEB163

Is prophylaxis against tuberculosis required for HIV-infected individuals in low incidence settings?

K. Manavi, J. Hosdon
University Hospitals Birmingham NHS Foundation Trust, HIV, Birmingham, United Kingdom
Presenting author email: kaveh.manavi@uhb.nhs.uk

Background: HIV infected patients are at high risk of reactivation of latent TB. Current data suggest combined antiretroviral therapy (cART) can reduce the rate of incident TB . The UK guidelines recommend screening of HIV infected patients for latent TB and offer of prophylaxis treatment to those with positive interferon gamma reactive assays (IGRA).
The recommendation is mainly based on data from settings with high incidence of TB that may not apply to settings with low incidence of the infection.
We investigated the effectiveness of TB prophylaxis in a HIV cohort in the UK.
Methods: This was an observational study on a cohort of HIV infected patients followed between 1st April 2011 and the 31st October 2013. Patients' countries of origin were classified in high and low risk groups. Patients from sub-Saharan African countries, Indian subcontinent, Eastern European countries (Russia, Latvia, and Ukraine) not on cART or on cART for less than two years were considered as high risk. Patients with culture proven TB after HIV diagnosis were classified as having "active TB".
A Kaplan-Meier plot was produced to show the survival time of patients to "active TB". The estimated "active TB" rates were then used to calculate the Number Needed to Treat (NNT) with TB prophylaxis to prevent one case of TB.
Results: 1,330 HIV infected patients were followed up for a median of 27 (quartiles: 14, 29) months; giving 2,385 patient-years (PY) of follow up. There were 16 cases of active TB in the period; an incidence of 6.7/1000 PY.
There were 301 patients who met the UK guidelines' criteria for being at risk of latent TB infection. The patients classified as high risk were significantly more likely to develop active TB than those that were low risk (Hazard Ratio=4.46; 95% CI=1.64-12.1; p=0.003). Prophylaxis TB treatment of every high risk patient at HIV diagnosis would prevent one case of TB for every 62 patients treated, within one year.
Conclusions: Patients meeting the criteria set by UK guidelines should be offered to start cART. TB prophylaxis for asymptomatic at-risk patients in cohorts with low incidence of active TB may not be necessary.

MOPEB164

The role of new molecular TB tests in South Africa's Xpert MTB/RIF algorithm: evaluation of Abbott RealTi*m*e MTB assay

A. David[1], M. Nduna[1], A. Black[2], W. Stevens[1,3], L.E. Scott[3]
[1]National Health Laboratory Services, Johannesburg, South Africa, [2]University of the Witwatersrand, WITS Reproductive Health and HIV Institute, Johannesburg, South Africa, [3]University of the Witwatersrand, Department of Molecular Medicine and Haematology, Johannesburg, South Africa
Presenting author email: anura.david@nhls.ac.za

Background: The WHO endorsed Xpert MTB/RIF (Sunnyvale, CA) test was implemented in South Africa in 2011. To date, >3 million tests have been performed as the initial diagnostic test for Pulmonary TB and this has dramatically increased the detection of TB.
Challenges still remain with the diagnosis of Paucibacillary patients whose bacterial burden is <130 cfu/mL. More sensitive molecular tests are therefore needed to improve TB case identification. A potential assay is the Abbott RealTi*m*e MTB assay (Des Plaines, IL) which uses the high-throughput *m2000* platform.
Methods: Presumptive TB patients attending the Hillbrow Community Health Centre in Johannesburg were consented and enrolled in the study. Participants were requested to provide 2 sputa at 2 visits (7 days apart) in order to perform Abbott RealTi*m*e MTB testing, Xpert MTB/RIF, culture (species confirmation by GenoType MTBDR*plus* V2 {Hain Lifescience, Germany}, and DST), smear and GenoType MTBDR*plus* V2 (direct pellet). The Abbott RealTi*m*e MTB- and Xpert MTB/RIF were tested on raw sputa and NALC-NaOH pellets.
Results: Preliminary culture results on 62 (out of 79 enrolled to date) patients yielded 44% (26/59) MTBC positives. The sensitivity and specificity using culture as the gold-standard were: smear 58% (95% CI: 37-77%) and 97% (95% CI: 84-99.5%); MTBDR*plus* V2 (direct pellet) 77% (95% CI: 56-91%) and 39% (95% CI: 56-91%); Abbott RealTi*m*e MTB 92% (95% CI: 75-99%) and 79% (95% CI: 61-91%); Xpert MTB/RIF 92% (95% CI: 75-99%) and 94% (95% CI: 80-99%). On raw sputa, the sensitivity and specificity were: Abbott 92% (95% CI: 75-99%) and 85% (68-95%); GeneXpert 77% (95% CI: 56-91%) and 97% (84-99%).
Conclusions: The Abbott RealTi*m*e MTB assay evaluated on this preliminary small sample size has comparable performance with Xpert MTB/RIF on decontaminated sputa for identification of MTBC. This assay identified 4 additional patients' directly off raw sputa and therefore has the potential to support an existing Xpert MTB/RIF screening program. The reduced specificity and reflex testing for DST needs to be addressed.

MOPEB165

Optimal timing of initiation of antiretroviral therapy in HIV-infected adults with newly diagnosed pulmonary tuberculosis: a systematic review and meta-analysis of randomised controlled trials

O. Uthman[1], C. Okwundu[2], K. Gbenga[3], J. Volmink[4], D. Dowdy[5], A. Zumla[6], J. Nachega[7]
[1]Warwick-Centre for Applied Health Research and Delivery (WCAHRD), Division of Health Sciences, Warwick Medical School, University of Warwick, Coventry, United Kingdom, [2]Centre for Evidence-Based Health Care, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa, [3]Julius Centre for Health Sciences and Primary Care, University Medical Centre Utrecht, Utrecht, Netherlands, [4]South African Cochrane Centre, South African Medical Research Council and Stellenbosch University Centre for Evidence-Based Health Care, Cape Town, South Africa, [5]Johns Hopkins Bloomberg School of Public Health, Epidemiology, Baltimore, United States, [6]Division of Infection and Immunity, University College London, and NIHR Biomedical Research Centre, University College London Hospitals, London, United Kingdom, [7]Pittsburgh University Graduate School of Public Health, Epidemiology, Pittsburgh, United States
Presenting author email: jbn16@pitt.edu

Background: Concomitant tuberculosis (TB) and HIV treatments remains challenging due to non-adherence, drug-drug interactions, overlapping side effects and tuberculosis immune response inflammatory syndrome (TB-IRIS). We aimed to assess the evidence from randomised controlled trials (RCTs) for the optimal timing of initiation of ART in HIV-infected adults with newly diagnosed pulmonary TB.
Methods: We conducted a systematic review with meta-analysis and trial sequential analysis (TSA) including a comprehensive literature search from October 1, 1980 to September 30, 2014, including PUBMED, EMBASE, Cochrane CENTRAL, Conference Abstracts and Clinical trials.gov. Eight RCTs (N = 4,563) met our study eligibility criteria, evaluating 'early' ART initiation (2 to 4 weeks after starting TB treatment), versus 'delayed' ART initiation (8 to 12 weeks after starting TB treatment), or 'deferred' ART initiation (end of 6 months of TB treatment).
Results: Overall, early ART reduced all-cause mortality compared to delayed ART initiation (6 trials: RR = 0.82, 95% CI 0.67 to 1.01, p=0.06, I^2 = 17%). TSA showed insufficient evidence to confirm or refute a 25% or greater relative risk reduction for all-cause mortality. In pre-specified subgroup analysis, early ART reduced all-cause mortality compared with delayed ART among patients with baseline CD4+ T-cell count <50 cells/mm^3 (3 trials: RR = 0.66, 95% CI 0.49 to 0.89, p=0.007, I^2=0%). However, patients with CD4+ T-cell counts >50 cells/mm^3, a mortality benefit among those taking early ART could not be demonstrated (3 trials: RR = 0.89, 95% CI 0.54 to 1.46, p=0.64, I^2=62%). 'Early' initiation of ART was associated with a higher incidence of TB-IRIS than 'delayed' ART (5 trials: RR = 2.19, 95% CI 1.77 to 2.70, p=0.00001, I^2=0%). All-cause mortality, ART adherence, TB cure rate, and grade 3 or 4 adverse events did not differ between patients with 'early' or 'delayed' ART initiation.
Conclusions: In this TB-HIV co-infected population, early ART initiation improves survival in those with CD4+ T-cell counts <50/mm^3, although this is associated with a two-fold higher frequency of TB-IRIS. In patients with higher CD4+ T-cell counts >50/mm^3, current evidence is insufficient to support or refute a survival benefit conferred by 'early' versus 'delayed' ART initiation.

MOPEB166

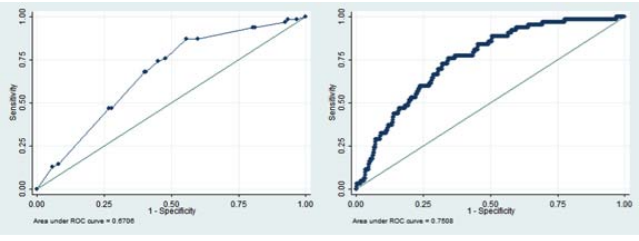
Prognostic indicators for severely ill HIV-infected patients with suspected tuberculosis

R. Griesel[1], A. Stewart[1], H. van der Plas[2], W. Sikhondze[1], M. Nicol[3], M. Mendelson[2], G. Maartens[1]
[1]University of Cape Town, Division of Clinical Pharmacology, Cape Town, South Africa, [2]University of Cape Town, Infectious Diseases and HIV Medicine, Cape Town, South Africa, [3]University of Cape Town, Microbiology, Cape Town, South Africa
Presenting author email: rulan.griesel@yuct.ac.za

Background: The World Health Organization (WHO) recommends an algorithm for the diagnosis of smear negative tuberculosis in HIV-infected patients with cough and danger signs (respiratory rate >30bpm; Heart rate >120bpm; temperature >39ºC; unable to walk unaided). The danger signs were decided by expert opinion and not proven to be associated with poor prognosis. We aim to determine the prognostic significance of danger signs and clinical covariates in this group, using death at 56 days as the primary outcome.
Methods: We enrolled 500 HIV-infected patients presenting with cough and danger signs. Using an outcome of death at 56 days after discharge we compared a multivariate regression model containing the WHO danger signs only (WHO-model), to a multivariate regression model containing the WHO danger signs and additional baseline characteristics; age, sex, CD4 count, whether the patient was on antiretroviral therapy (ART), and whether the patient was confused on admission (Augmented-model).
Results: Twenty three patients died during admission and 39 died after discharge (total 62/500, 12%). The median age was 36 years (IQR 30-42). Sixty-five percent of patients were female. The median CD4 count was 94cells/mm^3 (IQR 35-316) and 35% were on ART at the time of admission. Sixty-three percent (315/500) had a respiratory rate >30, 77% (383/500) had a heart rate >120, 51% (243/500) were unable to walk unaided, 16% (81/500) had temp>39ºC, and 18% (90/500) were confused on admission.
In the WHO-model, death was associated solely with being unable to walk unaided (adjusted odds ratio (aOR 3.56 [95% CI 1.92-6.60]). In the Augmented-model, death was associated with age (aOR for 10 year increase 1.4 [95%CI 1.05-1.87]); CD4 count (aOR for 100 cells/mm^3 increase 0.66; [95% CI 0.49-0.88]); and being unable to walk unaided (aOR 2.9 [95% CI 1.52.-5.52]).
The Augmented-model with AUC (area under ROC curve) of 0.75 (95% CI 0.69-0.81) performed better than the WHO-model (AUC 0.67; 95% CI 0.60-0.74) in predicting death at 56 days (likelihood ratio test p = 0.001).
Conclusions: In severely ill HIV-infected tuberculosis suspects, an augmented model including covariates, age and CD4 count, is a better predictor of 56 day mortality than the current WHO model.

Variable		Crude			Adjusted		
Category	N	OR	95% confidence interval	Wald's p-value	OR	95% confidence interval	Wald's p-value
Age in years (increasing in increments of 10)	500	1.42	1.1 - 1.83	0.007	1.4	1.05 - 1.87	0.024
Sex							
Female	327	Referent category			1.00		
Male	173	1.66	0.97 - 2.85	0.064	1.50	0.84 - 2.67	0.167
CD4 cells/mm3 (increasing in increments of 100)	499	0.66	0.51 - 0.86	0.002	0.66	0.49 - 0.88	0.006
Unable to walk							
No	243	Referent category			1.00		
Yes	257	3.40	1.85 - 6.27	0.000	2.9	1.52 - 5.52	0.001

[Crude and multivariate associations with death]



[Area under ROC curve for WHO- and Augmented-models]

MOPEB167

Performance of latent TB infection diagnostics in HIV-infected pregnant women in western Kenya

S. LaCourse[1,2], L. Cranmer[3], D. Matemo[4], J. Kinuthia[4,5], D. Horne[5,6,7], G. John-Stewart[2,5,8]
[1]University of Washington, Department of Medicine, Division of Allergy & Infectious Disease, Seattle, United States, [2]University of Washington, Department of Epidemiology, Seattle, United States, [3]Emory University School of Medicine and Children's Healthcare of Atlanta, Department of Pediatrics, Atlanta, United States, [4]Kenyatta National Hospital, Department of Obstetrics and Gynaecology, Nairobi, Kenya, [5]University of Washington, Department of Global Health, Seattle, United States, [6]University of Washington, Department of Medicine, Division of Pulmonary and Critical Care Medicine, Seattle, United States, [7]Firland Northwest TB Center, Seattle, United States, [8]University of Washington, Department of Medicine, Seattle, United States
Presenting author email: sylvial2@uw.edu

Background: Maternal HIV/TB co-infection is associated with poor maternal and infant outcomes. Pregnancy provides a unique opportunity for TB screening and prevention efforts including isoniazid preventive therapy (IPT). Both HIV and pregnancy may affect latent TB infection (LTBI) testing performance of tuberculin skin tests (TST) and interferon gamma release assays (IGRA). There are no published studies addressing the performance of LTBI diagnostics in HIV-infected pregnant women in sub-Saharan Africa.
Methods: Cross-sectional LTBI screening were performed on HIV-infected pregnant women in two antenatal clinics in Nyanza Province, western Kenya. Women underwent TST placement and IGRAs were performed in the KEMRI/CDC lab using QuantiFERON® TB Gold In-tube (QFT). Agreement was measured using kappa statistic. Indeterminate QFT results were excluded from kappa analysis.
Results: Between August 2014-January 2015, 100 women were enrolled with median age of 27 years (IQR 22-32), median CD4 of 586 cells/μL (IQR 340-740), and median gestational age of 28 weeks (IQR 20-32). The majority (84%) were on combination ART (cART). Eighty-nine had their TSTs read within 96 hours, of which 14.6% were positive. Of the 94 available QFT results, 35.1% (33) were positive, 48.9% (46) were negative, and 16.0% (15) were indeterminate. Among the 83 women with both available TST and QFT results, 10.8% (9) were concordant positive (QFT+/TST+), 44.6% (37) were concordant negative (QFT-/TST-). Twelve (14.5%) women had indeterminate QFT results (11 TST-, 1 TST+). A higher proportion of women had a positive QFT compared to TST (32/83 [38.5%] vs. 12/83 [14.5%], p = .0004). Excluding indeterminate QFT results, agreement between IGRA and TST was 64.8% (κ= 0.24, 95% CI 0.06-0.43). Discordant QFT+/TST- results were associated with reported household TB contact (OR 4.5, 95% CI 1.1-17.4, p= 0.03), and older median age (32 vs. 25 years, p=.007).
Conclusions: The performance of LTBI testing between QFT and TST differed significantly among HIV-infected pregnant women in western Kenya, with more QFT positive women compared to TST. A reliance on TST would miss >60% of women who could potentially benefit from IPT. Further research is required regarding impact of pregnancy stage and HIV status on LTBI diagnostics and cost-effectiveness of different LTBI screening strategies.

Other bacterial infections and parasitic infections (including malaria)

MOPEB168

Augment of CD4$^+$Tcells count and decrease of cellular activation are observed in HIV-co-infected patients with first episode of visceral leishmaniasis but not in those with previous VL relapses

J. Santos-Oliveira[1,2], M.L. Silva-Freitas[2], G. Cota[3], P. Dias-Lins[1], C. Giacoia-Gripp[2], A. Rabello[3], A. Da-Cruz[2]
[1]Federal Institute of Rio de Janeiro (IFRJ), Rio de Janeiro, Brazil, [2]Oswaldo Cruz Foundation (Fiocruz), Rio de Janeiro, Brazil, [3]CpRR - Oswaldo Cruz Foundation (Fiocruz), Belo Horizonte, Brazil
Presenting author email: joanna_reis@yahoo.com.br

Background: High incidence of visceral leishmaniasis (VL) occurs in HIV-1 co-infected patients. Both diseases cause lymphocytes depletion and augmented cellular activation, enabling the maintenance of *Leishmania* infection in a continuous vicious circle, causing frequent relapses. Previously, we pointed leishmaniasis as a cofactor to the heightened activation status in VL/HIV-1 patients despite anti-*Leishmania* and antiretroviral (ART) therapies. Thus, we now evaluated whether VL/HIV-1 presenting the first VL episode have quantitative and qualitative differences on T-cell effector response in comparison to those that suffered previous relapses.
Methods: VL/HIV-1 patients under ART and treated with amphothericin B were grouped: 1- first episode of VL (n=6) and 2- previous episodes of VL (n=7). Both groups were followed from

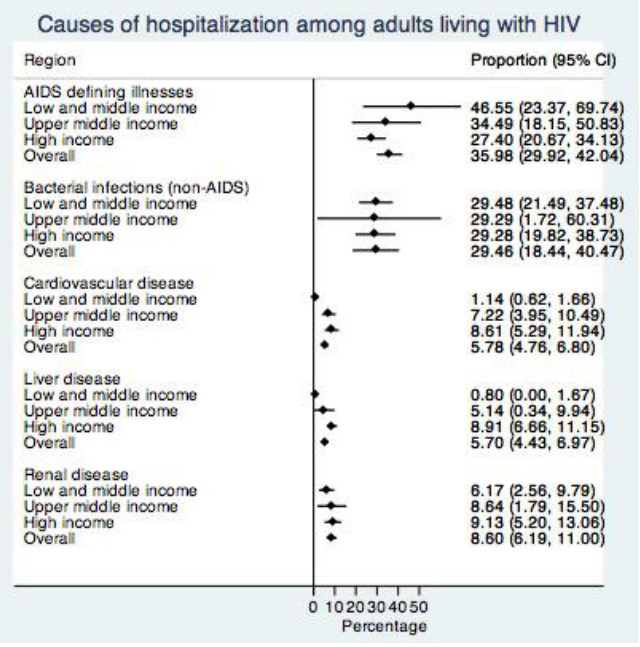
the active phase of VL up to 12 months post-treatment (mpt) and maintained amphotericin B as secondary prophylaxis. VL only (n=6), HIV-1 only (n=17) and healthy subjects (n=12) were included as controls. $CD4^+$T-cell counts, cellular activation degree ($CD38^+HLA\text{-}DR^+$), senescence ($CD57^+CD27^-$), effector memory (CD45RO/CCR7) and plasmatic sCD14 were performed.
Results: During active VL, both groups presented similar levels in all the parameters evaluated. However, at 12mpt group 2 remained with lower $CD4^+$T cells, while group 1 showed a significant increase of these cells ($p< 0.05$). At this time, group 2 patients presented higher median levels of $CD38^+/HLA\text{-}DR^+$ on $CD4^+$ and $CD8^+$T cells ($p< 0.05$) and elevated levels of sCD14, suggesting a persistent degree of immune activation. During this evaluation relapses were more frequent in group 2 than in group 1. The viral load remained low or undetectable without correlation with $CD38^+/HLA\text{-}DR^+$ levels. Both VL/HIV groups showed similar percentages of senescent and effector memory (T_{EM}) $CD4^+$T and $CD8^+$T cells, that were higher in relation to the controls ($p< 0.05$).
Conclusions: Secondary prophylaxis may help modify the natural history of VL in co-infection for individuals that are experiencing the first episode. The worsen capability of group 2 to downmodulate the activation levels in comparison with group 1, could be related to any functional impairment of effector response that was shaped at each previous relapses. Ongoing studies regarding the specific immune response may help clarify the different reactivation rate of VL in co-infected patients.

MOPEB169

Causes of hospitalization among people living with HIV/AIDS: a global review

C. Kirby[1], Z. Shubber[2], A. Calmy[3], G. Meintjes[4], S. Eholie[5], B. Grinsztejn[6], M.-A. Davies[4], L. Frigati[7], M. Vitoria[8], M. Doherty[8], N. Ford[8]
[1]Brighton and Sussex University, Brighton, United Kingdom, [2]Imperial College, London, United Kingdom, [3]Geneva University Hospital, Geneva, Switzerland, [4]University of Cape Town, Cape Town, South Africa, [5]CHU de Treichville, Abidjan, Cote D'Ivoire, [6]Fundação Oswaldo Cruz, Sao Paulo, Brazil, [7]Tygerberg Hospital, Stellenbosch, South Africa, [8]World Health Organization, Geneva, Switzerland
Presenting author email: fordn@who.int

Background: Mortality and morbidity due to HIV/AIDS has fallen globally as access to antiretroviral therapy has increased. Nevertheless, HIV remains a heading cause of hospitalisation, particularly in resource-limited settings. We assessed causes of hospitalization among people living with HIV/AIDS (PLHIV/AIDS) globally and by region, with a particular focus on 2007 onwards.
Methods: 6 databases were systematically reviewed from inception to 01 December 2014 for studies publishing causes of hospitalization among PLHIV/AIDS, provided they included data after 01 January 2007. Diseases were grouped according to the ICD-10 classification, and proportions pooled using random effects models.
Results: 79 cohorts, reporting data from 35 countries contributed to the analysis, including 40,608 adults and 4,459 children. The majority (51) of cohorts reported data exclusively post 2007. AIDS-defining illnesses remained the leading cause of hospitalization across all income categories, accounting for over a third of all hospitalizations. Among adults, tuberculosis (TB, 12.8%) and non-TB bacterial infections (29.5%) were leading causes of hospitalisation; this was similar across all settings. Other conditions accounting for over 5% of hospitalizations included renal disease (8.6%), cardiovascular disease (5.8%) and liver disease (5.7%) (Figure);



[Figure]

Cardiovascular and liver diseases were more important in high and upper middle-income settings. Among children, the leading causes were TB (14.1%), bacterial infections (45.6%), haematological disorders (18.0%), malnutrition (wasting and stunting, 17.6%), and malaria (6.3%).
Conclusions: At global level, infectious diseases, including TB and other bacterial infections, remain a leading causes of hospitalization among adults and children living with HIV. In high and middle-income settings, cardiovascular and liver disease accounts for an important proportion of cases.

MOPEB170

Incidence of malaria by cotrimoxazole use in HIV-infected Ugandan patients on antiretroviral therapy: a randomized placebo controlled study

R.P. Kasirye[1,2], K. Baisley[2], P. Munderi[1], J. Levin[1], Z. Anywaine[1], A. Nunn[3], A. Kamali[1], H. Grosskurth[2]
[1]MRC/UVRI Uganda Research Unit on AIDS, Entebbe, Uganda, [2]London School of Hygiene and Tropical Medicine, Infectious Disease Epidemiology, London, United Kingdom, [3]MRC Clinical Trials Unit at University College London, London, United Kingdom
Presenting author email: ronniekasirye@yahoo.com

Background: Previous trials have shown an increase in malaria incidence among HIV-infected patients on antiretroviral therapy (ART) who stop cotrimoxazole (CTX) prophylaxis; however these trials were not blinded. We investigated the effect of stopping CTX on malaria in HIV-infected patients on ART in a placebo-controlled trial (COSTOP-ISRCTN44723643).
Methods: HIV-infected adults on ART and CTX with CD4 cell count (CD4) ≥250 cells/μl were randomized (1:1) to continue CTX prophylaxis or receive matching placebo CTX. Participants were seen monthly for the first 3 months and 3 monthly thereafter and whenever they were ill. Follow-up was 12-38 months. Malaria was defined as fever and a positive blood slide, and considered severe if a participant had ≥1 clinical or laboratory feature of severity or was admitted to hospital for malaria. The incidence of all malaria episodes and rate ratios (RR) were estimated using random effects Poisson regression. Follow-up time was split into bands to investigate interaction of treatment with time. CD4 counts were stratified into ≥250 to < 350 and ≥350 to investigate the effect of enrolment CD4.
Results: 2180 participants were enrolled. 453 malaria episodes were recorded among 362 participants (range 1-5 episodes/participant). Median follow-up was 2.5 years; malaria incidence was 9.1/100person-years (pys) (95%CI=8.2-10.1) and was higher in patients on placebo (RR 3.47 (CI=2.74-4.39)). The effect of stopping CTX was similar by enrolment CD4 (≥250 to < 350 versus ≥350) (interaction p-value=0.27). Malaria incidence reduced over time (from 17.3/100pys in the first year in the placebo arm to 9.0/100pys after two years, P< 0.001); the effect of stopping CTX reduced slightly with time (interaction p-value=0.097). 15 patients experienced severe malaria (< 1%); overall incidence of severe malaria was 0.33/100pys (CI=0.20-0.55). There was one malaria related death (CTX arm).
Conclusions: Participants on ART who stopped CTX had 3.5 times more malaria episodes than those who continued; this rate difference is expected given the antimalarial properties of CTX and is significantly lower than previously reported. Only 1.2% of participants on placebo had severe malaria implying a need to carefully review the necessity of CTX prophylaxis to prevent malaria in ART treated individuals.

Syphilis

MOPEB171

Repeat syphilis among HIV-infected patients: a nationwide population-based cohort study in Taiwan

Y.-C. Chen[1], N.-Y. Lee[2], C.-W. Li[3], H.-Y. Liu[3], N.-Y. Ko[4], W.-C. Ko[3]
[1]International Cheng Kung University, Institute of Allied Health Sciences, Tainan, Taiwan, Province of China, [2]National Cheng Kung Hospital, Medicine, Tainan, Taiwan, Province of China, [3]National Cheng Kung Hospital, Tainan, Taiwan, Province of China, [4]National Cheng Kung University, Tainan, Taiwan, Province of China
Presenting author email: yenchin2427@gmail.com

Background: Among the individuals with human immunodeficiency virus (HIV) infection, syphilis is an important sexually transmitted disease (STD) and repeat infections are common. Identifying risk factors for and delineating the trends in repeat syphilis are essential for STD and HIV prevention.
Methods: A population-based cohort design was used, in which the Taiwan National Health Insurance Research Database from 2000 to 2010 was applied to identify 13,239 patients with HIV infection and 4,907 (39.1%) with regular syphilis screen tests. The syphilitic cases was defined by the International Classification of Disease, Ninth Revision, Clinical Modification, in combination with the prescription of antimicrobial therapy for syphilis. The Poisson regression test was used to identify risk factors for repeat syphilis.

Results: Of 4,907 patients with annual screen tests, 956 (19.5%) had an episode of syphilis and 524 (10.7%) repeat syphilis. The annual trend in repeat syphilis showed a significant increase in the study period (β = 0.23, p <0.001). The incidence rate of repeat syphilis was 3.3 (95% CI, 2.8-3.9) per 100 patient-years (PYs) in the second year after HIV diagnosis and 10.7 (95% CI, 6.9-16.6) per 100 PYs in the 11th year. By the Poisson regression models analysis, the individuals associated an increasing risk of repeat syphilis included 15-24 years of age at HIV diagnosis, male, a lower income, non-opioid dependence, a history of STDs, and more syphilis screening tests. The receipt of antiretroviral therapy with an adherence rate of ≥85% was associated with a reduced risk of repeat syphilis.
Conclusions: Individuals with repeat syphilis may represent a core group of STIs. Adherence to antiretroviral therapy is associated with a reduced risk of repeat syphilis among HIV-infected patients.

MOPEB172

The rapid syphilis test: is it useful for syphilis diagnosis among HIV-vulnerable groups? The Argentinean experience

A. Duran[1], L. Gallo Vaulet[2], M. Rodriguez Fermepín[2], R. Casco[3], D. Rossi[4], R. Marone[5], G. Orellano[6], M. Romero[7], C. Petracca[8], E. Benedetti[9], M.M. Avila[10], H. Salomón[10], M.A. Pando[10]
[1]Coordinacion SIDA, Ministerio de Salud, Buenos Aires, Argentina, [2]Laboratorio de Inmunología y Virología Clínica, Hospital de Clínicas José de San Martín, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, Buenos Aires, Argentina, [3]Programa de Enfermedades de Transmisión Sexual (PETS), Hospital de Clínicas José de San Martín, Universidad de Buenos Aires, Buenos Aires, Argentina, [4]Intercambios AC, Buenos Aires, Argentina, [5]Nexo AC, Buenos Aires, Argentina, [6]Asociación de Mujeres Meretrices de Argentina (AMMAR), Buenos Aires, Argentina, [7]Asociación de Travestis Transexuales y Transgéneros de Argentina (ATTTA), Buenos Aires, Argentina, [8]Programa de VIH-Sida e ITS, Municipalidad de San Martín, San Martín, Argentina, [9]Hospital en Red Especializado en Salud Mental y Adicciones (ex CENARESO), Buenos Aires, Argentina, [10]Instituto de Investigaciones Biomédicas en Retrovirus y SIDA (INBIRS), Buenos Aires, Argentina
Presenting author email: mpando@fmed.uba.ar

Background: In Argentina, syphilis, caused by infection with Treponema pallidum, subsp. pallidum, has been reported in high prevalence in HIV-vulnerable groups. A new syphilis-rapid test (RT) has recently been approved in the country. In order to evaluate this RT, it was included in the syphilis diagnoses algorithm during a cross sectional prevalence study among vulnerable groups.
Methods: A cross-sectional syphilis and HIV prevalence study was conducted at different settings (non-governmental organizations, hospitals and field visits) (September 2013-May 2014). Men who have sex with men (MSM), female transgender/travesties, drug users (DU) and female sex workers (FSW) were included. Syphilis diagnosis was done using: Alere Determine Syphilis TP, VDRL, TPHA and FTA. HIV diagnosis was also done (Allere Determine HIV-1/2, Genscreen Ultra HIV Ag&Ab, bDNA Versant HIV RNA).
Results: 1517 individuals were tested. Comparison of syphilis-RT with standard laboratory diagnosis showed that 53 samples non-reactive for syphilis-RT were positive for syphilis according to other laboratory tests. Among these, 16 had reactive TPHA, 5 had reactive VDRL/FTA and 31 had both. Seventeen samples that were reactive for syphilis-RT were confirmed as negative by standard laboratory. Sensitivity and specificity for syphilis RT was 81.3% and 98.8% respectively (PPV: 93.1%, NPV: 96.4%). Prevalence of syphilis was 17.7% (179/1014, 95% CI 15.2-20.0) for MSM, 47.3% (78/165, 95% CI 39.3-55.2) for transgender/travesties, 7.7% (20/259, 95% CI 4.3-11.2) for DU and 14.1% (11/78, 95% CI 5.7-22.5) for FSW. Co-infection with HIV was detected among 17,0% transgender/travesties, 4.2% MSM and 0.8% DU. In few patients clinical data were obtained: 78.2% (43/55) with reactive RT and 90% (10/11) with no-reactive RT (but reactive by laboratory assays) presented clinical manifestations that justified penicillin treatment.
Conclusions: Early detection and treatment of syphilis is critical in preventing severe long-term complications, co-infection with agents like HIV and transmission to sexual partners. Syphilis-RT implementation could aid early diagnosis. Since treponemal RT cannot distinguish between active and past infection, treatment of all RT-positive individuals will result in over-treatment. However, given the high prevalence of infection in vulnerable groups and the serious consequences of missed treatment, the benefits of syphilis-RT implementation should be considered in some settings.

MOPEB173

What men don't know *can* hurt them. Prospective survey on syphilis knowledge and behaviours in the ANRS CO3 Aquitaine cohort of HIV-infected men, 2014

A. Valdes[1,2], C. Cazanave[3], F. Dabis[1,2], D. Neau[3], D. Lacoste[2,4], V. Gaborieau[5], S. Farbos[6], M. Dworkin[1,7], Groupe D'épidémiologie Clinique du Sida en Aquitaine (Gecsa)
[1]INSERM U 897, ISPED, Université de Bordeaux, Bordeaux, France, [2]COREVIH Aquitaine, Bordeaux, France, [3]Service de Maladies Infectieuses et Maladies Tropicales, Hôpital Pellegrin, Centre Hospitalier Universitaire (CHU), Bordeaux, France, [4]Service de Médecine Interne, Hôpital Saint-André, CHU de Bordeaux, Bordeaux, France, [5]Service de Médecine, Hôpital François Mitterrand, Pau, France, [6]Centre Hospitalier de la Côte Basque, Bayonne, France, [7]School of Public Health, University of Illinois at Chicago, Chicago, United States
Presenting author email: francois.dabis@u-bordeaux.fr

Background: The incidence of syphilis among HIV-infected men who have sex with men (MSM) has risen substantially in the last 15 years in France, including in the Aquitaine (South-western) region. We investigated sexual behaviour and knowledge about syphilis in persons living with HIV (PLHIV) in care in the ANRS CO3 Aquitaine Cohort to better understand this trend and inform future interventions.
Methods: An anonymous self-administered questionnaire was proposed to all male PLHIV attending seven Aquitaine Cohort clinics between September 22nd and October 24th, 2014. Knowledge, attitudes and behaviours towards syphilis were explored.
Results: Among 302 patients surveyed, all were under ART. 34% of respondents (n=298) reported having syphilis at least once and were more often aware that a "skin rash" (RR=1.67 [1.23-2.27]) and "sore on skin" (RR=1.83 [1.35-2.47]) were syphilis symptoms than those who never had syphilis. Sixty-nine patients (23.5%) reported using recreational drugs for intercourse and had more often a history of syphilis (RR=1.62 [1.18-2.22]) than non-users. Less than half (43.5%; n=292) were aware that syphilis increases HIV transmission; 20.7% (n=300) thought that syphilis could not be contracted more than once and 31.1% (n=299) were unaware that syphilis could be transmitted by oral sex. About half of all respondents (51.5; n=272) estimated that their risk of getting syphilis was very low or non-existent. A majority (56.4%; n=156) did not know that syphilis was increasing in MSM in South-western France. Among patients reporting having sex with men in the last 12 months (n=160), 70.6% reported rarely or never using condoms for oral intercourse whereas 71.9% reported using often or always condoms for anal intercourse; 58.8% were ready to change their sexual behaviour if they were informed that syphilis was more diagnosed among MSM.
Conclusions: These preliminary findings reveal misinformation about syphilis among PLHIV in care in Aquitaine and potential receptiveness to behavioural change if informed.

Other sexually transmitted infections (including herpes simplex infection)

MOPEB174

Vaginal cytomegalovirus shedding before and after initiation of antiretroviral therapy in Rakai, Uganda

S. Gianella Weibel[1], A.D. Redd[2], M.K. Grabowski[3], A.A.R. Tobian[4], D. Serwadda[5], K. Newell[6], E.U. Patel[7], S. Kalibbala[8], P. Ssebbowa[8], R.H. Gray[3], T.C. Quinn[2], S.J. Reynolds[9]
[1]University of California San Diego, Medicine, La Jolla, United States, [2]Johns Hopkins University and National Institutes of Health, Medicine, Bethesda, United States, [3]Johns Hopkins University, Bloomberg School of Public Health, Epidemiology, Baltimore, United States, [4]Johns Hopkins University and Bloomberg School of Public Health, Epidemiology and Pathology, Baltimore, United States, [5]Institute of Public Health, Makerere University, Rakai Health Sciences Program, Rakai, Uganda, [6]Frederick National Laboratory for Cancer Research, Clinical Research Directorate/Clinical Monitoring Research Program, Frederick, United States, [7]National Institute of Allergy and Infectious Diseases, Division of Intramural Resea, Bethesda, United States, [8]Rakai Health Sciences Program, Entebbe, Uganda, [9]Johns Hopkins University, National Institute of Allergy and Infectious Diseases, Rakai Health Sciences Program, Medicine, Bethesda, United States
Presenting author email: gianella@ucsd.edu

Background: Asymptomatic genital cytomegalovirus (CMV) replication in HIV-infected men is associated with increased systemic inflammation, HIV disease progression, end-organ disease and transmission of both viruses. Fewer data are available about the frequency of CMV shedding in the genital tract of HIV-infected women, or about factors affecting vaginal CMV shedding.
Methods: Vaginal shedding of CMV was measured among 96 women co-infected with HIV, herpes simplex type-2 (HSV-2) and CMV who began anti-retroviral therapy (ART) during a placebo-controlled trial of HSV-2 suppression with acyclovir in Rakai, Uganda. Monthly vaginal

swabs from 6 months before to 6 months after ART initiation were tested for HSV-2 and CMV DNA using a real-time quantitative PCR assay (n=1080). Poisson regression models with generalized estimating equations and robust variance were used to estimate prevalence risk ratios (PRR) of vaginal CMV shedding.

Results: Shedding of CMV was detected in at least one monthly visit among 75 of the 96 women (78.0%) and 379 of the 1080 individual visits (35.1%). In univariate analysis, ART status (PRR: 1.34 [95% confidence interval (CI): 1.13-1.59], p=0.001), younger age (PRR: 0.05 [95%CI: 0.01-0.18], p< 0.001), higher baseline plasma HIV RNA viral load (PRR: 2.00 [95%CI: 1.19-3.38], p=0.009), and presence of vaginal HSV-2 DNA the month preceding CMV shedding (PRR: 1.20 [95%CI: 1.00-1.44], p=0.05), were associated with detectable CMV DNA in vaginal swabs. CD4 count prior to ART initiation, study arm (acyclovir versus placebo), and HSV-2 shedding during the same month were not associated with increased CMV shedding. In a multivariate analysis, ART status (PRR: 1.34 [95%CI: 1.13-1.59], p=0.001), higher HIV viral load (PRR: 1.84 [95%CI: 1.09-3.11], p=0.02) and younger age (PRR: 0.05 [95%CI: 0.01-0.18], p< 0.001), remained significantly associated with higher frequency of CMV shedding. HSV-2 shedding the month prior was not significantly associated with CMV shedding after adjustment. Compared to pre-ART levels, CMV shedding peaked from month two to four after ART initiation (p< 0.01).

Conclusions: CMV DNA shedding significantly increased after ART initiation and may be associated with subclinical immune reconstitution inflammatory syndrome (IRIS). Further studies are needed to determine the clinical significance and long-term effects of asymptomatic CMV reactivation in ART-treated HIV-infected individuals.

Prophylaxis for HIV-associated infections

MOPEB175

Safety and immunogenicity of yellow fever vaccine in HIV+ patients: ANRS EP46 NOVAA

N. Colin de Verdière[1], V. Meiffrédy[2], C. Durier[2], O. Launay[3], S. Matheron[4], S. Mercier-Delarue[5], A. Boulay[5], J.-M. Molina[1], F. Simon[5], ANRS EP46 NOVAA Group
[1]Saint-Louis Hospital , APHP, Infectious Diseases, Paris, France, [2]SC10-US019, INSERM, Villejuif, France, [3]Cochin Hospital, APHP, CIC de Vaccinologie Cochin Pasteur, Paris, France, [4]Bicêtre Hospital, AP-HP, Infectious Diseases, Paris, France, [5]Saint-Louis Hospital, APHP, Microbiology, Paris, France

Background: Yellow fever vaccine (YFV) uses a live attenuated viral strain and is contraindicated in HIV-infected patients with <200 CD4 cells/mm3. Whether YFV is safe and efficacious in patients with higher CD4 count remains to be clarified. We performed a prospective, comparative, non randomized study to assess safety and immunogenicity of YFV in uninfected (HIV−) and HIV-infected (HIV+) adults with CD4 count >350/mm3.

Methods: 40 YFV-naïve HIV+ adults under antiretroviral therapy (ART) with CD4 >350/mm3 and plasma HIV RNA < 50 cp/ml for at least 6 months, and 31 HIV− healthy adults received primary vaccination with YFV 17D strain. Follow-up was performed at day 7, 14, 28, 91, 365. Safety was assessed by grading clinical and biological adverse events (AEs), detection of YFV viremia using RTPCR, CD4 count and plasma HIV RNA levels. Serologic response was assessed by neutralizing antibody titers using a reference plaque reduction neutralizing test (PRNT) and a new pseudotype based neutralization assay, with protection associated titers >10 and >95% neutralizing activity, respectively.

Results: At baseline, HIV+ subjects were mostly male (95%), median age: 44 years, median CD4: 702/mm3 (IQR 553, 840), 23% were CDC stage C. HIV− patients were mostly female (88%), median age: 35 years, median CD4: 902/mm3 (IQR 635, 1247). Adverse events were reported by 42% of HIV− and 30% of HIV+, mostly headaches, asthenia, myalgia and local reactions of grades 1 or 2. None of the 3 SAE reported, with 1 death, was related to vaccination.76% of HIV− and 82% of HIV+ subjects had positive YFV viremia at D7 only. There was a significant decrease in CD4 count in both groups at D7 which was more pronounced in HIV− than in HIV+ patients (261.5 vs 111.5 cells decrease from baseline, respectively, p=0.0003). There was no HIV breakthrough during follow-up. All patients (100%) in both arms developed protective neutralizing antibody levels with both assays since day 28 and for a year after injection.

Conclusions: In HIV+ patients with CD4 >350/mm3 and suppressed viral replication on ART, YFV was as safe and immunogenic as in HIV− subjects. Long-term follow-up will tell whether protection is maintained over time.

Immune reconstitution disorders / immune reconstitution inflammatory syndrome (IRIS)

MOPEB176

High CRP and low hemoglobin predict IRIS in a prospective multicenter international study

V. Sheikh[1], F. Sawe[2], D. Shaffer[2], B. Agan[3,4], A. Pau[1], R. DerSimonian[1], J. Wang[5], G. Roby[1], A. Rupert[5], N. Phanuphak[6,7], N. Chomchey[7], S. Tansuphaswadikul[8], J. Ananworanich[3], I. Sereti[1]
[1]National Institutes of Health (NIH), National Institute of Allergy and Infectious Diseases (NIAID), Bethesda, United States, [2]Kenyan Medical Research Institute (KEMRI)/Walter Reed Program (WRP) Clinical Research Center, Kericho, Kenya, [3]Walter Reed Army Institute of Research, U.S. Military HIV Research Program, Silver Spring, United States, [4]Henry M. Jackson Foundation for the Advancement of Military Medicine, Bethesda, United States, [5]Leidos Biomedical Research, Inc, Frederick, United States, [6]The Thai Red Cross AIDS Research Centre, Bangkok, Thailand, [7]SEARCH, Bangkok, Thailand, [8]Bamrasnaradura Infectious Diseases Institute, Department of Medicine, Nonthaburi, Thailand
Presenting author email: isereti@niaid.nih.gov

Background: Initiation of ART in severely lymphopenic HIV+ patients may be complicated by a dysregulated inflammatory response to a pre-existing (paradoxical) or subclinical (unmasking) infection known as immune reconstitution inflammatory syndrome (IRIS). The pathogenesis of IRIS is unclear and there are no available clinical prediction criteria.

Methods: IRIS was a prospective, multi-center, international study conducted in the US, Thailand (THAI) and Kenya (KEN) which enrolled HIV-infected individuals naïve to HIV therapy with CD4<100 cells/μL, between 2006 and 2014 (NCT00286767). The primary endpoints were incidence and predictors of IRIS in the 24 weeks following ART initiation. IRIS events were adjudicated by an independent end point committee using the ACTG criteria. Wilcoxon rank-sum, Fisher's Exact tests, and logistic regression were used for analysis.

Results: 506 individuals were enrolled; 206 in US, 100 in THAI and 200 in KEN with characteristics as shown in the table. There were 109 IRIS events, occurring in 97 (19.2%) individuals (23.8% US, 16.5% KEN, 15.0% THAI) at a median of 27 (IQR 14-54) days after ART initiation. Of these, 31.2% were TB IRIS, 16.5%, MAC IRIS, 33.0% viral IRIS, and 16.5% fungal IRIS. 47 participants (9.3% total, 9% US, 14.5% KEN, 10% THAI) died: 14.4% with IRIS vs 8.1% without IRIS (p=0.077).

At baseline, those who would develop IRIS had lower Hgb (10.0 vs 11.2 g/dL, p=<0.001), CD4 count (22 vs. 30 c/mcl, p=0.025) and CD8 count (357 vs 478 c/mcl, p=0.029) and higher plasma HIV viremia (5.37 vs 5.28 $\log_{10}$ c/ml, p=0.039), D-dimer (1.54 vs 0.99 μg/ml, p=<0.001) and CRP levels (9.06 vs 4.11 mg/L, p=0.001).

Having TB was also associated with IRIS (41.0% vs 15.2%, p=<0.001). Low Hgb (<10 g/dL) combined with CRP levels >5 mg /L remained an independent predictor of IRIS (39% vs 16 %, p=<0.001) after adjusting for TB, age and site.

	All (n=506)	US (n=206)	KEN (n=200)	THAI (n=100)	KEN vs THAI (p value)	KEN vs US (p value)	THAI vs US (p value)
Age (years)	37 (31-45)	38 (31-46)	36 (32-42)	36.5 (31-35)	0.417	0.067	0.566
Male (n,%)	307 (60.7%)	150 (72.8%)	95 (47.5%)	62 (62%)	**0.02**	**<0.001**	0.064
CD4 (cells/μl)	29 (11-56)	19 (8-46)	35 (14-61)	29 (12.5-55.5)	0.296	**<0.001**	**0.03**
CD8 (cells/μl)	457.5 (273-739.5)	412 (263-611)	530 (318-889)	481 (273-711)	**0.002**	**<0.001**	0.25
HIV VL (log10 c/ml)	5.3 (4.9-5.7)	5.1 (4.7-5.5)	5.4 (5.1-5.8)	5.4 (5.1-6.0)	0.050	**<0.001**	**<0.001**
Hgb (g/dL)	10.9 (9.6-12.4)	10.6 (9.7-12)	11.2 (9.8-12.8)	10.5 (9.0-12.5)	0.05	0.082	0.312
CRP (mg/L)	5.0 (1.3-16.7)	3.8 (0.9-10.2)	8.7 (1.6-37.3)	3.6 (1.1-13.6)	**0.002**	**<0.001**	0.475
D-dimer (mg/L)	1.4 (0.62-2.12)	0.97 (0.56-1.96)	1.18 (0.7-2.16)	0.96 (0.58-2.25)	0.180	**0.032**	0.801
IRIS (n,%)	97 (19.2%)	49 (23.8%)	33 (16.5%)	15 (15.0%)	0.877	0.083	0.098

[Baseline Variables & Outcomes (median with IQR)]

Conclusions: In this large cohort of severely lymphopenic HIV patients from 3 continents, we found that IRIS is common, and is frequently associated with TB. Anemia with high CRP levels may help identify at risk patients who may benefit from closer follow up or preventive interventions.

MOPEB177

Cryptococcal immune reconstitution inflammatory syndrome in HIV-infected Ugandans is associated with memory T cell phenotype and increased GXM capsule-specific cytokine responses

D. Meya[1,2,3], S. Okurut[4], P. Brent[5], G. Zziwa[4], S. Cose[6,7], P. Bohjanen[2], D. Boulware[2], Y. Manabe[8], E. Janoff[5,9]
[1]Infectious Diseases Institute, Research Department, Kampala, Uganda, [2]University of Minnesota, Medicine, Minneapolis, United States, [3]College of Health Sciences, Makerere University, Medicine, Kampala, Uganda, [4]Makerere University Walter Reed Project, Research Department, Kampala, Uganda, [5]Mucosal and Vaccine Research Program Colorado (MAVRC), University of Colorado, Denver, United States, [6]London School of Hygiene and Tropical Medicine, London, United Kingdom, [7]MRC/UVRI Uganda Research Unit on AIDS, Entebbe, Uganda, Kampala, Uganda, [8]Johns Hopkins University, Medicine, Baltimore, United States, [9]Denver Veterans Affairs Medical Center, Denver, United States
Presenting author email: david.meya@gmail.com

Background: Immune Reconstitution Inflammatory Syndrome (IRIS) occurs in up to 30% of HIV-infected patients with cryptococcal meningitis (CM), and is proposed to result from exaggerated immune responses upon initiation of antiretroviral therapy (ART). T cell responses in the immunopathogenesis of cryptococcal IRIS (CM-IRIS) are not well understood.
Methods: We assessed in vitro cytokine responses to cryptococcal Glucuronoxylomannan (GXM) capsular antigen in circulating T cells from 17 subjects with CM in Kampala, Uganda at CM diagnosis and the time of CM-IRIS (n=11) or a matched time for CM controls without IRIS (Controls) (n=6). We quantified T cell memory and activation phenotypes and measured intracellular interleukin (IL)-2, IL-17 and interferon-γ (IFN-γ) cytokine expression by flow cytometry.
Results: At CM diagnosis, central memory $CD4^+$ T cells ($CD27^+CD45RO^+$) and naive $CD8^+$ T cells ($CD27^+CD45RO^-$) were the predominant T cell phenotypes among CM-IRIS patients and Controls. GXM-induced $CD4^+IFN\text{-}\gamma^+$ T cells were more frequent among the CM-IRIS group vs Controls (median 13% vs 2%, respectively; p = 0.028). $CD4^+$ and $CD8^+$ T cell activation (HLA-DR expression) was similar at baseline between CM-IRIS and Controls.
At the time of CM-IRIS and the matched time point, $CD4^+$ central memory and $CD8^+$ effector memory ($CD27^-CD45RO^+$) T cells predominated among both groups. Subjects with CM-IRIS had a lower frequency of $CD4^+$ T cells vs CM Controls (median 6% vs 14%; p = 0.039) and a higher frequency of total $CD8^+$ T cells (median 95% vs 85% p = 0.018). Upon stimulation with GXM, subjects with CM-IRIS more frequently expressed poly-functional $IL\text{-}2^+/IL\text{-}17^+$ $CD4^+$T cells vs CM Controls (0.24% vs 0.02%,
p= 0.047). GXM-induced IL-2 responses were also more robust among $CD8^+$ central and effector memory T cells at CM-IRIS compared with paired patient-matched CM diagnosis cells and with time-matched CM-Control samples.
Conclusions: $CD4^+$ T cells from patients who later developed CM-IRIS appeared primed for response at baseline with increased GXM-induced IFN-γ. Indeed, polyfunctional T cells were also increased with GXM stimulation at the time of IRIS. Thus, distinct functional T cell cytokine responses to GXM may both predict and characterize CM IRIS.

Therapeutic vaccine trials

MOPEB178

HIV-1 reservoir dynamics after vaccination and antiretroviral therapy interruption are driven by dendritic cell-vaccine induced T cell responses

C. Andrés[1], M. Plana[1], A.C. Crespo[1], C. Alvarez-Fernandez[1], N. Climent[1], C. Gil[1], T. Gallart[1], A. León[2], B. Clotet[3], B. Autran[4], N. Chomont[5], J.M. Gatell[2], S. Sanchez-Palomino[1], F. García[2], DCV2/MANON07-ORVACS Study Group
[1]Hospital Clinic, IDIBAPS, University of Barcelona, Retrovirology and Viral Immunopathology Laboratory, Barcelona, Spain, [2]Hospital Clinic, IDIBAPS, University of Barcelona, Infectious Diseases Department, Barcelona, Spain, [3]AIDS Research Institute IrsiCaixa, Institut d'Investigació en Ciències de la Salut Germans Trias i Pujol, Universitat Autònoma de Barcelona, Badalona, Spain, [4]INSERM UMR-S 945 - Université Paris VI Pierre et Marie Curie. Hôpital Pitié-Salpêtrière, Paris, France, [5]Vaccine and Gene Therapy Institute Florida, Port St Lucie, United States
Presenting author email: fgarcia@clinic.ub.es

Background: We recently reported a peak decrease of viral set-point of 1.2 log10 associated with an increase in HIV-1-specific T cell responses in HIV infected individuals receiving autologous myeloid derived dendritic cells (MDDC) pulsed with autologous heat-inactivated whole HIV. Here we assessed if the HIV specific immune responses induced by the vaccine might have cleared some of the reservoir and drove the dynamics of replenisment of viral reservoir during the antiretroviral therapy (cART) interruption.
Methods: We measured total and integrated HIV-1 DNA in isolated CD4 T cells in 36 patients on cART randomized to receive 3 immunizations with MDDC pulsed with autologous HIV-1 (n=24) (DC-HIV-1) or with non-pulsed MDDCs (n=12) (DC-control) at 6 time-points: before any cART, before STOP1 (a first cART interruption 56 weeks before the first immunization to isolate virus for pulsing MDDCs), before and after vaccinations (VAC1 and VAC2) and at weeks 12 and 48 after second interruption of cART.
Results: Vaccinations did not influence HIV-1 DNA levels in vaccinated subjects. After cART interruption post-vaccination (week 12), while total HIV-1 DNA significantly increased in both vaccinees (n=24) and controls (n=12), integrated HIV-1 DNA did not change in vaccinees (1.8 to 1.9, p=0.22) and increased in controls (1.8 to 2.1, p=0.05) (p=0.03 for the difference between groups). HIV-1 specific T cells responses at VAC2 time-point were strongly and inversely correlated with total and integrated HIV-1 DNA after vaccination (r= -0.46, p=0.04 and r= -0.79, p<0.0001, respectively) and after cART interruption in vaccinees (r= -0.69, p=0.002 and r= -0.82, p<0.0001, respectively), while a direct correlation was observed in DC-controls (r= 0.72, p=0.03 and r= 0.67, p=0.05 total and integrated HIV-1 DNA after vaccination, respectively) and no correlations were found after cART interruption). These associations were mainly observed with HIV-1 specific T cell responses targeting gag p24 and p17 and nef antigens.
Conclusions: HIV-1 specific T cell immune responses elicited by therapeutic DC vaccines could drive changes in viral reservoir after vaccination and the replenishment of reservoir after cART interruption in chronic HIV-1 infected patients treated at early stages.

Nutrition and HIV

MOPEB179

Randomized control trial on the effect of protein supplementation and nutritional counseling on HIV-positive adults initiating antiretroviral therapy at Calcutta School of Tropical Medicine, India

A. Bhowmik[1], D. Chaudhuri[2], S.K. Guha[3], B.B. Rewari[4]
[1]Medical College and Hospital, Pediatric Centre of Excellence in HIV Care, Kolkata, India, [2]All India Institute of Hygiene and Public Health, Biochemistry and Nutrition, Kolkata, India, [3]School of Tropical Medicine, Tropical Medicine, Kolkata, India, [4]Department of AIDS Control, Government of India, Delhi, India
Presenting author email: ananya50@gmail.com

Background: Nutrition plays an important role in the treatment of HIV patients on antiretroviral therapy (ART). The basic ART package of Nation AIDS Control Organization of India includes free antiretroviral to all eligible clients and counseling services by trained counselors for psycho-social, adherence, nutrition and prevention counseling. The role of elaborate nutritional counseling and nutritional supplement on such patients remains unclear. Hence, this study was designed to observe the effect of the above interventions on PLHIV.
Methods: Three hundred ART naïve patients were randomly assigned to one of the four arms while starting ART. Arm-1 providing basic ART package as control arm, Arm-2 provided additional nutritional counseling, Arm-3 provided protein supplementation and Arm-4 provided both additional nutritional counseling and protein supplementation. The supplementation comprised of 16 gm of protein/ day and additional nutritional counseling was done by a clinical nutritionist by administration of 6 specifically developed modules for the study over a period of 6 months.
The patients were observed for 6 months. BMI, Triceps skin fold (TSF), mid upper arm circumference(MUAC), grip strength(GS), CD4, serum albumin, total protein, hemoglobin and food frequency data was collected at baseline and at the end of six months. SPSS 16.0 was used to do t test, ANOVA and LSD.
Results: All study parameters of Arm- 2, 3 & 4 were compared with those of the control arm (Arm-1) at 6 months(Table-1)

PARAMETERS	COUNSELLING ARM	SUPPLEMENT ARM	SUPPLEMENT & COUNSELLING ARM
Clinical stage	.042*	.000**	.036*
Body mass index	.184	.046*	.002**
Grip strength	.011**	.000**	.000**
Mid arm circumference	.220	.006**	.001**
CD4 count	.009**	.004**	.006**
Triceps skin fold	.977	.567	.321
Albumin	.020*	.000**	.000**
Haemoglobin	.025*	.040*	.004**

[t test between control arm and intervention arms]

Significant improvement in GS, CD4 count, clinical staging and haemoglobin levels was recorded in all three arms as compared to control. Frequency of consumption of protein and energy also increased on counseling in both Arm-2 and 4. Arm-4, having both supplement and counseling as interventions, showed significant improvement in CD4 count (p=0.02) and serum albumin (p=0.04) as compared to Arm-2 & 3 after 6 months.
Conclusions: Supplementation and counseling proved to improve the nutritional and immunological status of PLHIV initiating ART. Hence, counselors of ART centres need to be trained specifically on nutrition' focusing on protein consumption. In addition, nutritional supplementation will further improve the health status of PLHIV.

MOPEB180

Efficacy and acceptability of outpatient nutritional rehabilitation among HIV-infected Senegalese children and adolescents under active follow-up in pediatric care: a pilot study within the MAGGSEN ANRS12279 cohort study

M. Varloteaux[1], B. Ouattara[2], N.G. Have[3], P. Msellati[4], N. Mbaye[2], H. Sy Signate[3], C. Cames[1]
[1]IRD, UMI 233, Dakar, Senegal, [2]King Baudouin Hospital, Dakar, Senegal, [3]Albert Royer Hospital, Dakar, Senegal, [4]IRD, UMI 233, Montpellier, France
Presenting author email: marie.varloteaux@ird.fr

Background: Severe (SAM) and moderate (MAM) acute malnutrition is highly prevalent in HIV-infected children, even when antiretroviral treatment (ART) is initiated. Since 2007, the United Nations recommend ready-to-use therapeutic foods (RUTF) for the outpatient rehabilitation of children <5 years with MAS. However, nutritional interventions take a long time to be assessed in HIV-infected children and adolescents with the aim of their integration in the "global care" of HIV-infection. The objective was to describe the efficacy and acceptability of outpatient rehabilitation with RUTF (Plumpy Nut® and Plumpy Sup®), in compliance with international recommendations, among HIV-infected children attending 2 hospital facilities in Dakar.
Methods: Children aged 6 months to 18 years with MAS, defined as Body Mass Index (BMI) < -3z-scores, were prescribed Plumpy Nut® (200kcal/kg of body weight/day) and those with MAM, -3 ≤ BMI < -2z-scores were prescribed Plumpy Sup® (75kcal/kg/day), until they reached their target weight defined as BMI ≥ -1.5z-score. Children were seen at the study sites every 2 weeks from enrollment for anthropometric measurements, RUTF provision and counting of used and non-used previous sachets returned by the patient. Acceptability of the intervention was assessed at week 2 and 8.
Results: From April to October 2014, 44 (n=22 girls) children were included in the pilot study and 27 had successful outpatient rehabilitation.

	Children with SAM n=18	Children with MAM n=26
Median age, year	14.3	11.0
In school, n	11	17
ART at enrollment, n	14	22
Discharged at target weight, n	8	19
Median duration to target weight, week	17.5	11.0
Mean weight gain, g/kg/week	9.5	7.2
Exited for ART initiation, n	6	2
Discontinued, n	3	5
Died, n	1	0

[Table: Characteristics of HIV-infected children en]

Among these, organoleptic acceptability of and adherence to RUTF were satisfactory but declined; notably in children with MAS, as rehabilitation duration increased. Eight children who failed to gain weight during the intervention were provisionally exited and referred to hospital care and ART or second line treatment initiation. The main reasons for intervention discontinuation were school resumption and living too far from the hospital. Overall, stigmatization and family leakage associated with RUTF provision were low in this study
Conclusions: This pilot study provides the first data on outpatient nutritional rehabilitation of HIV-infected children >5 years and adolescents in sub-Saharan Africa. The results are encouraging and address the main issues and challenges of such intervention in this particular and vulnerable population. The next step is scaling-up of the research in Senegal within the SNAC'S study, to start in 2015.

MOPEB181

Risk factors for mortality among malnourished HIV-infected adults eligible for antiretroviral therapy

S. Woodd[1], P. Kelly[2,3], J. Koethe[4], G. PrayGod[5], A. Rehman[1], M. Chisenga[3], J. Siame[3], D. Heimburger[4], H. Friis[6], S. Filteau[1]
[1]London School of Hygiene & Tropical Medicine, London, United Kingdom, [2]Barts & the London School of Medicine and Queen Mary University of London, London, United Kingdom, [3]University Teaching Hospital, Lusaka, Zambia, [4]Vanderbilt University, Nashville, United States, [5]National Institute for Medical Research, Mwanza, Tanzania, United Republic of, [6]University of Copenhagen, Copenhagen, Denmark
Presenting author email: john.r.koethe@vanderbilt.edu

Background: While many studies have reported risk factors for early mortality in patients starting ART, to our knowledge none have studied a large cohort of malnourished patients and included the high-risk period, usually 2-3 weeks in Africa, between referral for antiretroviral therapy (ART) and actually starting ART. We used the extensive data collected during the Nutritional Support for Africans Starting Antiretroviral Therapy (NUSTART) trial to increase understanding of this vulnerable population in the pre-ART and early ART period.
Methods: We analysed potential baseline risk factors from a randomised, double blind, controlled phase-III clinical trial in Lusaka, Zambia and Mwanza, Tanzania. Malnourished patients (n=1815; body mass index [BMI] < 18.5 kg/m^2) were recruited at referral to ART into a two-stage nutritional rehabilitation programme, randomised to receive a lipid-based nutrient supplement with or without added micronutrients. Demographics, measures of body composition, blood electrolytes and clinical conditions were investigated as potential risk factors for mortality using Cox regression models.
Results: The mortality rate from recruitment until 12 weeks after starting ART was 83.1 deaths/100 person-years (95% CI 75.0 to 92.1) and in the pre-ART period was particularly high at 110.9 (95% CI 94.5 to 130). In adjusted analyses low CD4 count, anaemia, high C-reactive protein and presence of oedema were risk factors for mortality throughout follow-up. Male sex and abnormal serum phosphate level carried a risk in the pre-ART period, while low BMI or mid-arm circumference had a stronger effect after starting ART. Being on TB treatment at recruitment was strongly protective (HR 0.46, 95% CI 0.32 to 0.66). Increased grip strength, a simple marker of functional lean mass, improved the chance of survival independent of BMI (HR 0.95 for every 1kg increase in strength, 95% CI 0.93 to 0.97) and mainly in the pre-ART period.
Conclusions: Mortality among this population of malnourished patients eligible for ART was extremely high, especially in the pre-ART period, pointing again to the need for earlier initiation of treatment. The positive effect of TB treatment suggests under-diagnosis of both TB and bacterial infections in this group. Grip strength measurement could be a useful tool in assessing risk among malnourished HIV patients.

MOPEB182

Malnutrition and pediatric HIV: prevalence and characteristics at inclusion from HIV-infected children enrolled in a nutritional protocol in Bamako, Mali

J. Jesson[1,2], A. Coulibaly[3], D. Masson[4], M. Sylla[3], C. Ndiaye[3], F. Dicko[3], V. Leroy[1,2]
[1]Institut de Santé Publique, d'Epidémiologie de de Développement (ISPED), Université de Bordeaux, Bordeaux, France, [2]Université de Bordeaux, Inserm U 897, Bordeaux, France, [3]Hôpital Gabriel Touré, Bamako, Mali, [4]Expertise France (Agence Française d'Expertise Technique Internationale), Département Santé, Paris, France
Presenting author email: julie.jesson@isped.u-bordeaux2.fr

Background: Malnutrition is highly prevalent among HIV-infected children in sub-Saharan Africa and nutritional care needs to be improved. The purpose of this study is to assess and describe the prevalence of malnutrition in a pediatric HIV care programme in Mali where a nutritional intervention is ongoing.
Methods: Between July and December 2014, HIV-infected children aged less than 15 years diagnosed with malnutrition during their routine follow-up in the University Hospital of Bamako, Mali, were included in a protocol to receive nutritional supplementation based on Ready-to-Use Therapeutic Food, and followed monthly until that they catch-up their growth. Malnutrition was determined using anthropometric indicators, expressed in Z-scores, according to the WHO child growth standards. Weight for Height Z-score (WHZ) for children < 5 years, and BMI for age Z-score (BAZ) for children ≥ 5 years, defined acute malnutrition, whereas Height for age Z-score defined chronic malnutrition. At inclusion, socio-demographic, immunological, viral, biological and treatment data were collected. Comparisons between children according to their nutritional status were made using Chi-square and Kruskal-Wallis tests.
Results: During the study period, 350 HIV-infected children were screened, of whom 200 (57%) were malnourished. Among them, 164 (82%) were enrolled in the nutritional protocol, 36 refused or lived outside of Bamako ; 13% of included children were followed for severe acute malnutrition, 45% for moderate acute malnutrition, 26% for moderate chronic malnutrition and 15% for severe chronic malnutrition. Median age was 9 years (EIQ: 6-12), 60% were boys, 40% were orphans; 96% were on antiretroviral therapy, with 42% of them on a protease-inhibitor based regimen; 99% were on cotrimoxazole. Twenty percent were severely immunodeficient,

median viral load was 109 (EIQ: 40-16900) copies/mL, 86% had anemia, median glucose and cholesterol rates were 4.3 (EIQ: 3.7-4.7) mmol/l and 3.7 (EIQ: 3.0-4.6) mmol/L respectively. The median age at ART initiation was higher in malnourished children than for non-malnourished children (4.4 years, EIQ 2.0-7.0 vs 2.2 years; EIQ: 1.4-4.6).
Conclusions: Prevalence of malnutrition was high in this pediatric HIV care center, highlighting the need to a nutritional support. Routine screening of malnutrition and appropriate care in HIV-infected children is needed to improve global pediatric HIV care.

MOPEB183

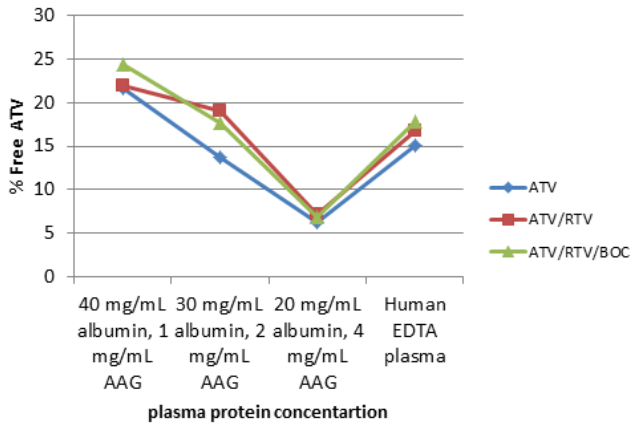
Plasma proteins binding of atazanavir and ritonavir with boceprevir

D.T. Chagwena, J. Hochreiter, R. DiFrancesco, G.D. Morse
NYS Center of Excellence in Bioinformatics and Life Sciences, Translational Pharmacology Research Core, Buffalo, United States
Presenting author email: tungadex@gmail.com

Background: HIV-1 protease inhibitors that are highly-bound to plasma proteins with high affinity to α1-acid glycoproteins (AAG) may be influenced by fluctuations in AAG due to HIV/HCV co-infection which in turn influence antiviral pharmacokinetics. Rapid equilibrium dialysis (RED) measures the free fraction of drugs using smaller sample volumes, increased sample throughput and is less labor intensive in comparison to tradition equilibrium dialysis procedures. RED procedure is more reproducible and less likely to be effected by nonspecific binding issues compared to ultrafiltration procedures. The objective was to validate an assay to measure the % free ATV in spiked human plasma. The effect of different concentrations of human albumin and AAG associated with different inflammatory and nutritional status and addition of boceprevir (BOC) and ritonavir (RTV) were also evaluated.
Methods: A novel approach to assimilate different inflammatory and nutritional status (normal, mild and severe hypoalbuminemia) was used. RED was performed for 22 hours at 37°C under rotation on samples that were pre-diluted with phosphate buffered saline (PBS). Both the plasma and buffered dialysates were measured for ATV using an ultra-performance liquid chromatography mass spectrometry method. The percent free was calculated as the ratio of the buffer to the plasma dialysate concentrations. After the RED method was optimized for human plasma, the effects of albumin and AAG concentration were investigated by adding ATV to different concentrations of proteins. Also tested was addition of RTV and BOC with ATV in human plasma of different albumin and AAG concentrations. As part of validation freeze/thaw cycles of plasma samples prior equilibrium dialysis were assessed.
Results: This method was accurate and precise within a concentration range of 1000 to 2.00 ng/mL for ATV. Free % ATV was related to the change in albumin and AAG concentration as opposed to addition of BOC and RTV.

		Mean % Free		
Drug	40 mg/mL albumin and 1 mg/mL AAG	30 mg/mL albumin and 2 mg/mL AAG	20 mg/mL albumin and 4 mg/mL AAG	Human EDTA plasma
ATV	21.6	13.7	6.23	15.1
ATV/RTV	22.0	19.0	7.14	16.8
ATV/RTV/BOC	24.4	17.7	6.92	17.8
Mean	22.7	16.8	6.77	16.5
STD	1.50	2.79	0.478	1.34
%CV	6.60	16.6	7.06	8.10

[Effects of plasma protein conc on % Free ATV]



[Percent free ATV in different plasma proteins conc]

Conclusions: The described validated RED method is accurate and precise in measuring ATV protein binding in human plasma. Care in processing and storing plasma samples must be considered due to lack of stability when samples are taken through freeze/thaw cycles. Our methodology facilitates analysis of samples from patients with different disease states and protein status.

MOPEB184

Serum zinc concentration and C-reactive protein in persons with human immunodeficiency virus infection in the Positive Living with HIV (POLH) study

K.C. Poudel[1], K. Poudel-Tandukar[2]
[1]School of Public Health and Health Sciences, University of Massachusetts Amherst, Department of Public Health, Amherst, United States, [2]School of Public Health and Health Sciences, University of Massachusetts Amherst, Department of Health Promotion and Policy, Amherst, United States
Presenting author email: krishna@schoolph.umass.edu

Background: Human Immunodeficiency Virus (HIV) infection has been frequently associated with zinc deficiency and chronic inflammation. Zinc deficiency can cause significant impairment in both adaptive and innate immune responses, and promotes systemic inflammation however no studies have investigated the association between serum zinc concentration and inflammation among HIV- positive people. To assess the association between serum zinc and C-reactive protein (CRP) concentration in a cohort of HIV-positive people.
Methods: A cross-sectional survey was conducted among 311 HIV-positive people (177 men and 134 women) aged 18-60 years residing in Kathmandu, Nepal. Serum CRP and zinc concentrations were measured by the latex agglutination turbidimetric method and the atomic absorption method, respectively. Relationships were assessed using multiple linear regression analysis.
Results: The geometric mean of serum zinc concentration in men and women were 73.83 ug/dL and 71.93 ug/dL, respectively, and of serum CRP concentrations were 1.63 mg/L and 0.96 mg/L, respectively. In multiple regression analysis, we found a significant inverse relation between log zinc and log CRP concentrations (beta for 1 unit change in log zinc; β = -1.56, p = 0.001). In sex-specific analysis, an inverse association between zinc and CRP concentrations was slightly stronger in women (β = -2.64, p = 0.008) than in men (β = -1.27, p = 0.03).
Conclusions: Serum zinc concentration is inversely associated with serum CRP concentrations in HIV-positive people. Further prospective study to confirm the role of zinc in inflammation among HIV-positive people is warranted.

Pharmacokinetics and outcomes of ARV in women during and after pregnancy

MOPEB185

Maternal tenofovir disproxil fumarate (TDF) use in pregnancy not associated with adverse growth outcomes at 6 weeks and 9 months among Kenyan HIV-exposed uninfected infants

J. Pintye[1], A. Langat[1], B. Singa[2], J. Kinuthia[1,3], B. Odeny[1], A. Katana[4], L. Nganga[4], G. John-Stewart[1], C. McGrath[1,5]
[1]University of Washington, Department of Global Health, Seattle, United States, [2]Kenya Medical Research Institute, Nairobi, Kenya, [3]Kenyatta National Hospital, Nairobi, Kenya, [4]Centers for Disease Control and Prevention (CDC), Nairobi, Kenya, [5]University of Texas, Medical Branch, Galveston, United States
Presenting author email: jillian.pintye@gmail.com

Background: Tenofovir disproxil fumarate (TDF) is commonly used in antiretroviral treatment (ART) and in pre-exposure prophylaxis (PrEP) regimens. Accruing TDF safety data among infants exposed to TDF in pregnancy is important, especially in sub-Saharan African settings.
Methods: Data from a cross-sectional survey of mother-infant pairs conducted July-December 2013 in 140 maternal-child health clinics throughout Kenya were analyzed to evaluate the relationship of maternal TDF use in pregnancy and growth outcomes among infants with PCR-confirmed HIV-negative status. Maternal ART regimen during pregnancy and birth information was determined by self-report and confirmed with clinic records. Anthropometric measurements from infants attending 6-week or 9-month immunization visits were assessed by mobile evaluation teams. Age & sex-adjusted z-scores for weight (WAZ), weight-for-length (WLZ), length (LAZ), and head circumference (HCAZ) were calculated using WHO Child Growth Standards and analyzed as continuous variables. Comparisons of HIV-exposed uninfected (HEU)

infants with and without TDF exposure were assessed using t-tests and multivariate linear regression models adjusted for maternal and infant demographic and medical characteristics accounting for clinic-level clustering.

Results: Overall, 277 HEU infants had mothers who used three-drug combination ART during pregnancy, of whom 63% initiated ART before pregnancy and 89 (32%) used TDF-containing regimens. Prenatal TDF use was associated with concurrent use of protease inhibitors (26% vs 7%, p< 0.001) and with WHO clinical stage III (14% vs 6%, p=0.030). No differences in birth weight (3.0 kg vs 3.1 kg, p=0.205) or gestational age at birth (38 weeks vs 38 weeks, p=0.160) were detected between TDF-exposed and unexposed infants. Mean WAZ at 6 weeks was lower among TDF-exposed infants in unadjusted comparison (-0.8 vs -0.4, p=0.033); the association was less significant in adjusted analyses, (p=0.057). There were no associations between maternal prenatal TDF use and WLZ (p=0.509), LAZ (p=0.998) and HCAZ (p=0.964) among infants in the 6-week postpartum cohort. Among infants attending 9-month visits, no association was detected between maternal prenatal TDF use and WAZ (p=0.349), WLZ (p=0.655), LAZ (p=0.514) and HCAZ (p=0.888) after adjustment.

Conclusions: Our results add to previous data suggesting that maternal TDF use during pregnancy is not associated with adverse infant growth outcomes compared to non-TDF ART use.

MOPEB186

Virological response among HIV-infected pregnant and lactating women initiated on Option B + attending the PMTCT program at Mulago National Hospital, Kampala, Uganda

R.A. Ayanga[1], Z. Namukwaya[1], E. Namara Lugoloobi[1], J. Nabweteme Mugerwa[1], S. Akasiima Afrika[1], A. Kakande[1], S. Kamya[1], J. Byamugisha[2], P. Musoke[1,3], M. Nolan[1]
[1]Makerere University Johns Hopkins University Research Collaboration, Kampala, Uganda, [2]Makerere University College of Health Sciences, Obstetrics andd Gynaecology, Uganda, [3]Makerere University College of Health Sciences, Pediatrics and Child Health, Kampala, Uganda
Presenting author email: ayangaracheal@gmail.com

Background: HIV-1 Viral load (VL) is a direct quantification of HIV replication and a marker of HIV disease progression. VL monitoring is recommended by WHO for clients on ART to detect early treatment failure resulting from poor adherence or drug resistance and allows intervention to reduce morbidity and preserve treatment options. Current WHO policy is ART for life for PMTCT clients with a treatment as prevention approach.

Methods: In Uganda, virological treatment failure is defined as detectable circulating viral load above a set threshold of 1000 copies/ml using plasma. The PMTCT program at Mulago National Referral Hospital has been offering ART according to adult treatment guidelines until October 2012 and ART for life (Option B+) to all HIV-infected pregnant and lactating women since October 2012. The Central Public Health Laboratory (CPHL) established VL testing in Kampala, Uganda and offered routine VL tests on plasma samples to all PMTCT clients from November 2014. Plasma samples were collected and transported to the CPHL and results received in a week. A retrospective analysis of VL data for PMTCT clients who had initiated ART for six months or more was done around 6, 12 and 24 months.

Results: Between 1st Nov, 2014 and 31st Jan, 2015, a total of 1,158 viral load tests were done. Of these, 757 (75.1%) were for clients on ART/Option B+ and 251 (24.9%) on ART/non-Option B+. Among clients on option B+, 70(9.3%) had been on option B+ for 6 months, 187(24.7%) for 12 months, 500(66.1%) for more than 24 months. 67/70(95.7%) women on option B+ had VL< 1000 copies/ml at 6 months, 174/187(93.1%) had VL< 1000 copies/ml at 12 months, 479/500(95.8%) had VL< 1000 copies/ml at 24 months.

Conclusions: At Uganda's national referral hospital, the majority (>93%) of the clients initiated on option B+ and in follow-up had virological suppression between 6 and 24 months after ARV initiation. However, intensive adherence counseling and close monitoring is still needed to achieve close to 100% viral suppression for women on option B+. Long term follow-up and effective linkage to ongoing care will be critical for individual and public health effectiveness of the Option B+ strategy.

Other issues related to pregnancy

MOPEB187

Socio-demographic and clinical predictors of preterm births, low infant birth weight, and pregnancy complications among women living with HIV (WLWH) in Ontario, Canada

R. Keshmiri[1,2], A. Ion[3], S. Greene[3], M. Yudin[4,5,6], K. Murphie[2,7,8], F. Smaill[9], S. Walmsley[10,11], A. Carvalhal[12,13], M. Loutfy[1,10]
[1]Women's College Research Institute, Women's College Hospital, Toronto, Canada, [2]University of Toronto, Institute of Health Policy, Management and Evaluation, Toronto, Canada, [3]McMaster University, School of Social Work, Hamilton, Canada, [4]Li Ka Shing Knowledge Institute, St. Michael's Hospital, Keenan Research Centre, Toronto, Canada, [5]University of Toronto, Obstetrics and Gynecology, Toronto, Canada, [6]St. Michael's Hospital, Centre for Research on Inner City Health, Toronto, Canada, [7]University of Toronto, Obstetrics and Gynaecology, Toronto, Canada, [8]Mount Sinai Hospital, Maternal Fetal Medicine, Toronto, Canada, [9]McMaster University, Pathology and Molecular Medicine, Hamilton, Canada, [10]University of Toronto, Faculty of Medicine, Toronto, Canada, [11]Toronto Hospital, Immunodificiency Clinic, Toronto, Canada, [12]St. Michael's Hospital, Medical Psychiatry, Toronto, Canada, [13]University of Toronto, Psychiatry, Toronto, Canada
Presenting author email: reyhaneh.keshmiri@mail.utoronto.ca

Background: Pregnancies amongst WLWH are increasing as a result of advances in combination antiretroviral therapy and the increasing proportion of WLWH of childbearing age. These women are also at increased risk of adverse obstetric outcomes. This study examined socio-demographic and clinical characteristics as correlates of premature birth (PB), low birth weight (LBW), and pregnancy complications (PC).

Methods: The HIV Mothering Study is an observational mixed methods study exploring psychosocial experiences and needs of mothers living with HIV in Ontario. Data during the 3rd trimester of pregnancy and at 3 months postpartum was obtained through surveys and medicals records. The UCLA Loneliness, HIV Stigma, Everyday Discrimination-Racism, and Medical Outcomes Study-Social Support Survey scales were used for psychosocial assessments. We employed the penalized-maximum likelihood logistic regression to eliminate small-sample bias and stepwise regressions to create final multivariate models. For each of the outcomes, covariates with p-values ≤ 0.20 were included, followed by backward elimination of covariates until best-fit models were reached.

Results: Of the seventy-six women in this analysis, eight deliveries were PB, eleven were LBW, and fourteen PCs were encountered (E.g. pre-eclampsia, gestational diabetes, antepartum hemorrhage; feet/hand swelling, prolonged vomiting). Having a CD4 count higher than 500cells/mm^3 correlated with a reduced chance of PB (OR=0.01; p=0.002), while history of cardiovascular disease increased the risk (OR=35.77; p=0.005). Interestingly, higher risk for LBW was found to be associated with prepartum depression (OR= 24.81; p=0.014), divorce/separation (OR=32.50; p=0.024), and reduced social support (OR=0.92; p=0.018). The strongest correlates of both delivery outcomes, PB and LBW, was having CD4 count lower than 200cells/mm^3 (OR=10.57; p=0.049) and depression (OR=0.21; p=0.016). As for maternal PCs, the significant correlates were low CD4 count (OR=0.004; p=0.004), use of protease inhibitors (OR=0.13; p=0.025), and experience of racism (OR=1.18; p=0.036).

Conclusions: Low CD4 count, history of cardiovascular disease, depression, marital status, use of protease inhibitors, social support, and racism can elevate the risk of adverse obstetric outcomes and pregnancy complications for pregnant WLWH. Specific strategies addressing these clinical and socio-demographic risk factors should be adopted prior to delivery in order to improve health trajectories for both mother and child.

MOPEB188

From option A to B+: exploring challenges of navigating evolving PMTCT strategies among postpartum women living with HIV in rural Uganda

L.T. Matthews[1], S. Ashaba[2], C. Psaros[3], B.F. Burns[4], E. Dunkley[5], J. Kastner[5], A.C. Tsai[6], M. Robak[7], J.E. Haberer[4], P.W. Hunt[8], J.N. Martin[9], Y. Boum[10], D.R. Bangsberg[1], A. Kaida[5]
[1]Massachusetts General Hospital, Division of Infectious Diseases and Center for Global Health, Boston, United States, [2]Mbarara University of Science and Technology, Mbarara, Uganda, [3]Massachusetts General Hospital, Department of Pscyhology, Boston, United States, [4]Massachusetts General Hospital, Center for Global Health, Boston, United States, [5]Simon Fraser University, Burnaby, Canada, [6]Massachusetts General Hospital, Division of Psychiatry and Center for Global Health, Boston, United States, [7]Harvard Medical School, Boston, United States, [8]University of California San Francisco, San Francisco, United States, [9]University of California San Francisco, Department of Epidemiology and Biostatistics, San Francisco, United States, [10]Epicentre Uganda Research Center, Mbarara, Uganda
Presenting author email: ltmatthews@partners.org

Background: In late 2012, Uganda adopted the WHO Option B+ strategy for preventing mother to child transmission (PMTCT) of HIV whereby pregnant HIV-positive women initiate antiretroviral therapy (ART) for life. National guidelines recommend breastfeeding for up to 6 months with maternal ART and Nevirapine prophylaxis for infants. How women understand and navigate evolving PMTCT guidelines remains unclear.
Methods: We conducted 20 in-depth interviews with HIV-positive women with pregnancy in the past 2 years, sampled from an on-going HIV cohort study in Mbarara, Uganda (February-August 2014). Interview guides explored women's conception, pregnancy, and postpartum experiences with a specific emphasis on how their HIV status affected their experiences. Content analysis of transcribed and translated interviews was conducted using NVIVO software.
Results: Twenty women were interviewed: median age 33 (IQR: 28,35), last CD4 cell count 677 cells/mm3 (IQR: 440-767), 2.3 years since ART initiation (IQR: 1.5-5.1), and 95% (n=19) were virally suppressed (< 400 copies/mL). Most women had more than one pregnancy since being diagnosed with HIV. An emergent theme was that women struggle to understand and adhere to evolving PMTCT practices. Personal and community experiences of having infected or uninfected children while following certain recommendations was sometimes more compelling than advice from healthcare professionals. For example, women who had, or knew of, a child infected during breastfeeding were afraid to breastfeed, even while on ART. Many women described negative provider experiences such as being scolded for being HIV-infected and pregnant, priming them to distrust novel information delivered by providers. Women reported increasing pressure from providers to comply with Option B+ requirements, such as increased frequency of infant testing. Difficulties complying with additional maternal and child clinic visits that are part of Option B+ was described, due to structural barriers including transportation costs, absent partner support, and the stigma of accessing PMTCT services.
Conclusions: HIV-positive women express confusion and concern about changing recommendations to reduce perinatal transmission. Effectively communicating the rationale for evolving strategies, reducing structural barriers to care, and working with providers to reduce stigma for women accessing PMTCT care is critical to maximizing uptake of recommendations, reducing perinatal transmission of HIV, and maximizing maternal-child health.

MOPEB189

Integration of TB screening in Kenyan PMTCT programs

L. Cranmer[1], A. Langat[2], K. Ronen[3], C. McGrath[4], S. LaCourse[3], J. Pintye[3], B. Odeny[3], B. Singa[5], A. Katana[2], L. Nganga[2], J. Kinuthia[6], G. John-Stewart[3]
[1]Emory University, Pediatric Infectious Disease, Atlanta, United States, [2]Centers for Disease Control and Prevention (CDC), Nairobi, Kenya, [3]University of Washington, Seattle, United States, [4]University of Texas Medical Branch, Galveston, United States, [5]Kenya Medical Research Institute, Nairobi, Kenya, [6]Kenyatta National Hospital, Nairobi, Kenya
Presenting author email: lisa.cranmer@emory.edu

Background: Integration of tuberculosis (TB) screening into prevention of mother-to-child transmission (PMTCT) programs provides an opportunity for improved TB detection and provision of isoniazid preventive therapy (IPT). We assessed the prevalence and correlates of maternal TB symptoms and TB exposure in a national survey of the Kenyan PMTCT program.
Methods: A cross-sectional survey of mother-infant pairs attending 6-week and 9-month immunization visits at 140 maternal and child health (MCH) clinics in Kenya was conducted between July and December 2013. Maternal sociodemographic information, clinical history of TB, TB exposure, World Health Organization (WHO) TB symptom screen (any fever, cough, night sweats or weight loss) and infant clinical data were collected by questionnaires and verified by MCH booklets. Among HIV-infected mothers, prevalence of maternal WHO TB symptoms and TB exposure was determined and maternal and infant correlates were assessed using t-tests or chi-squared tests and logistic regression.
Results: Among 498 HIV-infected mothers, median age was 28 years (IQR 22-32) and 11% reported a history of TB. Overall, 33% of mothers had a positive WHO TB symptom screen (31% in 6-week cohort and 35% in 9-month cohort). The most prevalent WHO TB symptom was cough, followed by fever, night sweats and, least commonly, weight loss. Maternal positive WHO TB screen was associated with household crowding (p=.05) and lower CD4 count (p=0.06), but not with partner HIV status or TB exposure. Compared to women without a positive WHO TB screen, women with a positive WHO TB screen were more likely to have an infant with TB symptoms, including cough (44% vs. 26%, p=0.002), fever (30% vs. 19%, p=0.05), and difficulty breathing (16% vs. 6.9%, p=0.01), and infant HIV (7.6% vs. 2.8%, p=0.02). TB exposure was reported by 11% of women, but only 15% of TB-exposed women received IPT.
Conclusions: HIV-infected mothers frequently had TB exposure and positive WHO TB symptom screen in this national survey. Maternal TB symptoms were associated with infant symptoms, suggesting potentially undiagnosed TB. Few mothers with TB exposure received IPT. Integration of maternal TB screening and prevention into PMTCT programs may improve maternal and infant outcomes.

MOPEB190

Reproductive choices of women with HIV-1 infection: the ELLA study

R. Kulasegaram[1], A. D'Arminio Monforte[2], J. Valdez Madruga[3], I. Krznaric[4], A. Samarina[5], E. Deig Comerma[6], I. Cassetti[7], B. Conway[8], M. Martinez-Tristani[9], M.J. Fournelle[9], J. van Wyk[10]
[1]St. Thomas's Hospital, London, United Kingdom, [2]Clinic of Infectious and Tropical Diseases, Department of Health Sciences, San Paolo University Hospital, Milan, Italy, [3]Centro de Referência e Treinamento DST/AIDS, São Paulo, Brazil, [4]Medical Center for Infectious Diseases Berlin (MIB), Infectious Disease Department, Berlin, Germany, [5]Saint Petersburg HIV Centre, Infectious Disease Department, Saint Petersburg, Russian Federation, [6]HIV-Infectious Diseases Unit, Internal Medicine Service, Hospital General de Granollers, Granollers, Spain, [7]HIV Clinic, Helios Salud, Buenos Aires, Argentina, [8]Vancouver Infectious Diseases Centre, Vancouver, Canada, [9]AbbVie Inc., Chicago, United States, [10]AbbVie Inc., Research and Development, Chicago, United States
Presenting author email: jean.vanwyk@abbvie.com

Background: The cross-sectional, noninterventional ELLA epidemiologic study examined barriers to care affecting women with HIV infection. The reproductive choices of these patients, including parity, willingness to have children, and birth control methods used, were examined.
Methods: ELLA enrolled HIV- positive women ≥18 years in 4 global geographic regions (China, Central/Eastern Europe [CEE], Latin America [LA], and Western Europe/Canada [WEC]). Women completed the Reproductive Choices questionnaire; responses were categorized by patient age group. The chi-square test was used to examine the association between age group and methods of birth control used in discordant couples.

Characteristic*	Region				
	China (n=120)	CEE (n=532)	LA (n=519)	WEC (n=760)	Total (N=1931)
Mean age (SD), y	37.7 (8.4)	33.2 (9.8)	42.2 (11.9)	44.0 (10.8)	40.1 (11.4)
Formal education <12 years	63%	46%	58%	40%	48%
Time from HIV diagnosis to enrollment, y					
<1	27%	6%	7%	3%	6%
1–5	49%	40%	33%	23%	32%
>5 to 10	16%	29%	27%	22%	25%
>10	4%	24%	27%	47%	33%
Unknown	4%	1%	5%	5%	4%
No. of live births					
0	34%	40%	19%	30%	30%
1	38%	39%	24%	25%	29%
2	22%	17%	28%	24%	23%
3	2%	3%	15%	12%	10%
4	4%	1%	9%	4%	5%
>4	1%	<1%	5%	4%	3%
Unknown	—	<1%	<1%	1%	<1%
Median (range)	1 (0–4) (n=119)	1 (0–7) (n=531)	2 (0–12) (n=512)	1 (0–9) (n=744)	1 (0–12) (N=1906)
No. of children living with patient					
0	53%	52%	35%	59%	51%
≥1	47%	48%	62%	38%	48%
Unknown	—	1%	1%	3%	2%
Median (range)	0 (0–3)	0 (0–4) (n=527)	1 (0–7) (n=513)	0 (0–6) (n=735)	0 (0–7) (N=1895)
Willingness to have children					
Yes	21%	46%	17%	23%	28%
No	72%	40%	75%	64%	61%
Unsure	8%	14%	8%	10%	10%
Unknown	—	1%	<1%	2%	1%
When wanting more children (if willing or unsure)	n=34	n=318	n=127	n=255	N=734
Within next year	12%	28%	32%	26%	27%
1–2 y from now	41%	20%	16%	20%	20%
3–4 y from now	15%	12%	8%	10%	11%
>4 y from now	0%	3%	6%	4%	3%
Don't know	32%	36%	35%	36%	36%
Not available	0%	2%	3%	5%	3%
Living status	n=120	n=532	n=519	n=760	N=1931
Living alone	21%	18%	14%	29%	21%
Living with others	9%	13%	40%	21%	23%
Living with partner/husband	70%	69%	46%	50%	55%
HIV status of partner†	n=84	n=365	n=238	n=380	N=1067
HIV positive	54%	41%	39%	59%	48%
HIV negative	40%	52%	54%	35%	46%
Unknown	6%	7%	7%	5%	6%
Procedures to prevent pregnancy	n=120	n=532	n=519	n=760	N=1931
Surgery, woman (tubal ligation or hysterectomy)	16%	6%	33%	15%	18%
Surgery, man	3%	1%	2%	2%	2%
Intrauterine device	21%	9%	13%	10%	11%
Birth control					
Male condoms	63%	59%	56%	47%	54%
Female condoms	2%	2%	3%	3%	3%
Pill	1%	6%	6%	5%	5%
Withdrawal, pulling out	1%	10%	2%	2%	4%
Emergency contraception	0%	1%	1%	1%	1%
Abstinence	7%	9%	20%	16%	14%
None	24%	27%	20%	26%	25%
Other	3%	3%	7%	5%	5%

*Percentages may not total 100% because of rounding.
†Partners cohabiting with subject.

[Table]

Results: A total of 1931 women (mean age, 40.1 years) completed the questionnaire (Table). In the total population, 70% had ≥1 live births, 61% were unwilling to have more children, and 48% lived with a discordant partner. The most common method to prevent pregnancy in all regions was the male condom (47%-63%). Between 20% (LA) and 27% (CEE) used no birth control. Abstinence (all time or at the time of ovulation) rates varied by region from 20% (LA) to 7% (China). Eighteen percent of women had a surgical sterilization procedure and 11% used an intrauterine device (IUD). Use of other forms of birth control (oral contraception, female condoms, withdrawal/pullout, and emergency contraception) was lower (1%-10%, by region). With increasing age, use of male condom, oral contraception, and withdrawal/pullout or any birth control method declined. Abstinence, IUD use, or surgery for women increased with increasing age group. There were no associations between methods used to prevent pregnancy for discordant (vs concordant) couples, except for a greater likelihood of IUD use in women aged 35-49 with a discordant partner (*P*=0.013).
Conclusions: Despite the considerable variability of reproductive choices across geographic regions and age groups, 25% of women overall in this study practiced no form of birth control, and approximately half reported use of barrier protection (male or female condoms). With increases in age, use of no birth control increased and male condom use decreased. Renewed efforts to educate women living with HIV regarding use of barrier methods to prevent HIV transmission should be considered.

Other sex- or gender-specific issues

MOPEB191

Safety, tolerability and efficacy of dual therapy in women in the GARDEL study

M.I. Figueroa[1], M.J. Rolon[1], P. Patterson[1], J. Andrade Villanueva[2], J. Ballesteros[3], J. Gathe[4], J.R. Lama[5], J.R. Arribas[6], P. Cahn[1], the GARDEL Study Group
[1]Fundacion Huesped, Clinical Research, Ciudad de Buenos Aires, Argentina, [2]Hospital Civil de Guadalajara 'Fray Antonio Alcalde', Serivicio Unidad de VIH, Guadalajara, Mexico, [3]Centro de Investigaciones del Salvador, Santiago, Chile, [4]Therapeutic Concepts, Houston, United States, [5]Asociación Civil Impacta Salud y Educación, Lima, Peru, [6]Hospital Universitario La Paz, Madrid, Spain
Presenting author email: pedro.cahn@huesped.org.ar

Background: The objective was to investigate the safety and efficacy of dual LPV/r-based therapy in women in the GARDEL study.
Methods: The GARDEL STUDY compared the efficacy and safety of a dual therapy (DT) combination of LPV/r +3TC to a triple therapy (TT) with LPV/r + 3TC or FTC and a third investigator-selected NRTI. We analyzed data regarding efficacy, tolerability and safety of this dual treatment in women.
Results: Among 416 dosed participants, 69 were women (16%), 35 were assigned to DT (51%) and 34 to TT (50%) Baseline characteristics were comparable in both arms.
At 48 weeks, 88.5% of women in DT and 67.6% in TT achieved a HIV RNA <50 copies/mL in ITT, NC = F analysis (p= 0.070, difference 21.3% while virologic response in men was 88.3 % in DT and 86.9 % in TT (p= 0.824, difference 1.4% Virologic response in women with bsl VL>100,000 copies/mL was 78.6% DT vs. 53.8% TT, and was 88.8% DT vs. 82.2% TT for men. Virologic failure was observed in 6 women (1 DT, 5 TT; p= 0.238) and in 16 men (9 DT, 7 TT; p=0,238). Median viral load at failure was 813 copies/ mL for women and 440 copies/ mL for men. CD4 increases (mean) showed no significant differences between gender or treatment arms. Safety and tolerability were generally similar between groups. A total of 33 Grade 2-3 clinical AE were reported in women, 48.5% (DT) and 51.5% (TT)(p=0.556) while 120 AEs were reported in men: DT, 40.8% and 59.5% TT (p=0.556)Numerically more discontinuations were reported in women 21 % vs 10.9% in men. Toxicity/tolerability-related discontinuations were more frequent in the TT arm for both genders(see tables 1 and 2)

HIV VL at Week 48	DT	TT	P value
VL < 50 (ITTe) women	88.5% (n31)	67.6% (n23)	(p=0.070, difference 21.3% [$CI_{95\%}$:-0.9% to +42.8%])
VL < 50 (ITTe) men	88.3% (n158)	86.9% (n146)	(p=0.824, difference 1.4% [$CI_{95\%}$:-6.2% to +8.9%])
VL > 100,000 (ITTe) women	78.6% (n11)	53.8% (n7)	(p=0.340, difference 24.8% [$CI_{95\%}$:-17.3% to +66.7%])
VL > 100,000 (ITTe) men	88.6% (n71)	82.2% (n60)	(p=0.355, difference 5.6% [$CI_{95\%}$:-5.9% to +19.0%])

[Table 1. Proportion of patient of plasma HIV-1 RNA less than 50 copies/ml by gender]

Adverse Events		DT	TT
Dyslipidemia	women men	14.3% (n 5) 10% (n 18)	11.7% (n 4) 7.15% (n 12)
Diarrhea	women men	11.4% (n 4) 5.6% (n 10)	5.9% (n 2) 7.1% (n 12)
Nausea	women men	5.7% (n 2) n 0	8.8% (n 3) 3.5% (n 6)
Vomits	women men	n 0 n 0	5.8% (n 23) 1.1% (n 2)
Dyspepsia	women men	2.9% (n 1) n 0	n 0 3.5% (n 6)

[Table 2. Adverse events at week 48 by gender]

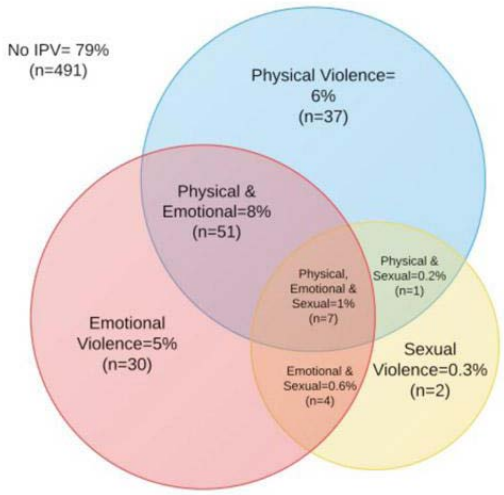
Conclusions: Albeit this substudy is not powered to support statistically significant results we observed that DT with LPV/r+3TC in women was non-inferior to triple therapy after 48 weeks of treatment, with a larger point estimate for the difference between arms in women in the lower baseline viral load strata. The DT regimen tended to have better safety and tolerability in both genders. Women discontinued more frequently due to tolerability/toxicity reasons.

MOPEB192

Intimate partner violence among HIV-infected pregnant women initiating antiretroviral therapy in South Africa

M. Bernstein[1], T. Phillips[1], A. Zerbe[2], J. McIntyre[3], L.-G. Bekker[4], G. Petro[5], L. Myer[1], E. Abrams[2]
[1]University of Cape Town, Division of Epidemiology and Biostatistics, School of Public Health and Family Medicine, Cape Town, South Africa, [2]ICAP at Columbia University, Mailman School of Public Health, New York, United States, [3]Anova Health Institute, Johannesburg, South Africa, [4]University of Cape Town, Desmond Tutu HIV Centre, Institute of Infectious Diseases & Molecular Medicine, Cape Town, South Africa, [5]University of Cape Town, Department of Obstetrics & Gynaecology, Cape Town, South Africa
Presenting author email: eja1@cumc.columbia.edu

Background: Intimate partner violence (IPV) during pregnancy may be common in many settings where HIV is prevalent but there are few data on IPV in populations of HIV-infected pregnant women. We examined the prevalence and predicators of IPV among pregnant women initiating lifelong antiretroviral therapy (ART) in a large primary care clinic in Cape Town, South Africa.
Methods: Consecutive pregnant women seeking antenatal care in Gugulethu, Cape Town were recruited into the MCH-ART study examining service models for postpartum ART care. IPV, depression, alcohol and drug use, and psychological distress were assessed using the 13-item WHO Violence Against Women questionnaire, the Edinburgh Postnatal Depression Scale (EPDS), alcohol and drug use disorders identification test (AUDIT/DUDIT) and the Kessler-10 (K-10) scale, respectively. Questionnaires were administered privately by trained interviewers. Women identified with specific IPV or mental health concerns were referred to appropriate services. Logistic regression was used to examine factors independently associated with experiences of IPV after adjusting for age and socioeconomic status.
Results: From April 2013-May 2014, 623 women were enrolled (median age, 28 years):97% reported being in a relationship, 38% were married and/or cohabiting and 70% reported not having discussed or agreed on pregnancy intentions prior to conception. Overall, 21%(n=132) reported experiencing ≥1 act of IPV in the past 12 months, including emotional violence(15%), physical violence(15%) and sexual violence(2%). Of those reporting any IPV, 48% reported experiencing multiple types (Figure 1). Emotional and physical violence were most prevalent among women 18-24 years old, while sexual violence was most commonly reported among women 25-29 years old. Women who reported not discussing or disagreeing on pregnancy intentions with their partners prior to conception were significantly more likely to experience violence(p=0.030), and women who experienced IPV reported higher levels of substance abuse, depression and psychological distress(p< 0.001 for all associations).
Conclusions: These data demonstrate high levels of IPV in this population. While the potential impact of HIV-infection, pregnancy and pregnancy intention on the risk of IPV and related factors require further research, IPV-related screening and support services should be considered as part of the package of care for ART in pregnancy.



[Figure 1: Venn diagram of types of intimate partner violence experienced in past 12 months]

MOPEB193

Antiretroviral drug use in a cohort of HIV-uninfected women in the United States

I. Chen[1], W. Clarke[1], S.S. Ou[2], M.A. Marzinke[1], A. Breaud[1], J.P. Hughes[2,3], P. Richardson[1], D.F. Haley[4], A.A. Adimora[5,6], C.E. Golin[5,7], C. Del Rio[8,9], I. Kuo[10], S.B. Mannheimer[11,12], L.E. Soto-Torres[13], A. Rompalo[14], J.E. Justman[15], S.L. Hodder[16], S.H. Eshleman[1], for the HPTN 064 Study Team
[1]Johns Hopkins Univ. School of Medicine, Dept. of Pathology, Baltimore, United States, [2]Fred Hutchinson Cancer Research Center, Vaccine and Infectious Disease Division, Seattle, United States, [3]Univ. of Washington, Dept. of Biostatistics, Seattle, United States, [4]Rollins School of Public Health, Emory Univ., Dept. of Behavioral Sciences and Health Education, Atlanta, United States, [5]Univ. of North Carolina School of Medicine, Dept. of Medicine, Chapel Hill, United States, [6]Gillings School of Global Public Health, Univ. of North Carolina at Chapel Hill, Dept. of Epidemiology, Chapel Hill, United States, [7]Gillings School of Global Public Health, Univ. of North Carolina at Chapel Hill, Dept. of Health Behavior, Chapel Hill, United States, [8]Rollins School of Public Health, Emory Univ., Dept. of Global Health, Atlanta, United States, [9]Emory Univ. School of Medicine and Center for AIDS Research, Dept. of Medicine, Atlanta, United States, [10]Milken Institute School of Public Health, George Washington Univ., Depts. of Epidemiology and Biostatistics, Washington, DC, United States, [11]Harlem Hospital Center, Dept. of Medicine, New York, United States, [12]Mailman School of Public Health, Columbia Univ., Dept. of Epidemiology, New York, United States, [13]National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, United States, [14]Johns Hopkins Univ. School of Medicine, Dept. of Medicine, Baltimore, United States, [15]Mailman School of Public Health, Columbia Univ., International Center for AIDS Care and Treatment Programs, New York, United States, [16]West Virginia Univ., Dept. of Medicine, Morgantown, United States

Background: Antiretroviral (ARV) drugs are used by HIV-uninfected individuals for pre- and post-exposure prophylaxis and to treat hepatitis B virus infection. Recent reports indicate that some ARV drugs are also used for recreational purposes. ARV drug resistance can emerge if individuals become HIV infected while using ARV drugs. We evaluated ARV drug use among HIV-uninfected women in the HPTN 064 study. The study enrolled 2,099 women at increased risk for HIV acquisition living in ten urban and periurban areas of the United States with high poverty rates and high HIV prevalence.
Methods: Plasma samples collected from 1,806 women who were HIV uninfected at the last study visit were analyzed. Enrollment samples from a randomly-selected subset of 364 HIV-uninfected women were also analyzed. Samples were screened for 16 ARV drugs from three ARV drug classes using a high-throughput, qualitative assay based on high-resolution mass spectrometry. Chi-square and Fisher's exact tests were performed to examine the association of ARV drug detection with participant and partner characteristics.
Results: ARV drugs were detected in 39 (2.2%) of the 1,806 women at the last study visit: 27/181 (14.9%) in Baltimore, MD and 12/179 (6.7%) in Bronx, NY. ARV drugs were not detected in samples from the other eight study sites. In Baltimore, efavirenz and protease inhibitors (nelfinavir, saquinavir, tipranavir, and indinavir) were detected; 22 women had one drug detected, and five had more than one drug detected. In Bronx, only efavirenz and indinavir were detected; nine women had one drug detected, and three had both drugs detected. ARV drugs were not detected in the random subset of enrollment samples.
Conclusions: Regionally-distinct patterns of ARV drug use were observed in HIV-uninfected women in the HPTN 064 study using a high-throughput ARV drug assay. Some of the drugs detected are rarely used in HIV care or prevention. Further research is needed to explore the prevalence of ARV drug use among HIV-uninfected individuals in different populations, the mechanisms by which those drugs are acquired, and the reasons for their use.

MOPEB194

Coercive sex as a mode of HIV acquisition among a cohort of women with HIV in Canada: an under-recognized public health concern

M. Loutfy[1,2], A. de Pokomandy[3,4], A. Benoit[1], V.L. Kennedy[1], J. Thomas-Pavanel[1], A. Carter[5,6], P. O'Campo[7], S. Greene[8], N. O'Brien[4], C. Logie[9], W. Tharao[10], J. MacGillivray[11], K. Proulx-Boucher[3], K. Beaver[1], V. Nicholson[6], P. Sereda[5], A. Nohpal[5], G. Colley[5], R. Hogg[5,6], A. Kaida[6], on behalf of the CHIWOS Research Team
[1]Women's College Research Institute, Women's College Hospital, Toronto, Canada, [2]University of Toronto, Toronto, Canada, [3]McGill University Health Centre, Chronic Viral Illness Service, Montreal, Canada, [4]McGill University, Department of Family Medicine, Montreal, Canada, [5]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada, [6]Simon Fraser University, Faculty of Health Sciences, Vancouver, Canada, [7]St. Michael's Hospital, Centre for Research on Inner City Health, Toronto, Canada, [8]McMaster University, Faculty of Social Work, Hamilton, Canada, [9]University of Toronto, Faculty of Social Work, Toronto, Canada, [10]Women's Health in Women's Hands Community Health Centre, Toronto, Canada, [11]St. Michael's Hospital, Toronto, Canada
Presenting author email: mona.loutfy@wchospital.ca

Background: Women experience coercive sex at alarmingly high rates, worldwide, due to entrenched gender and social inequities. We assessed the prevalence of and factors associated with HIV acquisition via coercive sex among women with HIV enrolled in the Canadian HIV Women's Sexual and Reproductive Health Cohort Study (CHIWOS).
Methods: Baseline survey data were analyzed for women with HIV (≥16 years), enrolled in a longitudinal, community-based cohort study in British Columbia (BC), Ontario (ON), and Quebec (QC). Coercive sex was assessed through self-report of 'non-consensual sex' as mode of HIV acquisition or sexual violence as a child or adult resulting in HIV. Univariate logistic regression analyses examined the relationship between self-reported coercive vs. consensual sex as the mode of HIV acquisition.
Results: Of 1,070 participants, 25% were from BC, 53% ON, and 22% QC, median age was 42 (IQR=35-50), 26 % identified as African/Caribbean/Black, 39% as Caucasian, and 25% as Aboriginal. Coercive sex was the second most dominant mode of HIV transmission at 17% (N=185) (vs. 57%-consensual sex, 15%-sharing needles, 4%-blood transfusion, 4%-perinatal, 4%-other). Amongst the women who acquired HIV from coercive sex, 38% (N=70) reported the assault occurring during war. In univariate analyses, covariates significantly associated with acquiring HIV from coercive vs. consensual sex included: province, ethnicity, birth country, year of arrival and legal status in Canada, sex at birth (p=0.009), sexual orientation (p=0.058), education (p=0.048), different regional residence in ON (p=0.005), living in an urban area, ever being in foster care or a group-home, ever being under Child Protection Services care (p=0.006), being incarcerated ever (p=0.038) and in the past year (p=0.022), recreational drug (p=0.010), illicit drugs (p=0.029) and injection drug (p=0.021) use, hepatitis C (p=0.034) and ever taking antiretrovirals (p=0.010) (p-values< 0.001 if not stated).
Conclusions: Coercive sex is a significant under-considered HIV risk factor among women. Given the high rates of self-reported coercive sex as a mode of HIV acquisition, it should be considered a distinct HIV risk factor, and reported separately from heterosexual transmission. The intersecting social determinants associated with coercive sex as an HIV risk factor warrant particular attention by policy makers and care providers.

Pharmacokinetics / pharmacodynamics / pharmacogenomics in children and adolescents

MOPEB195

A pharmacokinetics-based adherence measure for antiretroviral therapy in HIV-infected Kenyan children

W. Tu[1], W. Nyandiko[2,3], H. Lu[1], J. Slaven[1], M. Scanlon[3,4], S. Ayaya[2,3], R. Vreeman[2,3,4]
[1]Indiana University School of Medicine, Department of Biostatistics, Indianapolis, United States, [2]Moi University, College of Health Sciences, School of Medicine, Department of Child Health and Paediatrics, Eldoret, Kenya, [3]Academic Model Providing Access to Healthcare (AMPATH), Eldoret, Kenya, [4]Indiana University School of Medicine, Department of Pediatrcs, Children's Health Services Research, Indianapolis, United States
Presenting author email: rvreeman@iu.edu

Background: Traditional medication adherence measures do not accommodate the pharmacokinetic (PK) properties of the drugs and thus do not reflect patients' true therapeutic exposure. Medication Event Monitoring Systems (MEMS®) dose timers coupled with established PK parameters offer an opportunity to quantify the proximity of patient's actual drug exposure to its intended level.
We tested the concept by constructing a PK-based measure for nevirapine (NVP) adherence in HIV-infected Kenyan children.
Methods: We used a 1-compartment model with previously established PK parameters and actual MEMS®-recorded dosing times to estimate the mean plasma concentration of NVP (Cp) in individual patients after 1 month of follow-up. Intended NVP plasma concentration was calculated given a perfectly followed dosing regimen and frequency (Cp'). The difference between the 2 (Δ=Cp'-Cp) quantified the extent to which the patient's NVP actual exposure deviated from its intended level.
We validated Δ by evaluating its associations with MEMS®-defined adherence, CD4%, and spot-check NVP plasma concentrations assessed after 1 month.
Results: We analyzed data from 152 children (84 female). Mean age was 7.9 years (range 1.5-14.9). Subjects were on NVP for an average of 2.2 years. Children had moderate to severe clinical disease (61.7% were at WHO Stages 3 or 4) with mean CD4% of 27.7%. Mean MEMS® adherence was 78.6%. Figure 1 shows examples of fitted Cp "observed" and Cp' "optimal" curves of 4 patients; a larger Δ value suggests greater deviation of the observed plasma concentration from the intended level.
The mean Δ value was -0.04 ng/ml (SD 0.16 ng/ml). Δ was negatively associated with MEMS® adherence; patients with MEMS® adherence ≥90% had mean Δ value of -0.10 ng/ml versus mean Δ of 0.03 ng/ml in those with MEMS® adherence <90% (p< 0.0001), confirming a larger Δ was associated with non-adherence and thus a greater deviation from the intended level. A larger Δ was also associated with lower CD4% (p=0.0238) and spot-check plasma concentration (p=0.0008).

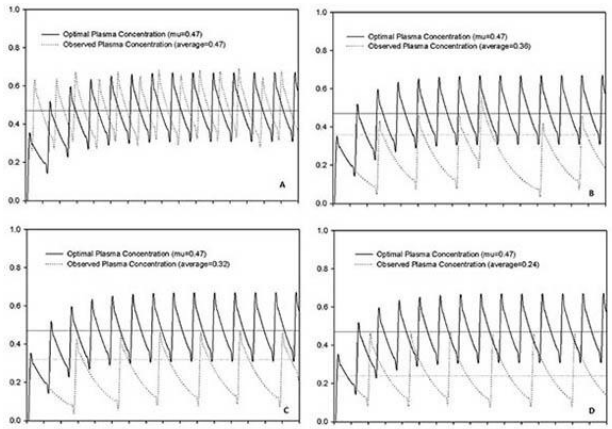


Figure Notes:
Curves plotted on graph with NVP drug concentration (y-axis) and time (x-axis). Observed (dotted) versus optimal (solid) NVP plasma concentration curves are shown for 4 pediatric patients (clockwise from top left, patient A, B, C, D) with varying levels of adherence: A has good adherence (Δ=-0.002), B has fair adherence (Δ=0.107), C has poorer adherence (Δ=0.146), and D has very poor adherence (Δ=0.231).

[Figure 1. Observed versus optimal plasma concentration using the PK-based measure in 4 pediatric patients]

Conclusions: The proposed adherence measure, Δ, captured patient drug-taking behaviors in addition to the PK properties of NVP; the measure's associations with MEMS®, CD4%, and spot-check plasma concentration confirmed its validity.

MOPEB196

Raltegravir (RAL) pharmacokinetics (PK) and safety in HIV-1 exposed neonates at high-risk of infection (IMPAACT P1110)

D.F. Clarke[1,2], E.P. Acosta[3], M.L. Rizk[4], Y.J. Bryson[5], S.A. Spector[6], L.M. Mofenson[7], M.E. Smith[8], H. Teppler[9], C. Welebob[4], M.P. Cababasay[10], B. Graham[11], K. Richards[12], M. Mirochnick[2], IMPAACT P1110 Protocol Team
[1]Boston Medical Center, Pediatric Infectious Diseases, Boston, United States, [2]Boston University School of Medicine, Pediatrics, Boston, United States, [3]University of Alabama at Birmingham, Clinical Pharmacology, Birmingham, United States, [4]Merck and Co., Inc., Whitehouse Station, United States, [5]David Geffen School of Medicine at University of California at Los Angeles, Pediatric Infectious Diseases, Los Angeles, United States, [6]San Diego and Rady Children's Hospital, Pediatrics, San Diego, United States, [7]Eunice Kennedy Shriver National Institute of Child Health and Human Development, Division of AIDS, National Institute of Health, Bethesda, United States, [8]National Institute of Health, NIAID, Division of AIDS, Bethesda, United States, [9]Merck and Co., Inc, Whitehouse Station, United States, [10]Harvard School of Public Health, Statistical and Data Analysis Center, Boston, United States, [11]Frontier Science and Research Technology Center, Data Management, Amherst, United States, [12]FHI 360, Durham, United States
Presenting author email: diana.clarke@bmc.org

Background: RAL is primarily metabolized by UGT1A1, whose activity is low at birth and increases exponentially over the first weeks of life. IMPAACT P1097 demonstrated that RAL crossed the placental well and elimination of transplacentally acquired RAL in infants whose mothers received RAL during pregnancy was highly variable and prolonged.
The objectives of IMPAACT P1110 are to evaluate the pharmacokinetics and safety of RAL and to determine an appropriate neonatal dose during the first 6 weeks of life using a two cohort adaptive design, where PK data from Cohort 1 are included in PK modeling to guide daily dosing in Cohort 2.
Methods: IMPAACT P1110 is a Phase I multicenter PK study of RAL in full-term HIV-1 exposed neonates at high risk of acquiring HIV-1-infection. Cohort 1 infants received RAL administered as a single oral 3 mg/kg dose within 48 hours of birth in addition to standard of care ARVs for PMTCT prophylaxis, and a second dose administered at 7-10 days of life. Pharmacokinetic sampling was done around the first dose (pre-dose and 1-2 hours, 4-8 hours, 12 hours, 24 hours post-dose, random sample on day 3-4 of life) and second dose (pre-dose and 1-2 hours, 24 hours post-dose). PK samples were analyzed for RAL concentrations on a rolling basis using a validated HPLC-MS-MS method. Protocol exposure limits for each subject are Cmax ≤ 19.6 μM and AUC12 ≤ 63 μMxhr.
Results: 6 mother-infant pairs enrolled in Cohort 1 (all RAL-unexposed in utero). Complete PK parameters following the first single dose are available for 5 of the 6 neonates (see Table). Although the Cmax upper limit was not exceeded by any subject, two patients exceeded the AUC12 upper limit. All infants tolerated the two single oral doses well.

Parameter	GM	%CV	Range
Cmax (μM)	6.9	27.6	4.5-9.6
AUC12 (μMxhr)	60.6	31.5	42.5-89.9
T 1/2 (hours)	12.8	19.6	9.9-15.7
T max (hours)	6.4	101.2	4.1-24
C24h (μM)	3.2	69.2	1.5-8.2
Vz/F (L/kg)	1.9	32.8	1.4-3.0
CL/F (L/kg/hr)	0.03	31.5	0.02-0.05

[Infant PK Parameters Following First Dose]

Conclusions: Given that 40% (2/5) infants exceeded the AUC12 target, these data suggest that daily neonatal dosing with RAL 3 mg/kg in RAL unexposed infants may be excessive. Dosing with 2 mg/kg for first dose is now under study. Neonates exposed to RAL in utero may require a different dosing strategy and are also being studied in P1110.

MOPEB197

Prevalence and correlates of CYP2B6-G516T polymorphisms in a cohort of HIV-infected women and children in Canada

F. Kakkar[1,2], S. Valois[1], D.G. Ramsey[3], A.M. Rezgui[3], V. Gagne[3], V. Lamarre[1,2], N. Lapointe[1], H. Soudeyns[1,4,5], P. Ovetchkine[2], M. Krajinovic[6]
[1]Centre Maternel et Infantil sur le SIDA (CMIS), CHU Sainte-Justine, Montreal, Canada, [2]CHU Sainte-Justine, Université de Montreal, Infectious Diseases, Montreal, Canada, [3]Centre de Recherche, CHU Sainte-Justine, Montreal, Canada, [4]Université de Montréal, Department of Microbiology, Infectiology & Immunology, Montreal, Canada, [5]Unité d'Immunopathologie Virale, Centre de Recherche du CHU Sainte-Justine, Montreal, Canada, [6]Division of Hematology-Oncology, CHU Sainte-Justine, Université de Montréal, Department of Pediatrics, Montreal, Canada
Presenting author email: fatima.kakkar@umontreal.ca

Background: The G516T polymorphism within the CYP2B6-gene affects the metabolism of non-nucleoside reverse transcriptase inhibitors (NNRTIs), with rapid NNRTI metabolism among homozygous GG individuals, and slow metabolism among those with TT genotype. The objective of this study was to describe the prevalence of the G516T genotypes among a cohort of HIV infected women and children in Canada, and associated clinical correlates.
Methods: HIV infected women and children were recruited from the Centre Maternel et Infantil sur le SIDA (CMIS) mother-child cohort between 2013-2014; family members were excluded from the study. DNA was extracted from saliva samples, and genotyping was performed using CYP2B6-G516T specific amplification and restriction fragment length polymorphism (PCR-RFLP).
Results: Genotyping was performed on 89 subjects (46 women, 43 children). Self-described ethnic distribution was African (46.1%), Haitian (31.5%), Caucasian (12.4%), and mixed origin (10%). Overall, 38.2% were GG (rapid metabolizers), 49.4% were GT , and 12.4% were TT (slow metabolizers). Among Africans, the GG genotype was most prevalent (46.3%), followed by GT (41.4%) and TT (12.2%). Among Haitians, the GT genotype was most prevalent (64.3%), followed by GG (21.4%) and TT (14.3%). Among Caucasians, 54.5% were GG, 36.4% were GT, and 9.1% were TT. There was a significant difference in the proportion of rapid metabolizers (GG) between Africans and Haitians (46.3% vs 21.4%, p=0.04), with an equal distribution of the GG genotype between patients from West Africa (43%) and Sub-Saharan Africa (44%). The highest proportion of slow metabolizers (TT) was among West Africans (21.5%), while the highest proportion of rapid metabolizers was among European Caucasians (75%). Among children treated with standard (weight/kg) doses of Efavirenz for whom unadjusted drug levels were available, 4/6 (67%) of GG genotype had trough drug levels in the lower therapeutic range (1-2 mg/L) at steady state, as compared to only 3/8 (38%) among the GT genotype. The single child with TT genotype had supra-therapeutic levels (>10mg/L) on standard dosing.
Conclusions: In this study population, the heterozygous GT genotype dominated, though there were significant differences within the predominant ethnic groups represented. Population-based knowledge of these genotypes may help tailor standard NNRTI dosing regimens to optimize their efficacy.

Therapeutic drug monitoring in children and adolescents

MOPEB198

Very high levels of drug resistance in HIV-infected children failing first line ART in Bobo-Dioulasso, Burkina-Faso

L. Serrano[1], M. Barro[2], B. Nacro[2], A.S. Ouedraogo[3], I. Ouattara[2], S. Sanou[3], E. Delaporte[1], M. Peeters[1], P. Msellati[1]
[1]IRD, UMI 233, Montpellier, France, [2]Centre Hospitalier de Bobo Dioulasso, Département de Pédiatrie, Bobo Dioulasso, Burkina Faso, [3]Centre Hospitalier de Bobo Dioulasso, Laboratoire, Bobo Dioulasso, Burkina Faso

Background: As access to ART for HIV-infected children is expanding in Africa, emergence of HIV drug resistance is inevitable, especially where biological monitoring is limited. The objective of this study was to describe drug resistance mutations in HIV-infected children that were clinically suspected to be on failing first line treatment in the outpatient clinic of paediatric department in Bobo-Dioulasso, Burkina Faso.
Methods: In October 2014, all children on first line ART (3TC+AZT/d4T+EFV/NVP, DDI/3TC/EFV) for more than 6 months and who were suspected failing ART (based on clinical and immunological) were invited in the outpatient clinic for a dried blood spot sample (DBS). Genotypic drug resistance testing in protease and reverse transcriptase was performed on DBS according to ANRS protocol. HIVDR was determined using the ANRS (v24.2014) HIVDR algorithm.
Results: Among 611 HIV infected children on first line ART, 72 (11.8%) were in clinical or immunological failure (35 male, 37 female) with a median age of 12 years (IQR 8-14). The median duration on ART was 45 months (IQR 30-74). For 63 children, CD4 counts were performed between January and October 2014: the median was 405 cells/mm3 (IQR 179-681). Genotyping was successful for 64/72 (89%) children: 61/64 (95%) were resistant to at least one drug, 58/64 (91%) to NRTIs and NNRTIs, 2/64 (3%) to NNRTIs and 1/64 (2%) to NRTIs. Overall, 43/64 (67%) were resistant to all drugs from their actual first line ART and 15/64 (23%) were on monotherapy. Moreover, they accumulated high numbers of mutations inducing cross-resistance to potential second line RTIs; i.e. ABC (30/64 (47%)),TDF (23/64, (36%)) or ETR (25/64 (39%).
Conclusions: This study shows the importance of early detection of treatment failure. The extensive accumulation of HIVDR and cross-resistance may compromise second-line regimens. These data stress the need of biological monitoring and advocate for more robust first-line regimens and surveillance of HIV drug resistance in HIV infected children.

Drug formulations in children and adolescents

MOPEB199

Two open label, randomized, cross-over, single-dose, bioavailability evaluations of abacavir sulfate/lamivudine dispersible tablets 60/30mg resp. 120 mg/60mg compared with that of EPZICOM® 600/300 mg tablets under fasting conditions

A. Deshmukh[1], S. Chakraborty[1], R. Chetan[1], A. Jaiswal[1], C. Issa[1], R. Dhobe[1], A. Nagaraj[1], P. Deshpande[2], A. Kanda[2], E. Patras[2]
[1]Mylan Laboratories Limited, Formulation Development, Hyderabad, India, [2]Mylan Laboratories Limited, Business Development, Hyderabad, India
Presenting author email: emmanuel.patras@mylan.in

Background: The development of pediatric fixed-dose combinations (FDCs) for later lines of therapy has become a priority to simplify dosing, increase adherence and thus improve pediatric care. This study analyzed the relative oral bioavailability of two newly developed pediatric FDCs of abacavir-sulfate and lamivudine (ABC/3TC) dispersible tablets 60/30 mg resp. 120 mg/60 mg and EPZICOM® (ABC/3TC) 600/300mg tablets.
Methods: In these two open label, randomized, two-period, two-treatment, cross-over, single dose evaluations, the relative oral bioequivalence was tested in 70 resp. 72 healthy adult human subjects under fasting conditions**.** In each period, an oral dose of ten FDC ABC/3TC dispersible tablets 60/30mg resp. five 120 mg/60mg and one reference EPZICOM® 600/300mg tablet was administered to the subjects. 23 blood samples per patient were collected pre-dose and at intervals over 48.0 hours after administration of each dose.
Subjects were monitored for safety and tolerability until the completion of the study. Primary pharmacokinetic (PK) parameters were: C_{max} and AUC_{0-t}. Secondary PK parameters were: t_{max}, $t_{½}$, $AUC_{0-\infty}$, $AUC_{\%\ Extrap\_obs}$, $AUC_{0-t}/AUC_{0-\infty}$ and K_{el}. PK parameters and descriptive statistics were evaluated for Abacavir and Lamivudine using Phoenix WinNonlin Version 6.3.
Results: Both the test and reference products were generally well tolerated by all study subjects, when administered in a single dose. For Abacavir and Lamivudine, the 90% confidence interval of the mean ratios (test/reference) for log-transformed primary pharmacokinetic parameters were within 80.00% to 125.00%, thus establishing bioequivalence.

Relative oral bioequivalence of two dispersible FDC ABC/3TC tablets 60/30 mg resp. 120/60 mg vs. 600/300 mg reference: Ratio of geometric means of test formulation vs. reference formulation			
10 x 60/30 mg vs. 1 x 600/300 mg N=70	Cmax (90%CI)	AUC (0-t) (90%CI)	AUC (0-∞) (90%CI)
ABC	107.45 (102.15 - 113.02)	97.75 (93.92 - 101.74)	97.72 (93.90 - 101.70)
3TC	110.19 (104.00 - 116.74)	99.36 (95.30 - 103.58)	99.14 (95.24 - 103.20)
5 x 120/60 mg vs. 1 x 600/300 mg N=72	Cmax (90%CI)	AUC (0-t) (90%CI)	AUC (0-∞) (90%CI)
ABC	113.75 (107.50 - 120.36)	104.29 (100.98 - 107.72)	104.18 (100.86 - 107.60)
3TC	114.37 (108.27 - 120.81)	104.37 (99.41 - 109.59)	103.97 (99.20 - 108.97)

[Relative Oral Bioequivalence]

Conclusions: Based on the results obtained in these two studies, ABC/3TC dispersible tablets 60/30 mg resp. 120/60 mg manufactured by Mylan Laboratories Limited, India and EPZICOM® (ABC/3TC) 600/300 mg tablets of ViiV Healthcare, Research Triangle Park, NC USA are found to be bioequivalent in healthy human adult subjects under fasting conditions. These new pediatric FDCs provide an easy-to-use ARV backbone.

MOPEB200

Relative bioavailability of a dolutegravir (DTG) dispersible tablet and the effect of low and high mineral content water on the tablet in healthy adult volunteers

S. Weller[1], F. Jerva[1], A. Buchanan[1], M. Holton[2], I. Conn[2], M. Choukour[3], H. Song[1]
[1]GlaxoSmithKline, Research Triangle Park, United States, [2]GlaxoSmithKline, Harlow, United Kingdom, [3]Parexel, Tampa, United States
Presenting author email: ann.m.buchanan@gsk.com

Background: A dispersible tablet formulation of DTG has been developed as an alternative to the granule formulation for administration to pediatric populations. The oral bioavailability of DTG is affected by metal cation-containing supplements. This study was conducted to evaluate the relative bioavailability of the dispersible tablet compared to the granule formulation and to compare DTG pharmacokinetics (PK) when tablets are dispersed in either low or high mineral content water.
Methods: This was a randomized, open-label, 5-way, single-dose crossover study in healthy adults. Treatments consisted of 20 mg DTG administered as:
(A) DTG granules in purified water and consumed immediately,
(B) dispersible tablets (4 x 5mg) dispersed in low mineral content (LMC) water, consumed immediately,
(C) dispersible tablets in high mineral content (HMC) water, consumed immediately,
(D) dispersible tablets in LMC water, consumed after standing for 30 minutes,
(E) dispersible tablets in HMC water, consumed after standing for 30 minutes.
Safety evaluations and serial PK samples were collected during each treatment period. DTG PK parameters were determined by noncompartmental methods and compared between treatments by analysis of variance (ANOVA). A palatability questionnaire was administered after the first period.
Results: Fifteen subjects were enrolled into the study and completed all treatment periods. Summary ANOVA results from treatment comparisons are presented in the following table.

PK Parameter	Geometric Least Square Mean Ratio (90% Confidence Interval)			
	Trt B / Trt A	Trt C / Trt B	Trt D / Trt B	Trt E / Trt C
AUC(0-∞)	1.06 (1.02, 1.11)	0.94 (0.90, 0.99)	1.03 (0.98, 1.07)	1.04 (1.00, 1.09)
Cmax	1.12 (1.06, 1.19)	0.92 (0.87, 0.97)	0.99 (0.93, 1.05)	1.05 (0.99, 1.11)
C24	1.03 (0.97, 1.09)	0.96 (0.90, 1.02)	1.07 (1.00, 1.13)	1.01 (0.95, 1.08)

[Table 1]

AUC(0∞) = area under the curve extrapolated to infinity; C24 = concentration 24 hours post-dose; Cmax = peak concentration.

The DTG dispersible tablet was bioequivalent to the granule formulation. Neither water mineral content within the range evaluated nor 30 minute delay in dispersed tablet consumption affected DTG PK. Study treatments were well tolerated. All adverse events (AEs) reported were mild, and no subjects were withdrawn due to AEs. Based on the limited palatability assessment data, the granule formulation seemed to be more acceptable than the dispersible tablets.
Conclusions: The dispersible tablet is suitable for further development and the formulation is being adjusted to improve taste.

Adherence in children and adolescents

MOPEB201

Virological suppression among adolescents and young adults living with HIV in Canada

A. Palmer[1], H. Wong[1], N. Oliveira[2], C. Miller[3], A. Kaida[3], W. Small[3,4], A. Burchell[5], C. Cooper[6], M. Klein[7], M. Loutfy[8,9], N. Machouf[10], J. Montaner[4,11], J. Raboud[9,12], C. Tsoukas[13,14], R. Hogg[2,3], The CANOC Collaboration
[1]British Columbia Centre for Excellence in HIV/AIDS, Drug Treatment Program, Vancouver, Canada, [2]BC Centre for Excellence in HIV/AIDS, Population Health and Epidemiology, Vancouver, Canada, [3]Simon Fraser University, Faculty of Health Sciences, Burnaby, Canada, [4]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada, [5]Ontario HIV Treatment Network, Toronto, Canada, [6]University of Ottawa, Ottawa, Canada, [7]McGill University Health Centre, Montreal, Canada, [8]Maple Leaf Medical Centre, Toronto, Canada, [9]University of Toronto, Toronto, Canada, [10]Clinique Medicale L'actuel, Montreal, Canada, [11]University of British Columbia, Vancouver, Canada, [12]University Health Network, Toronto, Canada, [13]McGill University, Montreal, Canada, [14]Montreal General Hospital, Montreal, Canada
Presenting author email: apalmer@cfenet.ubc.ca

Background: Compared with adults, adolescents and young adults (AYA) living with HIV have poorer treatment and clinical outcomes. AYA are an important treatment population, yet the reasons for poorer outcomes are poorly understood. The aims of this study are to assess time to virological suppression in the first year of cART among AYA and to explore factors associated with suppression.
Methods: Participants are HIV-positive individuals from a multi-site Canadian cohort of antiretroviral-naive patients initiating cART on/after 1 January 2000. Participants were censored after one year on treatment. Virologic suppression was defined as time to the first of at least two consecutive viral load measurements < 50 HIV-1 RNA copies/mL in a one-year period. Life tables were used to estimate probabilities of virologic suppression. Univariate and multivariable models were conducted to explore factors associated with virologic suppression among AYA aged 18-29.
Results: Of 755 AYA included in this analysis, (Median age=26) 562 (74%) experienced virologic suppression within one year of beginning cART. The median time to suppression was 7.5 months. In the adjusted multivariable model, people with a history of IDU (Adjusted Hazard Ratio [aHR]: 0.70, 95% CI=0.55-0.89, p=0.004) and those with treatment interruptions (aHR: 0.48 CI=0.38-0.61, p< 0.001) were less likely to suppress within one year. In addition, more frequent viral load monitoring (per year) was associated with increase likelihood of viral suppression (aHR: 1.08, IQR: 1.03-1.13, p< 0.001).
Conclusions: One-quarter of AYA are not reaching virological suppression within the first year of treatment. An increased number of VL tests was associated with VL suppression, which may reflect levels of engagement in care. AYA with a history of IDU may be experiencing chaotic lifestyles and in need of increased supportive services to understand lived experiences and help them prioritize their health. It's imperative that we implement evidence-based services to improve management programs for a wider community.

MOPEB202

Treatment interruptions common among adolescents and young adults living with HIV in Canada

A. Palmer-Fluevog[1,2], H. Wong[1], N. Oliveira[1], C. Miller[2], A. Kaida[2], W. Small[1,2], H. Samji[1], A. Burchell[3], C. Cooper[4], M. Klein[5], M. Loutfy[6,7], N. Machouf[8], J. Montaner[9,10], J. Raboud[7,11], C. Tsoukas[12,13], R. Hogg[1,2], The CANOC Collaboration
[1]BC Centre for Excellence in HIV/AIDS, Population Health and Epidemiology, Vancouver, Canada, [2]Simon Fraser University, Faculty of Health Sciences, Burnaby, Canada, [3]Ontario HIV Treatment Network, Toronto, Canada, [4]University of Ottawa, Ottawa, Canada, [5]McGill University Health Centre, Montreal, Canada, [6]Maple Leaf Medical Centre, Toronto, Canada, [7]University of Toronto, Toronto, Canada, [8]Clinique Medicale L'actuel, Montreal, Canada, [9]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada, [10]University of British Columbia, Vancouver, Canada, [11]University Health Network, Toronto, Canada, [12]McGill University, Montreal, Canada, [13]Montreal General Hospital, Montreal, Canada
Presenting author email: apalmer@cfenet.ubc.ca

Background: Adolescents and young adults (AYA) comprise nearly one-quarter of all Canadian HIV-positive tests. Despite available treatment, AYA face on-going challenges with adherence to cART. Incomplete adherence and treatment interruptions (TIs) result in viral rebound and are associated with treatment failure, HIV resistance, suboptimal clinical outcomes and increase potential for HIV transmission. This study will examine correlates of treatment interruptions.
Methods: Participants are HIV-positive individuals from a multi-site Canadian cohort of antiretroviral-naive patients initiating cART on/after 1 January 2000. A TI was defined as a gap in treatment >90 consecutive days during the follow-up time. Univariate and multivariable analyses were conducted to explore factors associated with treatment interruptions (TIs) among AYA.
Results: 9262 people living with HIV were included in this analysis, with 1304 (14%) aged 18-29 (AYA). Approximately 30% of AYA were female, 5.1% identify as Indigenous, 37% identify as MSM, and 19.2% report a history of injection drug use (IDU). AYA were more likely to experience treatment interruptions (26.2% vs. 18.9%, p< 0.001). In the adjusted analysis, factors associated with TIs among AYA were female gender (adjusted hazard ratio [AHR]: 1.86; 95% confidence interval [CI]: 1.46-2.36, p< 0.001), self-identifying as Indigenous (AOR: 1.66; 95% CI:1.11—1.66, p< 0.001), having a history of IDU (AHR: 2.25; 95% CI: 1.71-2.96, p< 0.001), having a baseline CD4 cell count >350 cells/µl (AHR: 1.71; 95% CI: 1.30-2.26, p< 0.001) and starting cART in earlier years (2000-2003) (AHR: 1.77; 95% CI: 1.19-2.64, p=0.017) relative to 2007-2012.
Conclusions: AYA disproportionally experienced treatment interruptions than non-AYAs over the study period. Despite the universal health care setting and cART availability, a quarter of AYA are not remaining on treatment. Tailored health care strategies are needed to support AYA to remain in care and to receive the full benefits of cART.

MOPEB203

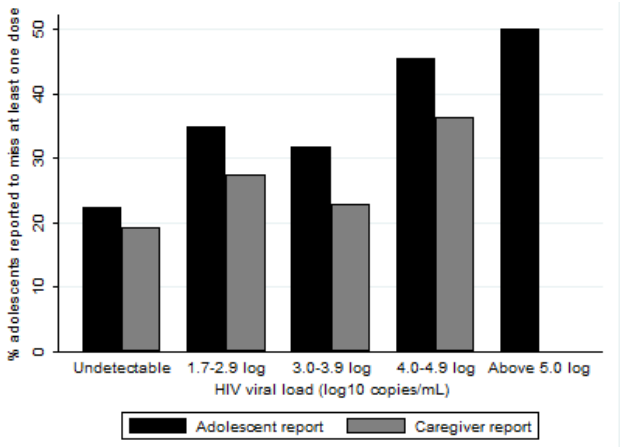
Antiretroviral therapy adherence in perinatally-infected adolescents in Cape Town, South Africa

K. Brittain[1], N.A. Asafu-Agyei[1], J. Hoare[2], L.-G. Bekker[3], H. Rabie[4], J. Nuttall[1], P. Roux[1], D.J. Stein[2], H.J. Zar[1], L. Myer[5], Cape Town Adolescent Antiretroviral Cohort
[1]University of Cape Town, Department of Paediatrics & Child Health, Cape Town, South Africa, [2]University of Cape Town, Department of Psychiatry & Mental Health, Cape Town, South Africa, [3]University of Cape Town, Desmond Tutu HIV Centre, Institute of Infectious Diseases & Molecular Medicine, Cape Town, South Africa, [4]Tygerberg Academic Hospital & Stellenbosch University, Department of Paediatrics & Child Health, Cape Town, South Africa, [5]University of Cape Town, Division of Epidemiology & Biostatistics, School of Public Health & Family Medicine, Cape Town, South Africa
Presenting author email: landon.myer@uct.ac.za

Background: Improvements in access to antiretroviral therapy (ART) for perinatally-infected children have resulted in increasing numbers surviving to adolescence, particularly in South Africa. Adolescents may face unique barriers to maintaining optimal ART adherence, but data are limited, and there are few insights into the performance of adherence measures reported by adolescents versus their caregivers.
Methods: We examined the association between ART adherence and HIV viral load (VL) in a cross-sectional analysis of enrolment data from the Cape Town Adolescent Antiretroviral Cohort, a longitudinal study of perinatally-infected adolescents ages 9-14 years using ART >6 months. Adherence was assessed by trained interviewers using 30-day recall, conducted separately for adolescents and their caregivers, and VL testing used Abbott RealTime HIV-1 testing. Logistic regression was used to examine the association between adherence reports and detectable VL (>50 copies/mL) after adjusting for child age and gender.
Results: Between July 2013 and October 2014, 305 adolescents (median age, 12.1 years; 46% female) enrolled; 60%, 29% and 11% of caregivers were biological parents, other family members, and non-family members, respectively. In adolescent and caregiver report, 26% and 21% reported at least one missed ART dose in the preceding 30 days, respectively, but agree-

ment between adolescents and caregivers was low (kappa, 0.19). Agreement between adolescent and caregiver report was significantly lower among non-family caregivers (kappa, -0.01) compared to biological parents and other family members respectively (kappa, 0.20 and 0.22). Adolescent reports of missed doses increased with age (odds ratio [OR]:1.18; 95%CI:1.01-1.39). 25% of adolescents had detectable VL. Although no association was observed between VL and caregiver report of adherence, detectable VL was significantly more likely among adolescents who reported missed ART doses independent of adolescent age (OR:1.88; 95%CI:1.07-3.31); this association was strongest in girls (OR:2.80; 95%CI:1.17-6.66). No association was observed between type of caregiver and either reported adherence or VL.

Conclusions: These novel data suggest that non-adherence increases with adolescent age and that adolescents' self-reported ART adherence may be a reasonable indicator of raised VL, particularly in girls. Better methods to measure ART adherence and interventions to improve adherence in perinatally-infected African adolescents are needed.



[Viral load according to 30-day recall of adherence]

MOPEB204

Managing children and adolescents with HIV treatment failure: results from a pilot project in Khayelitsha

J. Bernheimer[1], G. Patten[1], G. Van Cutsem[2,3], A. Shroufi[2], T. Makeleni[1], N. Mantangana[1], N. Dumile[1], V. Cox[1]
[1]Medecins Sans Frontieres, Khayelitsha, South Africa, [2]Medecins Sans Frontieres, Cape Town, South Africa, [3]Centre for Infectious Disease Epidemiology and Research, School of Public Health and Family Medicine, Faculty of Health Sciences, University of Cape Town, Cape Town, South Africa
Presenting author email: msfocb-capetown-deputymed@brussels.msf.org

Background: As HIV treatment programmes mature in Southern Africa, increasing attention has been given to adults failing antiretroviral treatment (ART). In contrast, despite reported high paediatric treatment failure rates, high viral loads (VL) in children on ART are often not addressed.
A pilot programme was introduced to identify and care for children and adolescents failing ART at two Khayelitsha primary care clinics. The programme consists of support groups for caregivers and adolescents, individual consultations to address adherence barriers, home visits, and genotyping to guide regimen switches when vireamia persists despite 3 months of adherence support.
Methods: Children and adolescents 0-19 years enrolled between July 2013 and November 2014 with last VL>1000 copies/µl or last two VL>400 were included. Routine data on ART regimens and VLs was used. VLs were performed every 3 months. Re-suppression was defined as achieving a VL< 400.
Results: Of 131 patients, median age at enrolment was 10 years (interquartile range 4.2-13.8); 60 (46%) were girls. Median time on ART was 4.03 years (IQR 2.6-7.6). VL suppression at first, second and third follow-up VL was 55% (58/105), 72% (55/76) and 84% (38/45) respectively. Patients >12 years were less likely to re-suppress compared with those < 12 (67% [10/15] vs. 93% [28/30], p=0.02). 77% (36/47) on PI-based regimens re-suppressed at their 2nd VL without switching, compared with 28% (7/25) on NNRTI-based regimens. Of those switched from NNRTI to PI regimens, 40% (10/25) re-suppressed. 34 genotypes were performed, with 43% (6/14) and 100% (20/20) resistant to PI and NNRTI-based regimens respectively. Patients resistant to PIs await 3rd line ART availability.
Conclusions: HIV programmes need systems to identify and support children and adolescents failing ART, since simple interventions can lead to high rates of re-suppression. Most children failing NNRTI-based regimens showed resistance and required switching to a PI-based regimen. Conversely, most children on PI regimens re-suppressed with adherence support, indicating their robustness and the potential benefit of adopting WHO recommendations for first line PI-based ART for children. Despite overall high rates of re-suppression, adolescents in the pilot programme required innovative support strategies to attain durable re-suppression.

HIV-exposed uninfected children (including effects of ART exposure during pregnancy)

MOPEB205

The effects of maternal HIV infection on infectious morbidity of HIV exposed uninfected (HEU) infants in South Africa

A. Slogrove[1,2,3], M. Cotton[1], T. Kollman[2], D. Speert[2], M. Esser[4], J. Singer[3], J. Bettinger[2]
[1]Stellenbosch University, Paediatrics & Child Health, Cape Town, South Africa, [2]University of British Columbia, Pediatrics, Vancouver, Canada, [3]University of British Columbia, School of Population & Public Health, Vancouver, Canada, [4]Stellenbosch University, Department of Pathology, Cape Town, South Africa
Presenting author email: slogrove@gmail.com

Background: HEU South African infants, comprising 30% of the infant population, may be at risk for substantial infectious morbidity, potentially explained by advanced maternal HIV disease. To understand the relationship between maternal CD4 count, viral load, antiretroviral therapy and infant infectious morbidity we compared these parameters in HEU infants with and without infectious cause hospitalizations.
Methods: The Mother-Infant Health prospective cohort study conducted from 2012-2014 identified HIV-infected and HIV-uninfected mothers at delivery from a single community midwife unit. Infants were enrolled at 2 weeks and followed to 6 months. Maternal antenatal CD4 counts were retrieved from the public health laboratory database and delivery CD4 counts and HIV viral loads were performed by the study. The primary outcome, infectious cause hospitalization before 6 months, was determined through active surveillance using the province-wide electronic hospital administration system allowing complete outcome determination on all infants. We present a descriptive analysis of the HIV-infected mothers and their HEU infants.
Results: 94 HIV-infected mothers and their HEU infants were enrolled. 48 mothers (51.1%) had HIV diagnosed pre-pregnancy and 47 (50.0%) received combination antiretroviral therapy (cART) during pregnancy. Seventeen (18.1%) HEU infants experienced an infectious-cause hospitalization. There were no differences between hospitalized and not hospitalized infants in timing of maternal HIV diagnosis, cART or zidovudine prophylaxis, maternal CD4 count or HIV viral load at delivery (Table 1). Neither were there differences in infant gestational age, birth weight, exclusive breastfeeding at 2 weeks or complete immunizations by 6 months. Infants of mothers on zidovudine prophylaxis were more often anaemic at 2 months than infants of mothers on cART (26/36(55.6%) vs. 14/42(33.3%), p = 0.03). Nineteen (40.4%) mothers on zidovudine prophylaxis had CD4 counts < 350 cells/mm^3 at delivery and 43 (46%) HEU infants were not receiving trimethoprim-sulphamethoxazole prophylaxis at 8 weeks.

	Total N=94	Infants hospitalized N=17	Infants not hospitalized N=77	P
Timing of maternal HIV diagnosis				0.23
Pre-pregnancy	48(51.1%)	10(58.8%)	38(49.4%)	
During pregnancy or peripartum	46(48.9%)	7(41.2%)	39(50.7%)	
Maternal antiretroviral type				0.15
Combination antiretroviral therapy	47(50%)	8(47.1%)	39(50.7%)	
Zidovudine prophylaxis	44(46.8%)	7(41.2%)	37(48.1%)	
Antenatal CD4 count - median (IQR)	420(284,539)	458(384,640)	410(284,515)	0.19
Delivery CD4 count - median(IQR)	343(236,501)	308(202,694)	346(246,486)	0.87
Log10 HIV viral load - median(IQR)	2.05(1.59,3.22)	1.87(1.59,2.85)	2.11(1.59,3.31)	0.42

[Table 1: Maternal HIV factors]

Conclusions: Maternal CD4 count, HIV viral load and receipt of either cART or zidovudine prophylaxis were not associated with infant infectious morbidity. Of concern is the proportion of mothers with delivery CD4 counts below the threshold for cART and the low proportion of infants receiving trimethoprim-sulphamethoxazole.

MOPEB206

Perturbations in gut microbiome in infants born to HIV-infected mothers are related to maternal microbiome and human milk oligosaccharides

L. Kuhn[1], J. Bender[2], F. Li[2], S. Martelly[3], E. Byrt[4], V. Rouzier[3], P. Pannaraj[2], H. Adisetiyo[2], C. Santiskulvong[2], S. Wang[5], C. Autran[6], L. Bode[6], D. Fitzgerald[4], G. Aldrovandi[2]
[1]Columbia University, Epidemiology, New York, United States, [2]Children's Hospital Los Angeles, Los Angeles, United States, [3]GHESKIO, Port au Prince, Haiti, [4]Weill-Cornell Medical Center, New York, United States, [5]Columbia University, Biostatistics, New York, United States, [6]University of California, San Diego, United States
Presenting author email: lk24@columbia.edu

Background: Programs to prevent mother-to-child HIV transmission have been highly successful in reducing the risk of HIV transmission to the infant. However, these infants do not escape unscathed. HIV-exposed infants experience higher rates of morbidity and mortality than unexposed infants, even HIV-exposed uninfected (HEU) infants.
Here we investigate a potential mechanism to explain the higher rates of mortality and morbidity in this vulnerable group.
Methods: Infants born to 25 HIV-infected and 25 uninfected mothers were recruited at a nutrition clinic in Port au Prince, Haiti. All infants were breastfed and the mean age was two months (range one to three months). Mucosal samples were collected from each mother-infant pair (mother - breast milk, areola, vagina; and infant -stool, oral, and skin). For each sample we performed 16S bacterial metagenomic sequencing and analyzed the data using QIIME 1.8.0. Human milk oligosaccharides were characterized using high-performance liquid chromatography.
Results: Alpha diversity was significantly reduced in the gut microbiome of infants born to HIV-infected mothers. Taxonomic composition in the infant stool sample differed by maternal HIV status. Infants born to HIV-infected mothers had more *Proteobacteria* and *Actinobacteria* and less *Bacteroidetes* and *Fusobacteria* than unexposed infants. Classes within these phyla were also significantly different. The Bacteroidetes to Firmicutes ratio has been used as a marker of diversity. This link to bacterial diversity was lost in infants born to HIV-infected mothers. Individual mother-infant pairs were significantly similar to each other with the strongest association being between maternal breast milk and infant stool microbiomes. The increases in *Proteobacteria* and *Actinobacteria* in HIV-exposed infants were explained by increases in the concentration of 3' sialyllactose (3'SL) in breast milk from HIV-infected mothers.
Conclusions: Both oligosaccharide composition of breast milk and infant stool microbiome were influenced by maternal HIV status. Maternal HIV infection may disrupt the bacterial robustness in developing infants. Perturbations caused by HIV in the oligosaccharide composition of breast milk or in the maternal microbiome may lead to these perturbations in infants. Close linkage between maternal and infant microbiomes may help explain some of the increased vulnerabilities of HEU infants

MOPEB207

Health outcomes among HIV-exposed uninfected infants in Quebec, Canada

S. Wizman[1], S. Valois[2], H. Soudeyns[2,3,4], N. Lapointe[1,2], V. Lamarre[1,2], F. Kakkar[1,2]
[1]CHU Sainte-Justine, Université de Montreal, Infectious Diseases, Montreal, Canada, [2]Centre Maternel et Infantil sur le SIDA (CMIS), CHU Sainte-Justine, Montreal, Canada, [3]Université de Montréal, Department of Microbiology, Infectiology & Immunology, Montreal, Canada, [4]Unité d'Immunopathologie Virale, Centre de Recherche du CHU Sainte-Justine, Montreal, Canada
Presenting author email: valerie_lamarre-pediatrie@ssss.gouv.qc.ca

Background: HIV exposed uninfected (HEU) infants are at increased risk of adverse health outcomes when compared to unexposed uninfected infants, though the precise cause is yet unknown. Our objective was to study the association between maternal health status at the time of delivery and infant health outcomes.
Methods: HEU infants followed in the CMIS mother-child cohort were eligible for the study. Infants born to mothers with CD4 count < 350 cells/mm^3 and detectable viral load (VL) at time of delivery were matched by year of birth, gender and ethnicity to infants born to mothers with delivery CD4 count >350cells/mm^3 and undetectable VL (n=133). Data on health outcomes was extracted by chart review, and compared among infant groups defined by maternal health status.
Results: There were no significant differences in gestational age, birthweight, APGAR scores, or growth parameters (weight, length and head circumference) at 6 and 12 month of age, or rate of hospitalization in the first two years of life, among infants born to mothers with delivery CD4 count < 350 cells/mm^3 (n=67) vs. >350cells/mm^3 (n=66). There was however a higher rate of infection in the first 6 months of life (0.05/person-week vs. 0.02/person-week, p=0.002). Infants born to mothers with detectable VL (n=41) had lower birthweight and mean gestational age as compared to infants of mothers with undetectable VL (n=89) (2914±621g vs. 3201±614g, p=0.01; and 37.9 ±2.83 weeks vs. 38.7 ±2.2 weeks, p=0.055), though there were no differences in their subsequent growth parameters. While there was no difference in the overall rate of infection in the first 6 month of life, there was a significantly higher rate of hospitalization (0.61/person-year vs. 0.22/person-year, p=0.001) in the first two years of life among infants born to mothers with detectable VL.
Conclusions: Maternal CD4 count and VL at delivery may have an impact on health outcomes among HEU infants, with increased rate of infection seen among infants born to mothers with CD4 count< 350 cells/mm^3, and higher rate of hospitalization seen among infants born to mothers with detectable VL at the time of delivery. Further work needs to be directed at understanding the contributing factors.

MOPEB208

Leukocyte telomere length (LTL) dynamics in a cohort of HIV-exposed uninfected (HEU) infants exposed to combination antiretroviral therapy (cART) *in utero*

A. Ajaykumar[1], H. Soudeyns[2,3], F. Kakkar[3], J. Brophy[4], A. Bitnun[5], A. Alimenti[6,7], D. Money[7,8,9], A. Albert[7,9], H. Côté[1,7,9], CIHR Team on Cellular Aging and HIV Comorbidities in Women and Children (CARMA)
[1]University of British Columbia, Department of Pathology and Laboratory Medicine, Vancouver, Canada, [2]University of Montréal, Department of Microbiology, Infectiology and Immunology, Montreal, Canada, [3]University of Montréal, Department of Pediatrics, Montreal, Canada, [4]University of Ottawa, Department of Pediatrics, Ottawa, Canada, [5]University of Toronto, Department of Pediatrics, Toronto, Canada, [6]University of British Columbia, Department of Pediatrics, Vancouver, Canada, [7]BC Women's Hospital and Health Centre, Vancouver, Canada, [8]University of British Columbia, Department of Obstetrics, Vancouver, Canada, [9]Women's Health Research Institute, Vancouver, Canada
Presenting author email: abhinavajaykumar.91@gmail.com

Background: Maternal cART in pregnancy could have long-term consequences for HEU children. Some antiretrovirals and HIV proteins inhibit telomerase, a potential mechanism of injury as LTL reflects cellular aging and is linked to age-related morbidities. We evaluated the impact of HIV and cART exposure on LTL by comparing a cohort of HEU and HIV-unexposed uninfected (HUU) control infants at birth, over the first 3-6 weeks prophylaxis period, and over the first three years of age.
Methods: Relative LTL was measured in 324 HEU (0-3y, n=215 had ≥2 blood samples collected) and 308 HUU children (0-3y, single blood sample each) via qPCR. Factors associated with LTL were investigated using linear regression modeling. Longitudinal LTL in HEU was analyzed via a generalized mixed effects additive model.
Results: In a cross-sectional analysis of LTL at birth (0-3d) in 115 HEU (56% male) and 91 HUU (54% male) children, maternal cART (duration or type) was unrelated to HEU LTL. Male sex was associated with shorter LTL (p=0.02). Maternal smoking in pregnancy (56% HEU, 43% HUU mothers smoked) was associated with significantly shorter LTL in HEU and longer LTL in HUU, indicating a significant smoking*HEU/HUU interaction (p<0.001). Percent change in LTL over the first 3-6 weeks was associated with birth LTL (p<0.001) whereby infants with longer LTL at birth showed greater LTL shortening. Overall, LTL slopes for the first six weeks were positive in both groups. In HEU, this was followed by rapid decline in LTL to ~one year of age, then leveling out. Although a similar model could not be built for HUU, LTL attrition rates were similar in both groups among a subset of age and sex-matched children (n=214:214, p=0.69).
Conclusions: This first detailed investigation of human LTL dynamics early in life suggests an initial apparent gain in LTL during the first 6 weeks of life followed by a rapid decline that levels off up to age three. These results further support that exposure to maternal HIV/cART *in utero* does not affect infant LTL, a reassuring finding. Rather, maternal smoking acts as a major modulator of infant birth LTL, likely through *in utero* stresses.

MOPEB209

Effects of smoking on telomere length in cohorts of HIV+ and HIV- pregnant women and HIV-exposed uninfected (HEU) and HIV-unexposed uninfected (HUU) infants

A. Ajaykumar[1], S. Saberi[1,2], B. Sattha[1], A. Albert[3], A. Alimenti[4], E. Mann[4], J. Van Schalkwyk[3,5], D. Money[3,4,5], H. Côté[1,2,3], CIHR Team in Cellular Aging and HIV Comorbidities in Women and Children (CARMA)
[1]University of British Columbia, Department of Pathology and Laboratory Medicine, Vancouver, Canada, [2]Centre for Blood Research, Vancouver, Canada, [3]Women's Health Research Institute, Vancouver, Canada, [4]BC Women's Hospital and Health Centre, Vancouver, Canada, [5]University of British Columbia, Department of Obstetrics, Vancouver, Canada
Presenting author email: abhinavajaykumar.91@gmail.com

Background: Antiretroviral drugs, HIV proteins, immune activation, and oxidative stress can affect telomerase activity and/or leukocyte telomere length (LTL), a marker of aging and lifespan predictor. HIV and smoking are associated with shorter LTL in adults, and smoking is known to have significant adverse affects in pregnancy, but the mechanism is not fully worked out. We explored the relationships between HIV status, maternal smoking, and cART on LTL in cohorts of HIV+ and HIV- pregnant women and HIV-exposed uninfected (HEU) and HIV-unexposed uninfected (HUU) infants.

Methods: Relative LTL was assessed in 89 HIV+ (all on cART) and 58 HIV- pregnant women at 31-40 weeks of gestation, as well as 115 HEU and 91 HUU infants at birth. Mouth swab TL was also measured in 34 HEU and 18 HUU infants. Linear regressions and correlations were used to examine and compare the factors associated with LTL.
Results: Smoking at visit was univariately associated with shorter maternal LTL (p=0.006), although the effect size was greater among HIV+ women (p< 0.001). In all infants, male sex (p=0.02) and higher birth weight (p=0.07) were most associated with shorter LTL. In addition, there was a significant (p< 0.001) interaction whereby maternal smoking (56% of HIV+ and 43% of HIV- mothers smoked ever in pregnancy) was associated with shorter LTL in HEU and longer LTL in HUU. Given an imbalance in smoking by ethnicity, whereby Aboriginal and Black women were significantly more and less likely to smoke respectively, a sub analysis of White mothers only (n=93, 53% smokers) was performed and showed a similar LTL pattern. An interaction was also seen in infant mouth swab TL (p=0.014) with longer TL in HUU infants exposed to maternal smoking. Among HEU, cART was not related to birth LTL.
Conclusions: Pregnant women who smoke have shorter LTL irrespective of HIV status. In infants, the counterintuitive effect observed in both LTL and mouth swab TL in association with maternal smoking may relate to a physiologic response to intrauterine stress. This smoking in pregnancy effect may be modulated by HIV/cART exposure in HEU infants.

Behavioural health outcomes in children and adolescents (including sexual risks, substance use and poor adherence)

MOPEB210

"I want to be called daddy": needs assessment of sexual and reproductive health among perinatally infected adolescents in Zambia

S. Okawa[1], S. Mwanza[2,3], M. Mwiya[2], K. Komada[4], M. Jimba[5], N. Ishikawa[4]
[1]The University of Tokyo, Tokyo, Japan, [2]Paediatric HIV Center of Excellence, University Teaching Hospital, Lusaka, Zambia, [3]University of Zambia, Lusaka, Zambia, [4]National Center for Global Health and Medicine, Tokyo, Japan, [5]University of Tokyo, Tokyo, Japan
Presenting author email: sumiyo1024@hotmail.com

Background: Expanded access to antiretroviral therapy has improved survival of perinatally infected children in sub-Saharan Africa. They are reaching the age of adolescence and facing new challenges on sexual and reproductive health (SRH). This study examined challenges and needs of SRH among HIV-positive adolescents.
Methods: A cross sectional study was conducted at the University Teaching Hospital of Zambia from April to July 2014. In total, 200 HIV-positive adolescents who were already aware of their HIV-positive status were recruited. Structured questionnaires including open-ended questions were administered. Descriptive analysis was done about their basic background, knowledge of HIV and sexual health, their sexual behaviors, and SRH needs. For the participants aged less than 17 years, we obtained parental assents.
Results: A total of 190 adolescents were included in the analysis: 110 (57.9%) girls; and 80 (42.1%) boys. Sixty-three (33.5%) were in relationships with boyfriend/girlfriend at the time of survey, and 38 (20.4%) had ever disclosed their HIV status to their boyfriend/girlfriend. Of these 38 adolescents, 28 reported supportive relationships with their boyfriends/girlfriends over time. Regarding sexual and reproductive health issues, they felt comfortable to talk with friends (17.7%) and mothers (16.6%), but 17.1% answered that they were not comfortable to talk to anyone. Pharmacy/clinic/hospital were the major places to obtain condom (51.4%) and birth control methods (65.1%). About half (49.4%) had concerns about their marriage, such as serostatus disclosure, fear of partner's response after disclosure, potential risk of transmission to partner and children. The majority of them (87.4%) showed intention to have a child in the future, and 172 (91.0%) knew the risk of mother-to-child transmission, whereas 35 (18.5%) did not know how to prevent it. Thirty-eight adolescents (22 girls, 16 boys) had ever had sexual intercourse at their median age of 16 years and partners' median age of 18 years. At the first sexual intercourse, 21 had already known their HIV status, 18 used condom, and 7 had forced sexual intercourse.
Conclusions: Adolescents living with HIV have unmet needs of sexual and reproductive health, which needs to be urgently addressed to improve their quality of life.

MOPEB211

Self-reported HIV risk assessment and risk factors among adolescents from the high HIV prevalence area in the USA

N. Rakhmanina[1], N. Ellenberger[2], K. Ganesan[2], J. Payne[2], S. Morrison[2]
[1]Childen's National Health System/Elizabeth Glaser Pediatric AIDS Foundation, Washington, United States, [2]Children's National Health System, Washington, United States
Presenting author email: nrakhman@childrensnational.org

Background: Adolescents are at risk for acquiring HIV due to high rates of unprotected sex and sexually transmitted infections (STIs). Youth frequently lack awareness about the risk of acquiring HIV. In Washington, DC, with 2.5% overall HIV prevalence, 0.2% of adolescents (13-19 years) and 1.0% of youth (20-29 years) are infected with HIV. This study aimed to evaluate self-reported HIV risk assessment and risk factors among adolescents tested for HIV at the pediatric Emergency Department (ED) located in a community hospital in Washington, DC.
Methods: A self-reported questionnaire with multiple choice answers on HIV risk and risk factors was offered to adolescents (≥13 years) at the United Medical Center ED during March 2013-August 2014. The questionnaire was distributed after adolescents received their HIV test results. Adolescents with positive HIV test results were excluded from participating in the survey. Descriptive statistics were used for data analysis.
Results: A total of 405 adolescents (median age - 16 years) completed the survey. The majority
(70%; n=285) were female and Black (95%; n=385). The majority (63%; n=254) reported being sexually active either currently, in the past, or both. Among adolescents with sexual history, more than half
(57%; n=144) reported using condoms "always" or "almost always". Less than half (45%; n=115) reported that they knew their partner's HIV status. Almost a third (27%; n=68) of sexually active youth reported at least one prior STI, with 66% reporting chlamydia (n=55) and 23% gonorrhea (n=19), with 15% (n=10) reporting both STIs. The large majority of surveyed adolescents (91%; n=369) did not believe that they were at risk for acquiring HIV.
Conclusions: In an urban area with a high HIV prevalence, majority of tested and surveyed predominantly female adolescents did not believe that they were at risk for acquiring HIV. Although more than half of adolescents with sexual history reported using condoms consistently, almost a third of them had a history of at least one STI. Better understanding of young people's perception of their risks for HIV and STIs is important in order to develop effective messaging and communication with youth about risks and prevention of HIV and STIs.

Transition into adult care

MOPEB212

Predicted efficacy of reverse transcriptase and protease inhibitors in pregnant adolescents with perinatally-acquired HIV infection: evidence of limited therapeutic options

D.M. Cecchini[1], I. Zapiola[2], S. Fernandez Giuliano[2], M. Martinez[1], C. Rodriguez[1], M.B. Bouzas[2]
[1]Hospital Cosme Argerich, PMTCT Working Group, Buenos Aires, Argentina, [2]Hospital Francisco J. Muñiz, Virology Unit, Buenos Aires, Argentina
Presenting author email: diegocec@gmail.com

Background: **A**dolescents with **p**erinatally acquired **H**IV infection **(APH)** are a vulnerable population, heavily exposed to antiretroviral treatment (ART), in which prevalence of drug resistance associated mutations (RAMs) is high. We aimed to describe the predicted efficacy of the three historically prescribed ART classes in APH who have transitioned from pediatric hospitals to an adult service during pregnancy.
Methods: Previous and latest genotypic resistance tests from pregnant APH (period 2008-2014) were analyzed in order to estimate prevalence of RAMs and to obtain genotypic sensitivity scores predicted by cumulative genotype. Prevalence of RAMs to NRTIs, NNRTIs and PIs was analyzed according IAS-USA update, 2014. Considering the genotype interpretation system (GIS) of Stanford HIVdb program (version 7.0), the predicted efficacy of each drug was classified within five categories: from susceptible to high-level resistance. The GIS categories "susceptible" and "potential low level resistance" were grouped together as "S" (susceptible), whereas "low level resistance" and "intermediate resistance" were grouped as "I" (intermediate) and the remaining as "R" (resistant).
Results: During the studied period, 27 treatment-experienced pregnant APH were transitioned. The median (IQR) of age, gestational age, viral load (VL) and CD4 T-cell count were: 18 years (17-19); 8 weeks (5-18); 1534 copies/mL (< 50-12103) and 298/µL (223-535), respectively. Genotypic resistance tests were available for 20 of them. Prevalence of RAMs was 84.2% for both NRTIs and NNRTIs, and 73.7% for PIs. The median (IQR) number drugs classed as S was 1 (0-5) for NRTIs, 1 (0-4) for NNRTIs, and 6 (0-7) for PIs. Predicted efficacy of NRTIs is shown in table 1.

Category	ABC	3TC	ZDV	D4T	ddI	TDF
Resistant (%)	25	35	40	40	25	15
Intermediate (%)	40	20	25	25	35	35
Susceptible (%)	35	45	35	35	40	50

[Table 1. NRTI predicted susceptibility]

Considering NNRTIs: 35% remain S to EFV/NVP; 45% S to RPV; 50% and 45% were S and I to ETR, respectively. Considering PIs, 10% and 35% were S and I to NFV; 55% and 20% to ATV/r, IDV/r, LPV/r and SQV/r; 55% and 25% to FPV/r; 65% and 15% to TPV/r; 80% and 20% to DRV/r, respectively.

Conclusions: Reduced predicted efficacy was observed for most NRTIs/NNRTIs and (in a lesser extent) to PIs, limiting ART options. In this context, prescription of newer drugs with limited experience in pregnancy may be considered.

MOPEB213

Prerequisite knowledge for transition from youth to adult HIV care services among perinatally HIV-infected youth in Thailand

V. Boon-Yasidhi[1], R. Lolekha[2], P. Leowsrisook[3], B. Manaboriboon[1], W. Nuchanard[2], W. Punpanich Vandepitte[3], Y. Durier[1], Y. Na Nakorn[3], C. Yuvasevee[2], S. Yadech[3], J. Tarugsa[1], T. Naiwatanakul[2], N. Ounjit[3], S. Kanakool[1], N. Jongchotchatchawal[2], M. Martin[2], K. Lapphra[1], K. Chokephaibulkit[1]

[1]Faculty of Medicine, Siriraj Hospital, Mahidol University, Department of Pediatrics, Bangkok, Thailand, [2]Global AIDS Program (GAP) Thailand/Asia Regional Office, Thailand Ministry of Public Health-U.S. CDC Collaboration (TUC), Nonthaburi, Thailand, [3]Queen Sirikit National Institute of Child Health, Department of Pediatrics, Bangkok, Thailand

Presenting author email: keswadee@gmail.com

Background: Many perinatally HIV-infected youth have begun to reach adulthood. Youth are moving from pediatric to adult clinics and taking more responsibility for their health and medical care. For a successful transition, youth should understand HIV and its management, know how to make and keep appointments, and know when to seek medical care. We assessed prerequisite HIV and medical care knowledge of HIV-infected Thai youth.

Methods: We interviewed HIV-infected youth aged 14-21 years receiving care at 2 tertiary care hospitals in Bangkok to assess prerequisite knowledge (i.e., 22 questions) important for the transition to adult HIV care. Score was calculated as the percentage of correct answers. We expect a score >80% will allow a smooth transition. Factors associated with a knowledge score greater than median were analysed using logistic regression.

Results: During March - June 2014, 192/245 (78%) eligible youth participated in the interview. Median age was 17 years (range: 14-21 years) and 41% were female. All youth received antiretroviral (ARV) treatment and 144 (75%) had HIV RNA < 50 copies/ml. The median score was 45% (Interquartile range (IQR) =32-55%). Only 8 (4%) youth had score >80%. Median knowledge score for ARV management (e.g., your current ARV, adherence, side effects) was 75% (IQR=50-75%); knowledge of their viral load (VL) and CD4 results and target levels was 0% (IQR=0-17%); understanding about how and when to access HIV care was 50% (IQR=25-63%); and knowledge of reproductive health and family planning was 67% (IQR=33-67%). One hundred forty seven (77%) youth were able to describe their education/career goals. In multivariate analysis, an overall knowledge score greater than the median was associated with receiving care at a University Hospital (adjusted odds ratio (aOR)=2.3 [95%CI, 1.1-4.9]), age ≥18 years (aOR=2.3 [95%CI, 1.1-5.3]), more than a junior high school education (aOR=2.9 [95%CI, 1.3-6.2]), and participating in the structured youth program activities at hospitals (aOR=3.0 [95%CI, 1.3-6.9]).

Conclusions: Most youth had low (< 80%) prerequisite knowledge score for transition to adult HIV care. Most youth did not know their VL and CD4 status. HIV-infected youth need better preparation for the transition to adult HIV care services to ensure a successful transition.

MOPEB214

Late enrollment in care and ART initiation among HIV patients in Ho Chi Minh City, Vietnam

T.T. Nguyen Thi[1], L.V. Le[2], P.Q. Bui Lieu[1], T.N. Nguyen Thi[1], M. McConnell[3], S. Lyss[3], J. Kaplan[4], S. Nguyen Thanh[2], M. Ackers[2], T.V. Tieu Thi[1]

[1]Ho Chi Minh City Provincial AIDS Committee, Ho Chi Minh City, Vietnam, [2]U.S. Centers for Disease Control and Prevention, Ho Chi Minh City, Vietnam, [3]U.S. Centers for Disease Control and Prevention, Ha Noi, Vietnam, [4]U.S. Centers for Disease Control and Prevention, Atlanta, United States

Presenting author email: mayth2003@gmail.com

Background: Vietnam's national guidelines for ART eligibility have changed in accordance with World Health Organization recommendations: before 9/2009 (Period 1), CD4 count <200 cells/mm^3 or clinical stage IV; 9/2009-11/2011 (Period 2), CD4 <250, <350 and stage III, or stage IV; and after 11/2011 (Period 3), CD4 <350 or stage III-IV. We assessed whether guideline changes were associated with changes in patient demographics and clinical indicators before ART initiation in Ho Chi Minh City.

Methods: We abstracted medical records of 2697 outpatients with initial clinic visits during 2007-2012 from all 21 community-based, adult, HIV clinics using random sampling with probability proportional to clinic size, intra-cluster correlation and weights. We applied OLS regression analysis to test for linear trends across proportions, and the Kruskal-Wallis test for differences in medians.

Results: Of 2697 patients, 1827 (68%) were ART-eligible at enrollment, and 1650 (61%) initiated ART. Over time, median age at registration slightly increased (Period 1=28 years, Period 2=29 years, Period 3=31 years; p<0.001); the proportion of enrollees who were women increased (Period 1=30%, Period 2=36%, Period 3=37%; p=0.022); and the proportion who injected drugs decreased (Period 1=40%, Period 2=28%, Period 3=22%; p=0.001).

Changes were insignificant for the proportion of enrollees with baseline CD4 <100 (Period 1=51%, Period 2=48%, Period 3=46%; p=0.219) or with CD4 >350 (Period 1=18.2%, Period 2=20.8%, Period 3=21.1%; p=0.247), although median baseline CD4 count increased (Period 1=96, Period 2=114, Period 3=132; p=0.0142).

The proportion with baseline clinical stages III-IV decreased but not significantly (Period 1=48%, Period 2=46%, Period 3=41%; p=0.402). The proportion of ART-eligible patients who initiated ART increased (Period 1=68%, Period 2=72%, Period 3=85%; p=0.001). Median time between establishing eligibility and initiating ART decreased (Period 1=42 days, Period 2=28 days, Period 3=28 days; p <0.001).

Conclusions: Despite improvement in the proportion of eligible patients receiving ART and the shortened duration between eligibility and initiation, patients were still initiating ART at low CD4 counts. In addition to guideline changes expanding ART eligibility, strengthened interventions- including routine HIV testing for key populations and immediate linkages to and retention in care- are needed to ensure timely ART initiation.

MOPEB215

Engagement in the HIV care cascade among perinatally HIV-infected patients transferred to an adult HIV clinic in Buenos Aires, Argentina

E. Cordova, C.G. Rodriguez

Hospital Cosme Argerich, Infectious Diseases Unit, Buenos Aires, Argentina

Presenting author email: dr_ecordova@hotmail.com

Background: Transitioning perinatally HIV-infected adolescents (PHI) patients into adult care is a complex process. In addition, few data of the management of these patients after transition is available.

The aim of this study was to characterize engagement in the HIV continuum of care among PHI-patients transferred from pediatric care to an adult HIV care in Buenos Aires, Argentina.

Methods: Retrospective chart review of PHI-patients transferred to our adult HIV care between 2000-2012. Percentages at each step of the cascade (transition, retention in care, on ART and viral load suppression) after 2 years of transition were determined. Bivariate analyses were performed to investigate factors associated with these outcomes.

Results: A total of 70 PHI-patients were transitioned to our centre during the study period. Median (range) age: 17 years (9-24). Female sex corresponded to 57%. Twenty seven percent of the patients were orphans. Use of drugs or alcohol was self-reported by 11%. Forty-eight percent of the patients had co-morbidities. The median CD4 T-cell count was 507/µL (3-1390) and 67% had ever had a CDC category C event. All patients except one were under antiretroviral treatment at the time of transfer and adherence issues were observed in 36%. Sixty seven percent of the patients were triple antiretroviral treatment (ART) experienced including 20% with triple-class ART resistance. Detectable viral load was observed in 52% of the patients. During the first 2 years after transition, 78% were retained in care, 73% continued ART, and 52% had undetectable viral load (72% of those on ART).

Female sex, and CD4 T-cell count < 200/µL at the time of transition were significantly associated with attrition along the cascade and adherence issues were significantly associated to a lack of virological suppression.

Conclusions: Despite significant efforts to address a successful transition, the engagement across the HIV Cascade remains a challenge, especially for female PHI-patients and those with a low CD4 T-cell count. Although the presence of a complex ART history and drug resistance profile, adherence is still the major barrier to achieve virological suppression in this population. Our results provide critical information to optimize engagement in care of PHI-patients after transition.

Hormonal contraception and HIV

MOPEC398

Genital inflammatory profiles associated with progestin-only injectable contraception and reproductive tract infections among women at high-risk of HIV

J. Deese[1], L. Masson[2], M. Wang[3], K. Ahmed[4], K. Agot[5], T. Crucitti[6], S. Abdellati[6], C. Morrison[1], L. Van Damme[7]
[1]FHI 360, Clinical and Epidemiological Sciences, Durham, United States, [2]University of Cape Town, 2. Centre for Infectious Disease Epidemiology and Research, Cape Town, South Africa, [3]FHI 360, Biostatistics, Durham, United States, [4]Setshaba Research Centre, Pretoria, South Africa, [5]Impact Research and Development Organization, Kisumu, Kenya, [6]Institute of Tropical Medicine, Antwerp, Belgium, [7]The Bill and Melinda Gates Foundation, Seattle, United States
Presenting author email: jdeese@fhi360.org

Background: Previous studies have found an association between mucosal inflammation and HIV acquisition. We evaluated the association between demographic and biological - specifically injectable progestin-only (IPOC) contraceptive use and reproductive tract infections (RTI) - risk factors for HIV infection and inflammatory marker concentrations in the female genital tract.
Methods: A cross-sectional analysis of 376 not pregnant, HIV uninfected women, selected on baseline contraceptive use and RTI status, was conducted using FEM-PrEP trial data. Inflammatory cytokines and secretory leukocyte peptidase inhibitor (SLPI) were measured in stored specimens and compared between a reference population, women using IPOC and women with RTI. Women were categorized into the following exposure groups:
1) referent (no hormonal contraception (HC) use/no RTI),
2) using Depot medroxyprogesterone acetate (DMPA)/no RTI,
3) using norethisterone enanthate (NET-EN)/no RTI,
4) *Neisseria gonorrhoeae* (NG) infected/no HC/no other RTI,
5) *Chlamydia trachomatis* (CT) infected/no HC/no other RTI,
6) *Trichomonas vaginalis* (TV) infected and having bacterial vaginosis (BV)/no HC/no other RTI,
7) having intermediate vaginal flora (Nugent 4-6)/no HC/no other RTI and
8) having BV (Nugent 7-10)/no HC/no other RTI.
Results: No significant variability in marker concentrations was observed by age or study site. DMPA users had significantly higher concentrations of 6/8 inflammatory markers (MIP-1α, MIP-1β, IL-8, IP-10, RANTES and IL-6). NET-EN users had a similar profile, but fewer overall markers of inflammation with significant elevation in IL-8, RANTES and IL-6. Although women with NG/CT/TV had fewer markers of inflammation compared to women using DMPA, several pro-inflammatory cytokines/chemokines were elevated, while SLPI was downregulated in women with NG and TV. Women with BV exhibited a mixed phenotype with some chemokines being upregulated and some pro-inflammatory cytokines being suppressed.
Conclusions: The finding of marked inflammation among DMPA users, and similar but overall less inflammation among NET-EN users, suggests a potential mechanism for the increased risk of HIV infection observed in some epidemiological studies. While the cross-sectional design limits causal interpretation, the results are strengthened by design control of important confounders, relatively large strata for several exposure groups and lack of observed variability within the reference population when stratified by age or site. Further mechanistic and clinical research is warranted.

Assessment of population viral load in epidemiology studies

MOPEC399

Validating a self-report measure for assessing viral suppression in observational studies: an analysis of linked survey and clinical data from the Canadian HIV women's sexual and reproductive health cohort study

A. Carter[1,2], A. Nohpal[1], P. Sereda[1], G. Colley[1], K. Proulx-Boucher[3], J. Thomas-Pavanel[4], V. Nicholson[5], K. Beaver[4], R.S. Hogg[1,2], A. de Pokomandy[3,6], M. Loutfy[4,7], A. Kaida[2]
[1]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada, [2]Faculty of Health Sciences, Simon Fraser University, Burnaby, Canada, [3]McGill University Health Centre, Chronic Viral Illness Service, Montreal, Canada, [4]Women's College Research Institute, Women's College Hospital, Toronto, Canada, [5]Simon Fraser University, Faculty of Health Sciences, Burnaby, Canada, [6]McGill University, Department of Family Medicine, Montreal, Canada, [7]Faculty of Medicine, University of Toronto, Toronto, Canada
Presenting author email: allison_carter@sfu.ca

Background: Assessment of viral suppression is essential towards evaluating progress on Treatment as Prevention (TasP) goals. Without laboratory data measuring viral load (VL), observational studies rely on self-report in surveys but the accuracy remains unclear. We assessed the validity of a self-reported measure of undetectable VL to assess viral suppression among women living with HIV (WLHIV).
Methods: We used survey data from WLHIV (≥16 years) enrolled in the Canadian HIV Women's Sexual and Reproductive Health Cohort Study (CHIWOS) in British Columbia (BC), Canada, the only study province (of three) where linkage to clinical data was possible through the BC Centre for Excellence in HIV/AIDS (a population-based registry capturing 100% of VL data in BC). Self-reported undetectable VL was assessed by the question: "What was your most recent VL, undetectable (i.e. below 50 copies/mL) or detectable (i.e. over 50 copies/mL)?" Laboratory measurements of VL < 50 copies/mL (closest to/before study visit) were the criterion for validity analyses. We measured positive and negative predictive values (PPV, NPV) and likelihood ratios (LR+, LR-) of self-reported undetectable VL.
Results: Survey data were linked to clinical data for 99.7% of participants (n=285); 13 were excluded due to missing self-report data. Median age was 45 (IQR: 37-51). 47% identified as Aboriginal, 36% Caucasian, and 6% African, Caribbean, or Black. 31% and 44% reported recent injection drug use and sex work. 83% were currently on ART and 93% enrolled in HIV care. 84% self-reported having undetectable VL while 82% had clinical data indicating suppression. Women reporting recent illicit drug use and current CD4 < 350 cells/mm^3 were significantly less likely to be virally suppressed. PPV was 94% (95% CI:89-96) indicating 94% of women who self-reported being undetectable truly were, and the NPV was 81% (95% CI:67-92) suggesting that 81% of women who self-reported being detectable truly were. LR+ was 0.1991 (SE: 0.0636) and LR- was 12.4264 (SE: 3.2312).
Conclusions: A brief self-reported measure assessing undetectable VL strongly predicted true viral suppression among a cohort of WLHIV in BC with a high prevalence of laboratory-confirmed viral suppression**.** This measure can be used in research settings without laboratory data to assess TasP-related goals.

Modelling the epidemiological impact of large-scale prevention programmes: approaches and results

MOPEC400

Impact of ART rollout on risky sexual behavior among HIV-negatives in rural KwaZulu-Natal, South Africa

N. Haber[1], F. Tanser[2], K. Herbst[2], D. Pillay[2], T. Bärnighausen[1,2],
Wellcome Trust Africa Centre for Health and Population Studies
[1]Harvard School of Public Health, Global Health and Population, Boston, United States, [2]Wellcome Trust Africa Centre for Health and Population Studies, Health Systems and Impact Evaluation, Mtubatuba, South Africa
Presenting author email: nhaber@mail.harvard.edu

Background: Understanding behavioral response to HIV/AIDS management systems is increasingly vital as the global roll-out of antiretroviral therapy (ART) approaches universal coverage. While behavior change of HIV-positive individuals in clinical care has been studied extensively, there is a lack of robust causal inference regarding the impact of public ART programs on the sexual behaviors of HIV-negative individuals. Risk compensation theory suggests

that ART programs would diminish expected negative consequences of risky sexual behavior, yielding riskier sexual behavior in the HIV-negative population.

Methods: The population for this analysis consists of 3,177 individuals from 2003-2011 who are unmarried, HIV-negative, and born after 1963. Data are from the Africa Centre Demographic Information System, a comprehensive population surveillance system, primarily from annual survey, covering a 478km^2, rural area of KwaZulu-Natal, South Africa. Six ART clinics were opened to offer ART and HIV-related services in this region between July 2005 and February 2007. While the locations of these clinics is likely to be endogenous to sexual behavior, this analysis takes advantage of plausibly exogenous variation in the timing of clinic opening. Observations are restricted to individuals living within 2km of a clinic, utilizing the differences between observations in open and unopened clinics to make a conservative causal estimate of clinic opening on sexual behaviors. Key outcomes include pregnancy and HIV infection rates, using survey data on beliefs regarding ART efficacy as a test of the risk compensation mechanism.

Results: The main results show an 8.4 percentage point (20%) increases in the probability of being ever-pregnant due to local clinic opening dates. However, there was a 0.6-0.9 percentage point (35%) reduction in the probability of testing HIV-positive within 36 months due to the roll-out. Interactions with belief in HIV efficacy are consistent with a risk compensation effect. Men are more likely to be impacted by risk compensation than women after stratifying on gender.

Conclusions: Risk compensation effects in the general population suggest that purely preventative strategies will become more important as universal coverage is approached in expectation of riskier sexual behavior. Efforts should be targeted at men in particular for slowing the spread of HIV.

STI control to prevent HIV transmission

MOPEC401

Factors influencing prevalence of HIV/AIDS among men who have sex with men (MSM) aged 18-24yrs in Mtwapa Town, Kilifi County, Kenya

O. Irungu
HAPA-Kenya, Member, Mombasa, Kenya
Presenting author email: oscar.irungu@yahoo.com

Background: Men who have sex with men (MSM) in Mtwapa Town, Kilifi County are at high risk of HIV infection. Probability sample surveys to determine HIV prevalence among MSM in Mtwapa are needed to inform prevention and care services.

Methods: In 2013, a cross-sectional survey was conducted among MSM aged 18-24 years old ,using respondent-driven sampling (RDS) in Mtwapa. Consenting MSM were tested for HIV (fingerstick rapid test). Population-based prevalence and 95% confidence intervals (CI) were estimated using RDS Analysis Tool (RDSAT).

Results: Among 274 MSM, the median age was 20 years (IQR:19-23 years). Fifty percent of MSM reported not selling sex, while 13.2% reported sex work as their "main occupation", and another 28.4% reported selling sex in the past two months (but not as their main occupation). Overall HIV prevalence was 19.2% (CI: 12.2-23.6%). HIV prevalence was higher among MSM who reported sex work as their main occupation (28.3%,CI: 12.1-42.3%) or selling sex in the past two months (26.6%,CI: 17.2-35.7%), than among MSM who did not sell sex (11.6%,CI: 7.0-18.1%).

Conclusions: : HIV prevalence among MSM were high than among Kilifi's general population aged 15-64 years (8.8%; 2010 KAIS) and highest in male sex workers. Health programs need to address concerns and modify services to meet needs of diverse subgroups of MSM. We recommend continued, periodic surveillance to monitor HIV prevalence among MSM in Mtwapa, and expansion to other areas in Kenya.

Male and female condoms and other physical barriers

MOPEC402

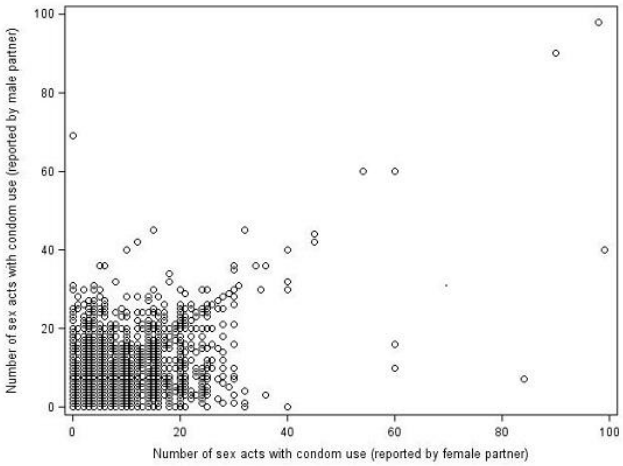
Discordance in unprotected sex reporting among African HIV serodiscordant couples

K. Ngure[1,2], R. Heffron[2,3], T. Hong[2], N. Mugo[2,4], E. Bukusi[2,4], P. Ndase[2], A. Mujugira[2], T. Muwonge[5], C. Celum[2,3,6], J.M. Baeten[2,3,6]
[1]College of Health Sciences Jomo Kenyatta University of Agriculture and Technology & Partners PrEP Demonstration Project, Clinical Sciences, Nairobi, Kenya, [2]University of Washington, Global Health, Seattle, United States, [3]University of Washington, Epidemiology, Seattle, United States, [4]Kenya Medical Research Institute, Center for Clinical Research, Nairobi, Kenya, [5]Makerere University, Kampala, Uganda, [6]University of Washington, Medicine, Seattle, United States
Presenting author email: k_ngure@hotmail.com

Background: For HIV serodiscordant couples participating in prevention studies, couple-level data can be compared to evaluate reporting consistency within couples and potentially provide information about reporting accuracy. We examined the frequency of discordance in reports of condom use among HIV serodiscordant couples enrolled in a HIV prevention trial in Africa.

Methods: Data were from the Partners PrEP Study, a randomized trial of daily oral PrEP for HIV prevention among HIV serodiscordant couples from Kenya and Uganda. At enrollment all couples were sexually active. Participants separately completed an interviewer-administered standardized questionnaire assessing frequency of sex and condom use at quarterly visits. We used descriptive methods to summarize the frequency of unprotected sex and discordant reports and generalized estimating equations to identify correlates of discordant condom use report. We defined couple-level unprotected sex as any self-reported unprotected sex within a partnership during a study visit.

Results: Of the 4747 HIV-1 serodiscordant couples enrolled in the Partners PrEP Study, 97.6% were married with a median of 7 (interquartile range [IQR]: 3-14) years living together and 2 (IQR 1-4) children together. 42.9% of couples reported discrepant condom use at ≥1 visit during study follow-up but only 15.4% of the reports were different by >3 acts (figure).



[Figure. Self-reported sex acts with condom use]

Additionally, 12.1% of follow-up visits had discordant reports about condom use during the last sex act with study partner. Couples with HIV infected female partners (adjusted odds ratio [aOR] = 1.14, 95% confidence interval [CI] 1.01-1.29), currently pregnant (aOR=2.28, 95% CI 2.05-2.53), children together (aOR=1.25, 95% CI 1.03- 1.52) and having more sex together (aOR=1.09, 95% CI 1.08- 1.1, for each additional sex act), were more likely to have at least one partner report unprotected sex.

Conclusions: Although discordant reports on condom use among HIV serodiscordant partners were frequent, the discrepancies were small and not likely to have substantial effect on perceived level of need for biomedical HIV prevention.

Male circumcision

MOPEC403

Satisfaction and discomfort in PrePex™ device circumcision in Mozambique: programmatic implications

B. Cummings[1], H. Muquingue[2], E. Necochea[3], M. Mahomed[4], T. Ferreira[4], D. Bossemeyer[4], L. Nhambi[4], K. Curran[3]
[1]CDC Mozambique, Maputo City, Mozambique, [2]Jhpiego, Monitoring & Evaluation, Maputo, Mozambique, [3]Jhpiego, Baltimore, United States, [4]Jhpiego Mozambique, Maputo City, Mozambique
Presenting author email: mehebub.mahomed@jhpiego.org

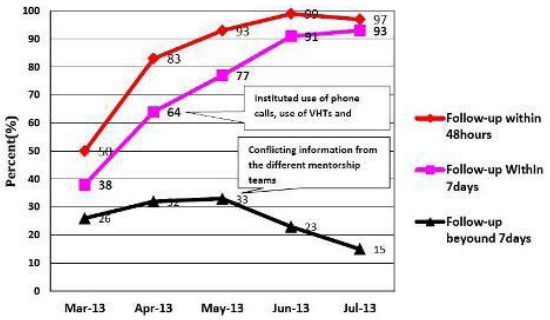
Background: Device circumcision could reach greater numbers of males with fewer human resources and surgical capacity that conventional surgery. As a result, devices may be important circumcision tools in high priority countries like Mozambique, where shortages of medical providers and infrastructure have limited progress to date. Because device circumcision requires men to wear the device for one week, acceptability among prospective clients is critical. This study describes acceptability of the PrePex™ device in an introductory study in Maputo, Mozambique.
Methods: Healthy, HIV-negative males, aged 18-49 years who presented for surgical circumcision services in a Maputo clinic were asked to participate in a study that included assessing the acceptability of a circumcision device. Consenting males received medical screening and genital examination to determine that they were in good physical health and eligible for device circumcision. Routine clinical forms and self-administered surveys were used to collect data at various times during the circumcision process. A visual analogical scale was used to measure pain intensity. Data were analyzed using statistical software.
Results: 504 men received device circumcision between May and July, 2013. Device placement was painless for 98.2% of males. During removal 38.5% reported intense but brief pain and 44.6% moderate pain. Despite that, satisfaction with placement and removal was nearly equal with 91.5% and 93.8% of males very satisfied or satisfied, respectively. Clients were asked about comfort while wearing the device for one week. Most males (51.5%) were very comfortable or comfortable with the device in situ but 38.0% were uncomfortable or very uncomfortable. The most common difficulties with the device in situ were painful erections (29.1%), urination (16.4%) and hygiene (16.1%). Nearly one-quarter reported no difficulties. By the final clinic visit, 49 days post-device placement, 94.6% were very satisfied or satisfied with the procedure.
Conclusions: High levels of satisfaction were reported for device circumcision, despite the pain noted during removal and some specific challenges with the device in situ. Give the programmatic advantages and acceptability among males in this study, Mozambique should consider an integrated service delivery model that combines device circumcision when clinically appropriate as an additional option to conventional surgical circumcision.

MOPEC404

Using continuous quality improvement approaches and service data to improve management of adverse effects and follow-up of circumcised volunteers: the TASO experience

C. Agaba[1], L. Ssali[2], S. Okoboi[3]
[1]TASO Uganda, Programs, Kampala, Uganda, [2]The AIDS Support Organization, Programs, Kampala, Uganda, [3]The AIDS Support Organization, Research Department, Kampala, Uganda
Presenting author email: collin.agaba@gmail.com

Background: Male Circumcision (SMC) is one of the key HIV prevention services TASO provides as part of combination prevention for HIV transmission among HIV negative males. This project's aim was to reduce the proportion of circumcised clients who experienced moderate and severe adverse events from 4.8% to < 2% within 3 months and to improve follow-up of volunteers within 48hours, 7days and beyond 7days of circumcision at two of the TASO sites in Uganda.
Methods: Two quality improvement TASO SMC teams (Tororo and Mbarara) were constituted after Continuous Quality Improvement training in March 2014. We Conducted reviews in government health facilities nearer the camping site and schools, volunteers who experienced adverse effects were calling a telephone hotline. We engaged top health unit management to support SMC plan and involved health facility staff and Village Health Teams in the follow-up activities.
Results: Reviewed a total of 712 out of 1456 circumcised clients between April and August 2014Results show that the proportion of circumcised clients who returned for review within 48 hours increased from 48% to 95%, and from 44% to 63% seven days after surgery between March and August 2014; the rate of moderate and severe adverse events amongst circumcised clients reduced from 4.8% to 1.6% in the same period at Tororo site. At Mbarara site, there was marked improvement in information sharing that led to an increase in the number of clients being followed up.



[Chart 1: Proportion of circumcised clients who experienced adverse events and follow up outcomes]

Conclusions: Continuous Quality improvement approaches in service delivery impact greatly on the SMC service outcomes.

MOPEC405

Safety, feasibility, and acceptability of the PrePex device for adult male circumcision in Malawi

P. Kohler[1,2], B. Beth[3], F. Kilembe[4], S. Galagan[1], A. Kang'ombe[5], C. Hofstee[6], W. Msunguma[3], D. Chilongozi[4], D. Namate[4], M. Machaya[7], K. Kabwere[8], F. Chimbwandira[9]
[1]University of Washington, Global Health, Seattle, United States, [2]University of Washington, Psychosocial and Community Health, Seattle, United States, [3]US Centers for Disease Control and Prevention, Health Services, Lilongwe, Malawi, [4]University of Washington, International Training and Education Center for Health, Lilongwe, Malawi, [5]Banja La Mtsogolo, Blantyre, Malawi, [6]Medecins Sans Frontieres, Blantyre, Malawi, [7]Ministry of Health, Nsanje, Malawi, [8]Ministry of Health, Mulanje, Malawi, [9]Ministry of Health, Lilongwe, Malawi
Presenting author email: pkohler2@uw.edu

Background: Male circumcision programs in Malawi target more than 2 million procedures over 5 years. Non-surgical devices present an alternative to surgery where health infrastructure and resources are limited. This study aims to assess the safety, feasibility, and acceptability of the PrePex device for adult male circumcision in Malawi.
Methods: A prospective single-arm cohort study was conducted at three sites (one urban fixed, one rural fixed, one rural tent) in Malawi. Twelve providers were trained and enrolled, including registered nurses, clinical officers, nurse midwife technicians and a medical assistant. Confidence intervals were corrected for clustering at the clinic-level, and adverse event (AE) outcomes were stratified to include/exclude pain measures to be more comparable with previous studies.
Results: Among 937 men screened, 129 (13.8%) did not meet inclusion criteria, 13 (1.4%) withdrew before device placement, and 791 (84.4%) men received the PrePex device. The majority of participants were under the age of 30 (85.8%). Moderate and severe AEs totaled 6.6% including pain [95% Confidence Interval (CI): 3.2-13.0], and 3.5% excluding pain (95% CI: 2.4-5.1). Severe AEs included insufficient skin removal requiring surgical correction (n=4) and early removal (n=4). Among early removal cases, 1 had immediate surgical circumcision, 1 had surgery after 48 hours when swelling subsided, 1 declined surgery, and 1 did not return to our site though presented at a nearby clinic. More than half of men (51.9%) reported odor while the device was in place, however few (2.2%) stated that they would not recommend the device to others due to odor. Median levels of reported pain were 2 (IQR 2-4) during application and removal, and 0 (IQR 0-2) at all other time points. At each visit of the 5 visits, >90% of participants stated that they were satisfied with the procedure and results.

	Moderate, n (%)	Severe, n (%)	Device-related, n (%)
Pain	21 (2.7)	3 (0.4)	0 (0.0)
Bleeding after removal	10 (1.3)	0 (0.0)	0 (0.0)
Infection	6 (0.8)	0 (0.0)	0 (0.0)
Insufficient skin removed	0 (0.0)	4 (0.5%)	0 (0.0)
Swelling	3 (0.4)	0 (0.0)	0 (0.0)
Wound dehiscence	1 (0.1)	0 (0.0)	0 (0.0)
Device displacement	0 (0.0)	0 (0.0)	2 (0.3)
Self-removal	0 (0.0)	0 (0.0)	2 (0.3)
Total	41 (5.2)	7 (0.9)	4 (0.5)

[Adverse events in PrePex Malawi pilot study, N=791]

Conclusions: The PrePex procedure was highly acceptable among adult men in Malawi. Severe adverse events were rare and similar to other programs, however immediate access to surgical services after displacement or early removal is a challenge. Cases of insufficient skin removal were linked to poor technique, suggesting provider training requires reinforcement and supervision.

MOPEC406

Effectiveness of a quality improvement strategy on the quality of voluntary male medical circumcision services: the Ugandan experience

S. Muhumuza[1], I. Sebuliba[1], I. Lutalo[1], F. Mulekya[1], R. Baryamutuma[1], E. Akello[1], R. King[2], W. Bazeyo[1]
[1]Makerere University School of Public Health, Monitoring and Evaluation Technical Assistance (META) Project, Kampala, Uganda, [2]University of California, Global Health Sciences, San Francisco, United States
Presenting author email: smuhumuza@musph.ac.ug

Background: Ensuring high quality voluntary medical male circumcision (VMMC) services is essential for the realization of the HIV transmission prevention impact of VMMC and increased demand for the service. The objective of this paper is to document Uganda's experience in improving the quality of VMMC services through integration of a quality improvement (QI) strategy in VMMC services.
Methods: In a before-after design, the quality of VMMC services were assessed at two points in time; at baseline in 2013 and follow-up in 2014, where training in QI approaches and onsite coaching and mentorship of VMMC service providers were integrated in 21 VMMC sites in 20 districts of Uganda. Improvement in VMMC service quality was measured through observations of 126 VMMC procedures and review of 13,581 and 11,173 client records at baseline and at follow-up, respectively. Percent scores on quality at baseline and follow-up were generated using the Ministry of Health VMMC quality assessment and performance indicator tools and compared.
Results: Overall, the quality of management systems and supplies for VMMC services increased from 44.3% and 52.5% at baseline to 81.9% and 70.1% (p<0.001) at follow-up, respectively. Health education and HIV testing services improved from 63.1% and 61.9% at baseline to 88.5% and 90.3% (p<0.001) at follow-up, respectively. The quality of the surgical technique increased from 75.8% at baseline to 94.8% (p=0.001) at follow-up. Monitoring and evaluation and infection prevention services improved from 58.2% and 73.1% at baseline to 80.9% (p=0.001) and 87.2% (p=0.012) at follow-up. The proportion of VMMC clients with at least one follow-up visit within 7 days post-surgery increased from 28.6% at baseline to 62.1% (p<0.001) at follow-up. The identification of moderate-severe adverse events increased from 0.24% at baseline to 0.69% (p<0.001) at follow-up.
Conclusions: Our findings suggest that integration of a carefully designed QI strategy into VMMC service delivery may help to achieve high-quality VMMC services. Improved client follow-up enables early identification of adverse events. Such measures are needed for increased efficacy of VMMC services and sustainable high demand for the service.

MOPEC407

Satisfaction with receiving voluntary medical male circumcision services in Nyanza, Kenya: a cross-sectional survey

B. Abunah[1,2], J. Ombaka[2], B. Guyah[2], R. Onkoba[3]
[1]AMREF Kenya, Research Advocacy and Business Development, Nairobi, Kenya, [2]Maseno University, Public Health and Community Development, Kisumu, Kenya, [3]Kemri CGHR, Health and Demographic Surveillance System, Kisumu, Kenya
Presenting author email: bonface.abunah@amref.org

Background: Male circumcision is an important component of a comprehensive multifaceted national HIV prevention policy aimed at reducing the risk of HIV acquisition and ultimately reducing HIV in the general population. Though voluntary medical male circumcision (VMMC) services are free-of-charge at all stages of client care, strategically set targets for its minimum package are not being met.
The goal of this study was to measure the level of satisfaction among circumcised clients, determine facilitatory and inhibitory factors of VMMC follow-up uptake, and elicit opinions on how VMMC services can be improved.
Methods: Between December 2012 and September 2013, men who received VMMC services at one of five public facilities in Nyanza Province were recruited to participate in a telephone interview between the 21st and 31st day after surgery. An experienced research nurse called participants and administered a structured questionnaire. Descriptive analyses were conducted using SPSS. Qualitative data on facilitatory and inhibitory factors and opinions on improving VMMC were coded, grouped and analyzed using N-Vivo software.
Results: Of 1853 males screened to participate, 277 eligible participants were enrolled in the study. Almost half of the participants (45%) were between 18 and 25 years of age and 40% had completed secondary education. The most common response was 'somewhat satisfied' with pre-operative counselling (33.9%), theatre services (37.2%), and the discharge process (37.6%). Half (49.5%) of participants were 'very satisfied' with the outcome of their surgery. Health education/instruction during counselling (31.4%) was the main motivation for returning for follow-up appointment while occupational engagement and presumption of healing (54.3%) was the main inhibitory factor.
Respondents advocated for the introduction of client compensation, nationwide VMMC roll-out, moonlight service provision, Ministry of Health Clinical staff empowerment, SMS alert system and intensified mobilization to improve service delivery.
Conclusions: Men are generally satisfied with VMMC services; improvement is required to ensure VMMC targets are being met. Several factors were found that facilitate and inhibit the holistic care of clients. This study has highlighted areas that health care partners and policy makers could consider to improve VMMC service provision.

MOPEC408

Scaling up of voluntary medical male circumcision (VMMC) services for HIV prevention in South Western region of Uganda

M. Mera[1], E. Natumanya Kajungu[1], B. Nanteza[2], J. Seclen-Palacin[3], E. Bitarakwate[1]
[1]Elizabeth Glaser Pediatric AIDS Foundation, USAID-STAR-SW Project, Mbarara, Uganda, [2]Ministry of Health- Uganda, Kampala, Uganda, [3]Elizabeth Glaser Pediatric AIDS Foundation, Washington, D.C., United States
Presenting author email: mmera@pedaids.org

Background: Studies have suggested that scale-up of voluntary medical male circumcision (VMMC) to 80% of eligible men in developing countries with generalized HIV epidemics could avert up to 3.4 million new HIV infections and save up to $16 billion in treatment costs by 2025. SouthWest (SW) Uganda has an HIV prevalence of 8.0% and circumcision is not common place among its population. In 2010, the country's Ministry of Health (MOH) targeted reaching 80% of eligible men (769,489) with VMMC services by 2016 to positively impact HIV prevention. Since 2011, The Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) a lead on the USAID-STAR SW project, in partnership with the Uganda MOH, provided support to ensure effective and accessible VMMC services to 48 facilities across all 13 districts in SW Uganda. Program performance reviews conducted by EGPAF to ensure promising practices in program strategy were utilized to ensure program implementers were on track to meet targets.
Methods: A systematic review of monthly data generated from site-level VMMC registers was conducted by EGPAF in 2012. We disaggregated and analyzed data from the VMMC registers by service delivery model: site-based or targeted outreach models over time to determine the contribution of each model to VMMC outcomes. After observing that outreaches yielded more numbers, we then deliberately focused on this model hence the progressively increasing service outputs. Site-based VMMC involves offering those services to clients as they visit a hospital whereas targeted outreach VMMC are offered at lower-level health sites by travelling hospital staff (who visit these outposts, bringing surgical equipment to provide services to community residents following community sensitization/advertisements in the catchment area of the site).
Results: The vast majority of circumcisions in SW Uganda were accomplished through targeted outreach: 85% (193,387/229,277) of all circumcisions performed in 2011-2014 occurred through targeted outreach. See Table; Progress of VMMC service utilization in SW Uganda (2011-2014)

Period	N of men circumcised in 48 VMMC Site-Based clinical services	N of men circumcised in Targeted Outreach clinical services	Total VMMC Procedures
2011	1,582	1,279	2,861
2012	10,649	22,687	33,336
2013	14,774	66,211	80,985
2014	8,885	103,210	112,095
Total	35,890	193,387	229,277

[Progress of VMMC service utilization in SW Uganda]

Conclusions: Targeted outreach significantly contributed to reaching VMMC program targets. This observation has been used to inform district health authorities to create greater buy-in and demand around targeted outreach VMMC. Further analysis is needed to identify challenges around site-based health facility-based circumcision.

MOPEC409

Projected costs and impacts of increasing coverage of 20- to 29-year-olds as voluntary medical male circumcision is scaled up in Zimbabwe

K. Kripke[1], K. Hatzold[2], D. Taljaard[3], K. Curran[4,5], D. Castor[6], E. Njeuhmeli[7]
[1]Avenir Health, Glastonbury, United States, [2]PSI, Harare, Zimbabwe, [3]CHAPS, Johannesburg, South Africa, [4]Jhpiego, Washington, United States, [5]Johns Hopkins Bloomberg School of Public Health, Baltimore, United States, [6]U.S. Department of State, Office of the Global AIDS Coordinator, Washington, United States, [7]USAID, Office of HIV/AIDS, Washington, United States
Presenting author email: khatzold@psi-zim.co.zw

Background: Most countries scaling up voluntary medical male circumcision (VMMC) for HIV prevention have aimed to increase circumcision coverage to 80% among 15- to 49-year-olds. However, VMMC implementers have reported that the majority of clients are ages 10 to 19, with proportions of clients ages 20 and above decreasing over time. This suggests that high coverage among men ages 20 and older may not be achievable. A team from the USAID- and PEPFAR-supported Health Policy Project created more realistic scale-up scenarios based on trends in implementation data from Zimbabwe and examined the potential costs and impacts of increasing efforts to recruit clients ages 20 to 29.
Methods: Zimbabwe VMMC program data were used to examine historical trends in male circumcision coverage by age and project these trends into the future. The projection informed a base scenario supposing that over five years, it would be possible to achieve 80% circumcision coverage among males ages 10-19 and to increase coverage by 25%, 15%, and 10% among males ages 20-24, 25-29, and 30-49, respectively. Two other scenarios assumed that the program could double or triple the increase in coverage among clients ages 20-29 by doubling or tripling the effort (represented as the unit cost in the model), respectively, with a maximum circumcision prevalence of 80% for any age group. The DMPPT 2.0 model for Zimbabwe was used to project costs and impacts, assuming a VMMC unit cost of $79 and a discount rate of 3%.
Results: Increasing circumcision coverage among men ages 20-29 averts more HIV infections. The number of VMMCs required to avert one infection over 15 years decreases as coverage increases in this age group. Assuming that effort (unit cost) is directly related to the increase in coverage among this age group, the cost per HIV infection averted in the 2x scenario is less than the base and 3x scenarios.

Scenario	Base	2x 20-29	3x 20-29
HIV infections averted	56,000	77,000	99,000
Total cost	$207 Million	$268 Million	$390 Million
% infections averted	17	22	29
VMMC per infection averted	46	38	33
Cost per infection averted	$6,200	$5,900	$6,800

[Cost and impact of different scenarios]

Conclusions: Under these assumptions, doubling the effort to attract clients ages 20-29 leads to increased cost-effectiveness of the program. The overall cost and impact of the program also increase. Programs should measure the relationship between increased effort and increased ability to attract this age group.

MOPEC410

Male circumcision and foreskin cutting practices may explain regional variations in HIV prevalence in Papua New Guinea

D. MacLaren[1,2], W. McBride[1], J.M. Kaldor[3], A. Vallely[4,5]
[1]James Cook University, Cairns, Australia, [2]Pacific Adventist University, Port Moresby, Papua New Guinea, [3]University of New South Wales, Kirby Institute, Sydney, Australia, [4]University of New South Wales, Kirby Institute, Darlinghurst, Australia, [5]Papua New Guinea Institute of Medical Research, Goroka, Papua New Guinea
Presenting author email: jkaldor@kirby.unsw.edu.au

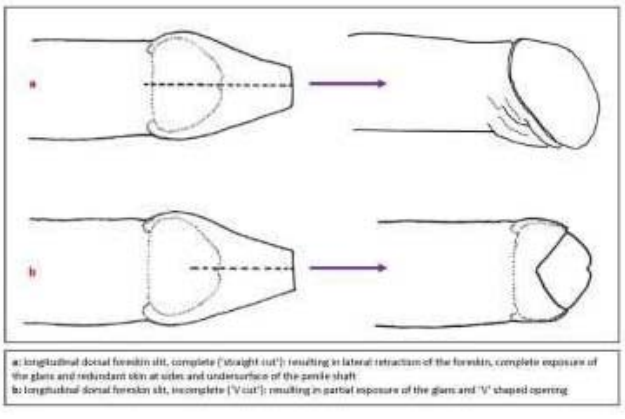
Background: Male circumcision (MC) has been shown to prevent heterosexual HIV acquisition in men. Epidemiological evidence from heterosexually driven epidemics indicates that populations with relatively high MC prevalence have relatively low HIV prevalence. Papua New Guinea (PNG) is an extremely diverse nation of 7 million people that speak over 800 languages with myriad socio-cultural practices, including MC and different forms of penile foreskin cutting. PNG has an estimated general adult HIV prevalence of 0.6-0.8% but there are significant variations in prevalence by geographical region and in different sub-populations.
Methods: Self-reported data on male circumcision and penile foreskin cutting were collected from 853 men in four provinces and used to construct maps indicating the prevalence of cutting in each of the country's four regions. National Department of Health HIV surveillance data were used to construct similar maps indicating variations in HIV prevalence by region.
Results: The prevalence of male circumcision varied from 8-9% in Southern and Highlands Regions, to 13% in Momase, and 23% in New Guinea Islands (NGI). Dorsal longitudinal foreskin slit was the most common form of penile cutting (Momase, 58%; NGI, 50%; Highlands, 45%; and Southern, 42%). The proportion of men without a cut was highest in Southern (50%) and Highlands (46%) Regions, and lowest in Momase (29%) and NGI (27%). Estimated adult HIV prevalence was 1.17%, 1.02%, 0.63% and 0.61% in Southern, Highlands, Momase and NGI Regions respectively. Male circumcision and longitudinal dorsal slit were strongly associated with HIV prevalence and able to explain 99% of the observed geographic variability in HIV prevalence in PNG ($p< 0.01$).
Conclusions: The geographical distribution of HIV infection in PNG appears to be closely correlated with the distribution of male circumcision and other forms of penile foreskin cutting. Given that complete dorsal longitudinal foreskin slit results in an appearance almost identical to that of MC we hypothesise that this form of foreskin cutting may confer a similar level of protection against HIV acquisition in men and thereby help explain the geographical distribution of HIV in PNG.

MOPEC411

Dorsal longitudinal slit of the penile foreskin may protect men against HIV acquisition in Papua New Guinea

A.J.B. Vallely[1,2], D. MacLaren[3,4], M. David[2], P. Toliman[2], A. Kelly-Hanku[2,5], R. Tommbe[4], Z. Kombati[6], K. Browne[7], C. Manineng[3], P. Kaima[8], L. Simeon[4], C. Ryan[2,9], H. Wand[1], P. Hill[10], G. Law[7], J. Millan[11], P. Siba[2], W.J. McBride[3], J.M. Kaldor[12]
[1]University of New South Wales, Kirby Institute, Darlinghurst, Australia, [2]Papua New Guinea Institute of Medical Research, Goroka, Papua New Guinea, [3]James Cook University, Cairns, Australia, [4]Pacific Adventist University, Port Moresby, Papua New Guinea, [5]University of New South Wales, Sydney, Australia, [6]Mt Hagen Hospital, Department of Pathology, Mt Hagen, Papua New Guinea, [7]National Department of Health, Port Moresby, Papua New Guinea, [8]Mt Hagen Hospital, Tininga Clinic, Mt Hagen, Papua New Guinea, [9]Burnet Institute, Melbourne, Australia, [10]University of Queensland, Brisbane, Australia, [11]PNG Sexual Health Society, Port Moresby, Papua New Guinea, [12]University of New South Wales, Kirby Institute, Sydney, Australia
Presenting author email: jkaldor@kirby.unsw.edu.au

Background: Papua New Guinea (PNG) is a diverse nation with myriad socio-cultural practices, including male circumcision (MC) and different forms of penile foreskin cutting. In earlier research we found that (a) foreskin cutting practices are common and widespread; (b) complete dorsal longitudinal foreskin slit results in an appearance almost identical to that of MC (Figure 1); and (c) variations in HIV prevalence by geographical region are closely correlated with the distribution of penile cutting practices in PNG.
These findings led us to investigate the association between penile foreskin cutting and HIV infection in more depth in this setting.



[Figure 1]

Methods: A prospective study among men attending voluntary HIV counselling and testing (VCT) clinics at six sites in the highlands region of PNG is underway. Following completion of informed consent procedures, participants undergo a face-to-face interview in which socio-demographic, behavioural and clinical information are collected, and a physical examination conducted in which foreskin cutting status is verified and categorised according to the degree of exposure of the glans penis. In addition to onsite HIV testing, participants provide venepuncture and urine specimens for offsite laboratory-based herpes simplex type-2 and syphilis serology, and polymerase chain reaction for chlamydia, gonorrhoea and trichomonas infection.
Results: Among 524 men enrolled to end-2014, 325 (62.0%) were uncut; 153 (29.2%) had a complete dorsal slit; 38 (7.6%) a partial dorsal slit; and 6 (1.1%) had MC. The prevalence of HIV was 9.3% overall (49/524) and was greatest among uncut men (36/325, 11.1%). Uncut men and those with a partial cut (in which the foreskin still covers part or all of the glans in the non-erect penis) were significantly more likely to have HIV infection compared to men with a complete dorsal longitudinal slit or full MC in unadjusted and adjusted analyses (Table 1).

NOTE: §=adjusted for age;§§=adjusted for age, condom use frequency in past 4 weeks and number of partners	N (%)	Unadjusted Odds Ratio (95% CI)	p-value	Adjusted§ Odds Ratio (95% CI)	p-value	Adjusted§§ Odds Ratio (95% CI)	p-value
Foreskin status based on exam findings (n=524; includes those with male circumcision)							
Longitudinal slit or male circumcision	159 (30.3)	1		1		1	
Uncut/partial cut	365 (69.7)	2.39 (1.10,5.22)	0.029	2.88 (1.29,6.47)	0.010	2.84 (1.26,6.41)	0.012
Foreskin status based on exam findings (n=518; excludes those with male circumcision)							
Longitudinal slit	153 (29.5)	1		1		1	
Uncut/partial cut	365 (70.5)	2.29 (1.05,5.02)	0.038	2.28 (1.25,6.33)	0.012	2.77 (1.22,6.26)	0.015

[Table 1]

Conclusions: Alternative forms of penile foreskin cutting that result in complete exposure of the penile glans and an appearance similar to MC may protect men against HIV acquisition. The final results of this study (expected end-2015) are likely to have implications for HIV prevention policy in countries where alternative forms of foreskin cutting are prevalent.

MOPEC412

Impact and cost of including adolescents ages 10-19 in programs to scale up voluntary medical male circumcision in South Africa

K. Kripke[1], K. Curran[2,3], C. Bonnecwe[4], D. Loykissoonlal[4], A. Thambinayagam[5], E. Gold[6], K. Seifert-Ahanda[7], D. Castor[8], E. Njeuhmeli[7]
[1]Avenir Health, Glastonbury, United States, [2]Jhpiego, Washington, United States, [3]Johns Hopkins Bloomberg School of Public Health, Baltimore, United States, [4]South African National Department of Health, Pretoria, South Africa, [5]USAID, Pretoria, South Africa, [6]Johns Hopkins University, Center for Communication Programs, Baltimore, United States, [7]USAID, Office of HIV/AIDS, Washington, United States, [8]U.S. Department of State, Office of the Global AIDS Coordinator, Washington, United States
Presenting author email: kelly.curran@jhpiego.org

Background: In 2011, the WHO and UNAIDS released a strategic action framework that set a goal of scaling up male circumcision prevalence to at least 80% among males ages 15-49 by 2016 in fourteen countries with generalized HIV epidemics and low prevalence of male circumcision. The 15-49 year age group was chosen because it includes the vast majority of sexually active males. As voluntary medical male circumcision (VMMC) programs were scaled up, implementers in these countries found that although the intended demand creation audience was adult men, the majority of clients accessing services were adolescents ages 10-19. This study, conducted by the USAID- and PEPFAR-funded Health Policy Project, examines the contribution of adolescent VMMC to the impact, cost, cost-effectiveness, and sustainability of VMMC programs in South Africa.
Methods: Using the DMPPT 2.0 model, we examined the impact of VMMC disaggregated by client age in South Africa. The model was populated with baseline male circumcision prevalence extracted from the South African National HIV Prevalence, Incidence and Behaviour Survey, 2012, and population and HIV incidence and prevalence projections from the South Africa national Spectrum/AIM file extended out to 2050.
Results: In a strategy to scale up male circumcision prevalence to 80% among men ages 10-34, 24% of the reduction in HIV incidence over 15 years can be attributed to circumcisions among the 10-19 year age group. This additional HIV incidence reduction requires circumcising an additional 4 million adolescents over 15 years, compared with a strategy providing VMMC only to clients ages 20-34. Inclusion of clients ages 10-14 within the scale-up strategy, while less cost-effective, can facilitate quicker transition from the scale-up phase to the sustainability phase.
Conclusions: Adolescents represent a key population for VMMC. They constitute the majority of clients. They have a right to HIV prevention services. They are essential to sustaining male circumcision coverage once the initial targets have been met. They contribute to the impact of VMMC on HIV incidence, and this impact increases over time. Inclusion of adolescents in the VMMC program requires resources and will require tailoring in-service communication to their specific needs.

MOPEC413

A sport-based intervention to increase uptake of voluntary medical male circumcision among adolescent male students in Bulawayo, Zimbabwe: process evaluation

J. DeCelles[1], R. Hershow[2], D. Ross[3], Z. Kaufman[3], K. Gannett[3], T. Ncube[4], A. Harrison[5]
[1]Grassroot Soccer, Cape Town, South Africa, [2]Grassroot Soccer, Research & Development, Cape Town, South Africa, [3]London School of Hygiene and Tropical Medicine, London, United Kingdom, [4]Grassroot Soccer, Bulawayo, Zimbabwe, [5]Brown University, Providence, United States
Presenting author email: rebeccah@grassrootsoccer.org

Background: Three randomized controlled trials have shown that VMMC reduces female-to-male transmission of HIV by 50-60%. Mathematical modelers estimate that, between 2011 and 2025, more than 3.3 million new HIV infections (570,000 in Zimbabwe alone - 42% of the projected new infections) could be averted through increased scale-up and uptake of VMMC. Despite progress in supply scale-up, Zimbabwe is falling well short of its target of 80% VMMC coverage. In this context, Grassroot Soccer developed "Make the Cut +" (MTC+), a short, scalable intervention facilitated by circumcised "coaches" and targeting 14-19 year-old male students in secondary schools in Bulawayo, Zimbabwe. MTC+ consists of a 60-minute soccer-themed educational session and logistical, behavioral reinforcement in the form of follow-up phone calls, coach accompaniment to the clinic, and small soccer-based incentives.
Methods: A process evaluation was conducted to help interpret VMMC uptake findings from a cluster-randomized trial conducted with 1226 male adolescent Zimbabwean students from March to July 2014. The process evaluation explores perceptions of VMMC, perceptions and acceptability of the MTC+ intervention, influential factors in deciding whether to undergo VMMC, the role of incentives (USD 5 value) in creating demand for VMMC, and to see if there was any evidence of coercion. The process evaluation includes 20 in-depth interviews (IDIs) with participants, 7 IDIs with MTC+ coaches, and structured observation of programme implementation.
Results: IDIs suggest participants enjoyed the educational session because they highly valued hearing their coaches' personal experiences with VMMC and connected with the soccer theme. Logistical reinforcement influenced participants' decisions to undergo VMMC. Additionally, qualitative findings suggest MTC+ coaches generally enjoyed and accepted the intervention. Responses to incentives were mixed, with some participants saying provision of incentives influenced their decision to undergo VMMC, while others did not feel it was influential. The IDIs with participants do not show any evidence of coercion.
Conclusions: This study provides strong evidence of MTC+'s effectiveness and acceptability in Bulawayo schools. If the intervention's effectiveness remains consistent at scale, the MTC+ intervention could generate substantial new VMMC demand among adolescent males and should be included in a package of effective demand creation tools.

MOPEC414

Association of demographics and sexual risk behaviour with adverse events among men accessing medical male circumcision in Ekurhuleni North, South Africa

C.M. Chetty-Makkan, V. Molapisi, M. Kgampe, O. Letlape, S. Ginindza, S. Charalambous, M. Maraisane
Aurum Institute, Research Department, Gauteng, South Africa
Presenting author email: cchetty@auruminstitute.org

Background: Medical male circumcision (MMC) reduces HIV infection by 60%. Swelling, bleeding and wound infection are common adverse events (AEs) which are suggestive of sex post circumcision before healing is complete. We investigated the relationship between post-circumcision AEs, demographics and sexual risk behaviour among men accessing routine MMC services.
Methods: At enrolment, questionnaires on demographics (age, language, ethnicity, employment status) and sexual risk behaviour (marital status, number of sexual partners in the past 6 months and condom use) were administered prior to circumcision (19 September 2011-21 May 2014). After circumcision, participants were invited to attend at least 2 follow-up visits where AE's were identified. Bivariate analyses and logistic regressions models were used to determine associations with post-circumcision AEs.
Results: A total of 20929 adult males (median age 26 years, range 18-69) completed questionnaires prior to circumcision. Among 12059 (57.6%) participants that attended at least 1 follow-up visit, we identified 128 post (1.1%) circumcision AE's. The common identified post circumcision AEs were wound disruption 44 (0.4%), infection/sepsis 37 (0.3%) and excessive bleeding 21 (0.2%). There were significant associations between age (x^2 (1, N = 12059) = 5.5, p = 0.02) and language (x^2 (2, N = 11839) = 7.1, p = 0.03) with post circumcision AEs respectively. Marital status, having 1 or more female partner/s and condom use were not associated with post-circumcision AE's. We included age, language and marital status into the multivariate model. Higher odds of being identified with an AE post circumcision was found with older age [(vs. young adults (18-24 years): 25-69 years OR 1.5; 95% CI 1.0-2.4] and speaking a non-indigenous language [(vs. Setswana/Sesotho: Non-indigenous OR 2.6; 95% CI 1.2-5.4].

Conclusions: While men who are 25 years and above are accessing MMC services, they may be at risk of being identified with an AE post-circumcision. It is possible that individuals who do not speak the local language may not fully understand the post-procedure instructions. Tailored age appropriate counselling in different languages on sexual abstinence post-circumcision is recommended for those accessing MMC services.

MOPEC415

Improving quality of voluntary medical male circumcision services thorough mentorship and coaching: an experience of East Central Uganda

R. Bbuye[1], M. Ndifuna[1], E. Tibenderana[1,2], S. Mashate[1,2], F.H. Kazibwe[1], A. Mugume[1], D. Namuganga[1]
[1]JSI Research &Training Institute Inc./Strengthening TB and HIV&AIDS Responses in East Central Uganda (STAR-EC) Program, Jinja, Uganda, [2]AIDS Healthcare Foundation/Uganda Cares, Kampala, Uganda
Presenting author email: rbbuye@starecuganda.org

Background: The World Health Organization and United Nations Program on AIDS recommend voluntary medical male circumcision (VMMC) to be part of comprehensive HIV prevention package. VMMC is known to reduce the risk of HIV infection by 60% and therefore provides a vital a avenue for averting new HIV infections especially the sexually active individuals. To achieve optimum benefit and successful scale of VMMC, there are minimum quality indicators that must be in place to ascertain safety and confidence among the beneficiaries. However, the baseline quality improvement assessments conducted in 2013 at 22 health facilities in East Central Uganda showed that adherence to Ministry of Health (MoH) quality improvement indicators for VMMC services was less than 60% as opposed to the acceptable standard 80% and above.
Methods: From 2013 through to 2014, The Strengthening TB and HIV&AIDS Responses in East Central Uganda (STAR-EC) with funding from USAID conducted onsite monthly mentorships and coaching at 22 VMMC health facilities that offer static and outreach VMMC services. The objective was to ensure that set MoH quality improvement standards are adhered to and sustained. The quality improvement areas on which coaching and mentoring focused on included: management systems; supplies, equipment and environment; registration and utilization of information, education and communication materials; individual HIV testing and counseling; adherence to standard male circumcision; infection control, monitoring and evaluation.
Results: § Ministry of Health quality standards for VMMC services improved from below 60% to over 80% in all quality indicators § The VMMC teams developed capacity to conduct continuous self-assessment to sustain quality§ There was improvement in day two post circumcision follow up of the beneficiaries by health workers from 40% to over 90%§ All the 22 health facilities were able to competently respond to any emergency due to the availability of fully constituted emergency kits § Post circumcision adverse events have been maintained at the acceptable limit of less 2%
Conclusions: On-site health facility mentoring and coaching is an effective and cost effective model of improving quality of VMMC services. This also provides a platform for monitoring and evaluating quality of VMMC services in resource limited settings.

Treatment as prevention

MOPEC416

Assessing TasP implementation one year after the publication of Brazilian national guidelines

M.A. Freitas[1], A.R. Pascom[2], F. Mesquita[2], J. Barbosa[3]
[1]Ministry of Health - Department of STD, AIDS an Viral Hepatitis, Care and Treatment Division, Brasília, Brazil, [2]Ministry of Health - Department of STD, AIDS and Viral Hepatitis, Brasília, Brazil, [3]Ministry of Health, Brasília, Brazil
Presenting author email: marcelaofreitas@gmail.com

Background: Brazil was the first developing country and the third country in the world to adopt the concept of Treatment as Prevention (TasP) in its national guidelines. Published in the end of 2013, the new national guidelines presented the recommendation of stimulating antiretroviral therapy (ART) initiation for all people living with HIV/AIDS (PLWHA) irrespective to CD4 count or clinical condition. The objective of this study is to assess TasP implementation one year after the publication of Brazilian ART guidelines.
Methods: A multiple cross-sectional study was made by analyzing data on antiretroviral dispensation and routine monitoring laboratory tests from two national information systems. Patients who were 18 or more years of age and had the first ARV dispensation in life between 2009 and 2014 were selected. Increase rate of new patients on ART, last CD4 count before ART initiation and viral suppression rate (below 1000 cp/ml) were analyzed.
Results: In 2014, 70.047 patients started ART in Brazil, 27% more than the 55.721 patients who initiated ART in 2013. Approximately 36% initiated ART with CD4 count higher than 500 cell/mm^3, what represented a twofold increase of the proportion observed in 2013. Consequently, the median CD4 count at treatment increased 26%, from 349 in 2013 to 439 cell/mm^3 in 2014. Moreover, viral suppression rate among patients who started ART with CD4 count higher than 500 cell/mm^3 in 2014 was 92%, higher than the average of 88% observed in the same year.
Conclusions: One year after TasP implementation in Brazil, the highest increase in the amount of PLWHA starting ART in Brazilian history could be observed. Similarly, early ART initiation was significantly improved. Morevover, this study showed a higher suppression rate in patients who started ART with CD4 count above 500 cells/mm3 than the average in 2014, what refutes the idea that these patients would present lower levels of adherence to treatment. By implementing innovative national strategies, Brazil shows that it may not only succeed in achieving the 90-90-90 goals by 2020 but also contribute to the end of the world epidemic levels of HIV/AIDS by 2030.

MOPEC417

Identification of factors associated with viral suppression and treatment failure when antiretroviral therapy is used for HIV prevention: results from the HIV prevention trials network (HPTN) 052 trial

J. Fogel[1], S.S. Ou[2], Y.Q. Chen[2], E. Piwowar-Manning[1], M. McCauley[3], D. Sabin[1], J. Eron[4], J. Gallant[5], T. Gamble[6], M.C. Hosseinipour[4,7], J. Kumwenda[8], J. Makhema[9], R. Panchia[10], J.G. Hakim[11], V. Akelo[12,13], N. Mwelase[14], S. Chariyalertsak[15], S.V. Godbole[16], N. Kumarasamy[17], B. Grinsztejn[18], J.H. Pilotto[19], B. Santos[20], K.H. Mayer[21,22], M.S. Cohen[4], S.H. Eshleman[1], for the HPTN 052 Study Team
[1]Johns Hopkins Univ. School of Medicine, Dept. of Pathology, Baltimore, United States, [2]Fred Hutchinson Cancer Research Center, Vaccine and Infectious Disease Division, Seattle, United States, [3]FHI 360, Washington, DC, United States, [4]Univ. of North Carolina School of Medicine, Dept. of Medicine, Chapel Hill, United States, [5]Southwest CARE Center, Sante Fe, United States, [6]FHI 360, Durham, United States, [7]UNC Project, Lilongwe, Malawi, [8]College of Medicine-Johns Hopkins Project, Blantyre, Malawi, [9]Botswana Harvard AIDS Institute, Gaborone, Botswana, [10]Univ. of the Witwatersrand, Perinatal HIV Research Unit, Johannesburg, South Africa, [11]Univ. of Zimbabwe, Harare, Zimbabwe, [12]Kenya Medical Research Institute, Kisumu, Kenya, [13]Center for Disease Control, Kisumu, Kenya, [14]Univ. of Witwatersrand, Clinical HIV Research Unit, Johannesburg, South Africa, [15]Chiang Mai University, Research Institute for Health Sciences, Chiang Mai, Thailand, [16]National AIDS Research Institute, Indian Council of Medical Research, Pune, India, [17]Y. R. Gaitonade Center for AIDS Research and Education, VHS, Chennai, India, [18]Instituto de Pesquisa Clinica Evandro Chagas, Fiocruz, Rio de Janeiro, Brazil, [19]Hospital Geral de Nova Iguacu and Laboratorio de AIDS e Imunologia Molecular-IOC/Fiocruz, Rio de Janeiro, Brazil, [20]Hospital Nossa Senhora da Conceição, Porto Alegre RS, Brazil, [21]Fenway Health, Boston, United States, [22]Harvard Medical School, Boston, United States
Presenting author email: jfogel@jhmi.edu

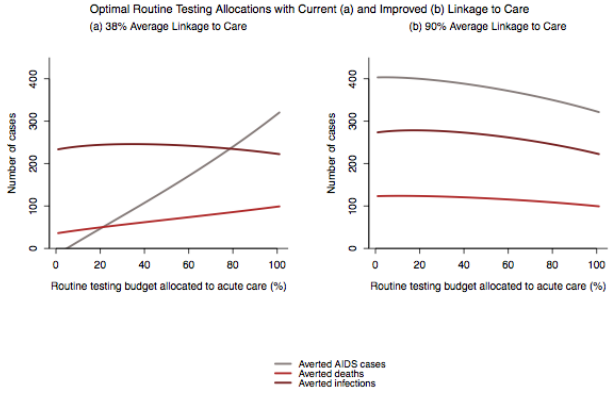
Background: In HPTN 052, early antiretroviral therapy (ART) prevented 96% of linked HIV infections in serodiscordant couples. In this setting, HIV transmission can occur after ART initiation before viral suppression (VS) or after ART failure. We analyzed VS and ART failure in HPTN 052.
Methods: Data through May 2011 (trial unblinding) was analyzed for 1,036 participants who had a viral load (VL) >400 at ART initiation (early arm: N=832, CD4 350-550 at ART initiation, 1,647 person-years on ART; delayed arm: N=204, CD4 < 350 at ART initiation, 219 person-years on ART). VS was defined as the first of two consecutive VLs ≤400. ART failure was defined as the first of two consecutive VLs >1,000 >24 weeks after ART initiation. Factors analyzed from the time of ART initiation included study arm, age, gender, CD4 count, VL, region (Americas/Asia/Africa), regimen (zidovudine/lamivudine/efavirenz vs. other), education level, marital status, and number of sex partners.
Results: Cumulative probabilities of VS at 1, 3, 6, and 12 months were 46.4%, 78.5%, 89.4%, and 92.9%. In a multivariate model, higher VL at ART initiation was associated with longer time to VS (hazard ratio [HR]: 0.87 [0.84, 0.91]; p< 0.0001). By May 2011, 93 participants in the early arm and 9 participants in the delayed arm failed ART. Time to ART failure and ART failure were analyzed for the early arm only. In univariate models, lack of VS by 3 months was associated with shorter time to ART failure (HR=9.34 [6.14-14.2]; p< 0.0001) and ART failure (odds ratio=8.99 [5.65-14.3], p< 0.0001). Findings were similar for lack of VS by 6 months. Weaker associations were observed for age and time to VS and for education level and failure outcomes.
Conclusions: Higher VL at ART initiation is associated with a longer time to VS, potentially increasing the risk of HIV transmission after ART initiation. A longer time to VS is associated with a shorter time to ART failure and ART failure, potentially increasing the risk of late transmission events. Further studies are needed to evaluate the relationships between VL, time to VS, ART failure, and HIV transmission when ART is used for HIV prevention.

MOPEC418

Reconciling the individual and community benefits of treatment as prevention through optimizing an HIV testing program

A. Nadaf[1], A. Adams[2], S. Kok[2], A. Rutherford[2], R. Gustafson[3], R. Barrios[4], K. Vasarhelyi[2,5]
[1]Simon Fraser University, Burnaby, Canada, [2]Simon Fraser University, IRMACS, Burnaby, Canada, [3]Vancouver Coastal Health, Vancouver, Canada, [4]British Columbia Centre for Excellence in HIV/AIDS, Vancouver, Canada, [5]Simon Fraser University, Faculty of Health Sciences, Burnaby, Canada
Presenting author email: anadaf@sfu.ca

Background: Treatment as Prevention (TasP) provides benefits to individuals and community, which may be shared disproportionately depending on how TasP is implemented operationally. We sought potential conflicts between individual and community TasP goals through a resource allocation analysis conducted to optimize the HIV testing program in Vancouver, Canada.
Methods: We carried out resource allocation simulations using a validated system dynamics model of the HIV care continuum in Vancouver, (doi:10.1007/s10729-014-9312-0). The model incorporates the major local testing programs, including high-cost/high-efficiency targeted testing and low-cost/high-efficiency routine testing in high-prevalence settings (HPS), both serving key populations of men who have sex with men (MSM) with 15% prevalence of HIV and the socially linked injection drug user and street-based female sex worker (IDU-FSW) populations with 18% prevalence of HIV. Relatively low-cost/low-efficiency routine testing in acute care serves these key populations as well as the general population with 0.1% prevalence of HIV. The cost of a targeted test is approximately 7 times the cost of a routine test. The optimal strategies for allocating a fixed budget were determined by incrementally reallocating resources until minimum morbidity, mortality or incidence was achieved. We considered HIV morbidity and mortality to represent individual outcomes and HIV incidence to represent community outcomes.
Results: Morbidity, mortality and new infections were all minimized when resources were predominantly allocated to routine testing. However, to minimize morbidity and mortality, resources had to be predominantly dedicated to routine testing in acute care, potentially averting 320 AIDS cases, 99 deaths, and 238 new infections. In contrast, minimizing incidence would require 44% of the budget to be allocated to routine testing in HPS and the rest to acute care; this strategy could avert 123 AIDS cases, 65 deaths, and 277 new infections. Further simulations showed that improving linkage to care in HPS to match acute care rates could harmonize individual and community benefits in HPS.
Conclusions: Understanding that individual and community benefits of TasP could be shared unequally is important for operational planning and policy. Analysis of the HIV care continuum as a system can uncover important inconsistencies, while optimization techniques can help make better use of scarce resources.



[Figure 1]

MOPEC419

Can targeting treatment as prevention to female sex workers in a concentrated HIV epidemic setting lead to local HIV elimination: a modelling study

A. Low[1,2], N. Nagot[3], I. Konate[4], N. Meda[4], M. Segondy[3], P. Van de Perre[3], P. Mayaud[1], P. Vickerman[2], Yerelon Study Group
[1]London School of Hygiene and Tropical Medicine, London, United Kingdom, [2]Bristol University, Bristol, United Kingdom, [3]Universite de Montpellier, Montpellier, France, [4]Centre Muraz, Bobo-Dioulasso, Burkina Faso
Presenting author email: andrea_low@hotmail.com

Background: Burkina Faso has a concentrated HIV epidemic where female sex workers (FSW) are thought to drive HIV transmission. In such settings, targeting antiretroviral treatment (ART) to FSWs could be an efficient strategy for reducing HIV transmission to low levels. The aim of this study was to compare the impact and efficiency of different targeted ART-based prevention strategies.
Methods: A dynamic deterministic HIV transmission model was developed using data from the Yerelon FSW cohort in Bobo-Dioulasso and general population surveys obtained from 1987 to 2010. The model categorises individuals into subgroups on the basis of gender and sexual behaviour and stratified FSW into occasional and full-time FSWs. Compared to current ART provision (status quo/SQ), the model estimated the proportion of HIV infections averted (%HIA) or incremental life-years-gained (LYG) per additional person-year of ART (PYAs) over 20 years from prioritizing ART to different subgroups, or expanding eligibility to all HIV-infected individuals. The model also estimated the impact of past increases in condom use.
Results: Modelling suggests that the scale-up of condom use within commercial sex averted 40% of past HIV infections. Continuing current levels of ART (SQ) over the next 20 years averts 35-47% of new infections compared to no ART, leading to local elimination by 2037. The most rapid decline in incidence is achieved by increasing the annual recruitment on to ART to 80% of all HIV-infected individuals (54-71 %HIA compared to SQ, over 20 years) with local elimination being achieved by 2016. If FSWs were targeted at the same recruitment rate, then a smaller impact (4-38 %HIA) is achieved, with local elimination occurring by 2027; however, targeting FSWs is more efficient in terms of LYG per 100PYAs (97.64 vs. 55.31 LYG/100PYAs, respectively). Importantly, condom use within commercial sex needs to be maintained at high levels (>80%) for HIV elimination to occur with expanded ART provision to FSWs.
Conclusions: Increasing FSW recruitment onto ART could be an efficient prevention strategy for eliminating HIV transmission in concentrated epidemic settings, but should not be undertaken at the expense of existing interventions for FSWs, particularly condom promotion.

Vaccines

MOPEC420

Parents' uptake of human papillomavirus vaccine for their children: a systematic review and meta-analysis

P.A. Newman, C. Logie, A. Lacombe-Duncan, P. Baiden, N. Doukas, A. Asey
University of Toronto, Factor-Inwentash Faculty of Social Work, Toronto, Canada
Presenting author email: p.newman@utoronto.ca

Background: Human papillomavirus (HPV), among the most common STIs worldwide, is a causal agent in genital warts, cervical, anal, penile and oral cancers, with morbidity among MSM and persons living with HIV much higher than the general population.
We synthesized results from quantitative cross-sectional investigations of parents' uptake of HPV vaccine for their children to understand rates and correlates of parents' uptake of HPV vaccine for their children.
Methods: We conducted a systematic search of the scientific literature across multiple electronic databases to locate empirical studies that examined rates and/or correlates of parents' uptake of HPV vaccine for their children. Standardized data extraction forms were used including descriptive information, methods, outcomes/key findings. We performed meta-analysis on studies examining similar correlates of HPV vaccine uptake and calculated effect sizes for each variable, with a random-effects model to compensate for clinical and methodological diversity between studies, following PRISMA guidelines.
Results: Out of 284 articles collected, 32 studies (n=334,823) from six countries met inclusion/exclusion criteria, the majority (n=25) from the US. Parental uptake of HPV vaccine for their children ranged from 1.6%-89.0%; weighted mean (WM)=12.8 (SD=21.6), with girls' uptake (WM=49.9; SD=16.3) higher than boys' (WM=1.6; SD=0.6, p< .0001). Correlates of uptake included healthcare provider (HCP) recommendation (r=0.54 [95%CI: 0.30-0.72]), parental preventative check-up (r=0.38 [95% CI: 0.21-0.52]), safety concerns (r=-0.30 [95% CI: -0.41- -0.19]), belief in vaccines (r=0.23 [95% CI: 0.07-0.38]), perceived HPV vaccine benefits (r=0.15 [95% CI: 0.04-0.25]), logistical barriers (r=-0.27 [95% CI: -0.42- -0.10]), vaccine covered

by health insurance (r=0.23, 95% CI: 0.03-0.07), HPV vaccine awareness (r=0.25 [95% CI: 0.21-0.29]), HPV knowledge (r=0.11 [95% CI: 0.01-0.21]), and urban vs. rural (r=0.15 [95% CI: 0.02-0.27]).

Conclusions: Low-to-moderate parental HPV vaccine uptake for their children, even lower for boys, and the primacy of HCP recommendation and parental preventive check-ups suggests that parents' interactions with the healthcare system, particularly HCP, present important opportunities to increase children's HPV vaccine uptake. Information to address HPV vaccine safety and efficacy, along with interventions to broaden insurance coverage (including boys), reduce vaccine cost, and mitigate logistical barriers may increase uptake.

MOPEC421

Willingness to participate in future HIV vaccine trials among adolescents and young adults (AYA) from the AYAZAZI study in Soweto, South Africa

J. Dietrich[1], L. Cotton[2], T. Smith[2], S. Hornschuh[1], K. Otwombe[1], E. Lazarus[1], F. Laher[1], G. Gray[1], M. Brockman[2], A. Kaida[3], AYAZAZI Research Team
[1]Perinatal HIV Research Unit, University of the Witwatersrand, Johannesburg, South Africa, [2]Simon Fraser University, Vancouver, Canada, [3]Simon Fraser University, Faculty of Health Sciences, Vancouver, Canada
Presenting author email: kangela@sfu.ca

Background: South Africa has the highest HIV burden globally; 139000 new infections occur among 15-24 year olds annually. With a 1.49% HIV incidence among adolescents and young adults (AYA), participation of AYA will be critical in preventative HIV vaccine trials conducted in South Africa. We measured willingness to participate (WTP) in HIV vaccine trials among AYA.

Methods: Baseline interviewer-administered survey data were analyzed for AYA (16-24 years) enrolled in AYAZAZI, a youth-centred, inter-disciplinary cohort study aimed at linking socio-behavioral, structural, clinical, and biomedical data to understand HIV acquisition risk among AYA. AYAZAZI is based at the Perinatal HIV Research Unit, in Soweto, South Africa and began enrollment in November 2014. Study procedures include: a survey, clinical screening and bloodwork. WTP in HIV vaccine trials was assessed using a 3-point Likert scale [very willing, neutral and very unwilling] and compared by gender using Pearson's Chi-squared test of proportions. Reasons for WTP in vaccine trials are presented. Statistical analyses were conducted using STATA v.12.

Results: We enrolled 111 participants, median age 18 (*IQR*: 17-21), 55% female. Forty nine percent were 'very willing' to participate in HIV vaccine trials, 21% reported a neutral response, and 22% were 'very unwilling'. There was no difference in WTP in HIV vaccine trials by gender (p = 0.59). The leading reason for WTP amongst "very willing" participants (n = 59) was "to make a difference and to contribute to new HIV knowledge" (n = 44, 75%). Other reasons included learning about HIV (n = 8) and access to free healthcare (n = 4). The main reason amongst 'very unwilling' participants (n = 27) was "being scared of becoming ill" (n = 20, 74%).

Conclusions: Half of participants in a youth-focused cohort reported WTP in future HIV vaccine trials with no significant differences by gender. WTP is motivated by altruistic intentions. Recruitment of AYA in future HIV vaccine trials should emphasize participants' ability to make a long term difference in decreasing HIV incidence through an HIV vaccine trial. With a large proportion of unwilling participants reporting fears of "becoming ill", vaccine research efforts should engage AYA in trial planning and communication efforts.

Strategies for identifying key populations

MOPEC422

'Meeting a sex partner downtown' as a risk factor for HIV and syphilis infection among MSM and trans women in Lima, Peru: a marker for larger sexual networks?

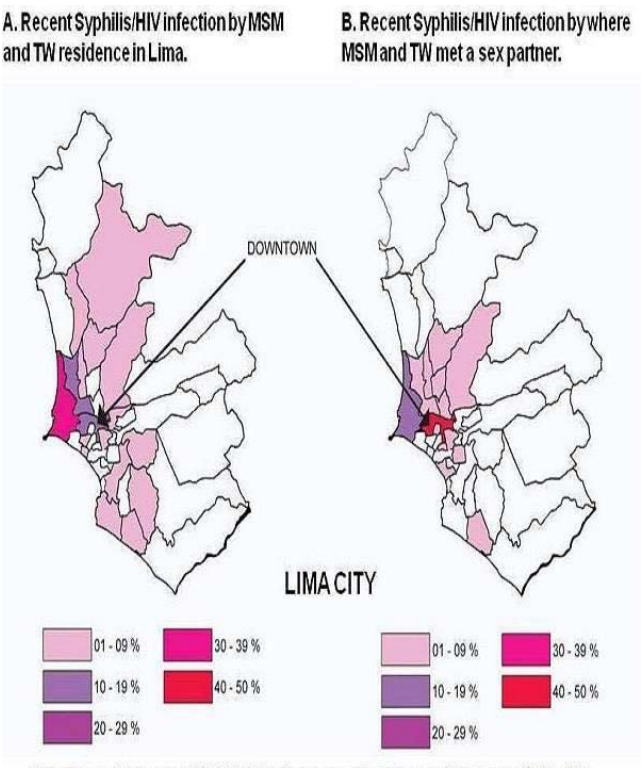
L.R. Carrera[1], K.A. Konda[2], S.R. Leon[1], G. Calvo[3], B. Brown[3,4], J.D. Klausner[2], C.F. Caceres[1]
[1]Universidad Peruana Cayetano Heredia, Unit of Health, Sexuality and Human Development, and Laboratory of Sexual Health, Lima, Peru, [2]University of California, Los Angeles, United States, [3]Epicentro, Lima, Peru, [4]University of California, Irvine, United States
Presenting author email: lourdes.carrera.a@upch.pe

Background: Syphilis and HIV are endemic among lower-income MSM and transgender women (TW) in Lima, where current prevention strategies have had low impact. Lima's population of 10 million has substantial sprawl, but also has a central hub sector with important social gathering locations for the working class, including clubs, bars and bath houses catering to MSM and TW. The objective of this analysis was to determine if meeting a sex partner in downtown Lima is associated with recent STI/HIV infection among MSM and TW.

Methods: High-risk MSM and TW who attended one of two STI clinics in Lima from June 2013 to May 2014 were invited to participate. Data on demographics, sexual risk behaviors and where they met sex partners in the last three months were collected using a computer-based questionnaire. Serologic testing for HIV and syphilis infection was conducted. Associations between recent HIV (reporting an HIV negative test within 6 months) or recent syphilis diagnoses (RPR >1:8) and reporting having met a recent sex partner in downtown Lima were analyzed using and multivariable Poisson regression to calculate adjusted prevalence ratios (aPR).

Results: A total of 253 MSM and TW reporting recently meeting a sex partner were surveyed, among these participants 45 (18%) had recent syphilis, 5 (2%) had recent HIV and 2 (1%) had recent HIV/syphilis co-infection. Among participants, 37% recently met a sex partner downtown.

Condomless anal sex, number of sex partners, being a sex worker and being a TW were similar in both groups and were not associated with recent syphilis/HIV infection (all p-values>0.05). Having recent syphilis or HIV infection was higher among MSM/TW who met a recent sex partner downtown (aPR 1.41, 95% CI 0.8-2.5) compared to those who had not met a partner downtown, adjusted for age and sex role.



[Recent syphilis and hiv]

Conclusions: Meeting a sex partner in downtown Lima indicates links to sex partners outside of participants' neighborhoods, suggesting broader, more diverse sexual networks. The association between higher prevalence of recent HIV/syphilis infection and reports of meeting sex partners in downtown Lima should be explored with ethnography and potentially lead to prevention strategies focused on this risk configuration.

MOPEC423

Transpinay: understanding the Philippine transgender women towards developing transgender-specific HIV prevention programs and related health services

R.P.N. Cortes[1,2]
[1]Philippine NGO Council on Population, Health and Welfare, Inc., ISEAN-Hivos Program, Pasay City, Philippines, [2]ISEAN Secretariat, ISEAN-Hivos Program, Jakarta, Indonesia
Presenting author email: raine.cortes@yahoo.com

Background: Unlike other neighboring Southeast Asian countries, the Philippines do not have a localized term to refer to transgender (TG) persons. In fact, the common local terms "bakla", "bading" and "bayot" are negatively used to refer to TG women. Even the Philippine Integrated HIV Behavioral and Serological Surveillance (IHBSS) do not disaggregate data for MSM and TG but are lumped together as one population, which creates both a socio-political and behavioral risk issue.

Thus, it is important to look at how TG women themselves define and understand the concept of TG in order to provide a context in developing TG-specific HIV prevention programs and related health services.

Methods: The method used was facilitating a self-administered questionnaire to forty-six (46) self-identified TG women, and conducted four (4) focus group discussions to TG women members from community-based organizations (CBOs) in Metro Manila, Cebu City and Davao City.
Results: The findings revealed that majority of the respondents/participants, being affiliated with a CBO, defines TG as persons whose gender identity and/or expression does not conform with their sex assigned at birth. Their differentiation of a TG woman from a transsexual (TS) is that the latter is related more to the concept of body modifications such as hormone replacement therapy, collagen injection and implants. Some TG CBOs coined "transpinay", "transwomen" and "binabae" as a local term for TG women rather than referring to them as "bakla". Lastly, in identifying TG women clients in peer education programs, peer educators can use qualifier questions or criteria but always respect the target clients' gender self-identification - both strategies should complement each other.
Conclusions: The study concludes that the use of local, indigenous and peer terms should be utilized in order to reach the unaware TG women community. Trans-specific health services should include both empowerment of their TG identities and addressing risky behaviors such as "versatile" sexual role and engaging in any form of body modifications, especially those who self-inject hormones and collagens, which is a potential risk to HIV. Lastly, members of TG CBOs should always be part of the consultative process in developing a comprehensive package of trans-health services and programs.

Use of the internet, social media, mobile phones and other e-devices for prevention

MOPEC424

Text messages increased HIV testing among young women in Kenya: a pilot study

N. Njuguna[1,2,3], N.R. Mugo[1,3,4], K. Ngure[1,3,5], E. Irungu[1], C. Sambu[1], C. Maronga[1], S. Gakuo[1], J. Baeten[3], R. Heffron[3]
[1]Partners in Health and Research Development, Nairobi, Kenya, [2]Kenyatta National Hospital, Nairobi, Kenya, [3]University of Washington, Seattle, United States, [4]Kenya Medical Research Institute, Nairobi, Kenya, [5]Jomo Kenyatta University of Agriculture and Technology, Juja, Kenya
Presenting author email: njambi@uw.edu

Background: More than half of all HIV infected individuals in Kenya are unaware of their status with young women carrying a disproportionate burden of incident HIV infections. We sought to increase HIV testing in young Kenyan women via a text messaging (SMS) intervention.
Methods: We conducted a randomized quasi-experimental study via SMS to increase HIV awareness among women 18-24 years old who had not tested for HIV in the preceding 12 months. We randomized women attending four technical training colleges in central Kenya. Women at two colleges received weekly SMS on HIV related topics with an option to text back for more information while women at the 2 control colleges did not receive any messages. Monthly 9-question SMS surveys were sent to all participants for 6 months to collect data on HIV testing, sexual behavior and HIV risk perception. We used multivariate Cox proportional hazards regression analysis to detect differences in the incidence of HIV testing among women in the intervention group compared to women in the control group.
Results: We enrolled 600 women between September 2013 and March 2014; 300 in each study arm. On average, women were 20 years of age (IQR 19-22), 68% had ever had sex in their lifetime and 73% had never tested for HIV. A total of 355 women reported testing for HIV within the 6 months of follow up: 67% were among the intervention arm and 51% were among the control arm representing a 52% increase in reported HIV testing among women in the intervention arm (95% CI 1.17-1.98, p=0.002) after adjusting for age, number of sex partners, condom use and HIV risk perception.
Conclusions: Use of HIV interventional text messages significantly increased rates of HIV testing among young Kenyan women in this pilot study and should be widely scaled up to have a substantial public health impact.

MOPEC425

Playing it safe: a game-based intervention to prevent HIV among young men who have sex with men in Mexico City

R. Buzdugan[1], Z. Andrade-Romo[2], L. Chavira-Razo[2], G. García-Plata[2], R. Grimball[1], E. Bertozzi[3], S. Bautista-Arredondo[2]
[1]University of California, Berkeley, United States, [2]National Institute of Public Health, Cuernavaca, Mexico, [3]Quinnipiac University, Hamden, United States
Presenting author email: sbautista@insp.mx

Background: Gamification modifies attitudes towards activities that individuals are unmotivated to undertake by embedding them in game-like environments, awarding points for targeted outcomes, and using 'leaderboards' (relative rankings) and non-financial rewards to create an atmosphere of supportive competition or collaboration. 'Serious' games increase participants' knowledge and self-efficacy skills.
We are developing a 'serious' game integrated in an online gamification platform to motivate young men who have sex with men (MSM) in Mexico City to learn about HIV/AIDS and get tested for HIV and syphilis; a first in developing settings.
Methods: The intervention is being developed based on findings from six iterative focus group discussions (FGDs) with 42 MSM aged 18-40 years from Mexico City, conducted in 2014-2015. Through prototype testing, FGDs inform the story, design, and specific game elements, and ensure that the intervention is engaging, motivating, and culturally relevant.
Results: We found that young MSM are highly interested in a web-based intervention exclusively for MSM, and positively reacted to gamification elements and principles. The FGDs informed the game element development process and adapted it for the Mexican context. In the game, players' objectives include persuading virtual partners to have sex, then figuring out how to sexually satisfy them; during this process they learn about the HIV risks associated with different sex acts and practice talking about HIV/AIDS. In addition to the game, the gamified intervention includes recruitment of peers, quizzes, an online forum, and real-world actions (HIV and syphilis testing). Via the gamification platform, these activities are rewarded using a point system and badges for pre-determined accomplishments
(e.g., HIV testing, higher scores on quizzes). Participants are motivated to participate and excel by comparing their scores to those of other participants via a leaderboard.
Conclusions: Iterative FGD data helped develop an HIV prevention intervention that leverages men's sexual curiosity to engage in a playful environment that also communicates pro-health and pro-social messages. The intervention will be piloted for 6 months among 300 MSM; we will assess participants' engagement, the acceptability and effect of the intervention on participants' level of knowledge about HIV/AIDS, self-reported safe sexual behaviors, and uptake of testing for syphilis and HIV.

MOPEC426

Variations in recruitment yield, costs, and speed and participant diversity across internet or social media platforms in a global study of HIV/AIDS and HIV testing knowledge

R. Merchant[1], W. Shao[2], W. Guan[2], M. Clark[2], T. Liu[2], C. Santelices[3], D. Cortes[3]
[1]Brown University/Rhode Island Hospital, Providence, United States, [2]Brown University, Providence, United States, [3]Northeastern University, Boston, United States
Presenting author email: rmerchant@lifespan.org

Background: For a global, internet-based study on HIV/AIDS and HIV testing knowledge among English- or Spanish-speakers, we compared:
(1) the yields, speed and costs of recruitment across 17 internet or social media platforms; and
(2) participant diversity among participants recruited from these platforms.
Methods: English- or Spanish-speaking persons worldwide of any age self-identifying as HIV uninfected were recruited over a six-week period from July to August 2013. Recruits were solicited from internet or social media platforms in English and Spanish to the study website through:
(1) free postings on 13 platforms,
(2) paid advertising or postings on 3 platforms (Amazon Mechanical Turk, Google, and Find-participants), and
(3) separate free postings and paid advertisements in sequential time periods on Facebook.
Separate uniform resource locators (URLs) were employed to identify the platforms recruits used to access the study website. Platforms were compared by study completions (yield), time to completion (rate), completion to enrollment ratios (CERs), and costs/completion; and by participants' demographic characteristics, HIV testing history, and health literacy levels.
Results: Of the 482 English-speaking participants, 42% were from India, 37% from the United States, and 8% from the Philippines. Of the 335 Spanish-speaking participants, 27% were from the United States (including Puerto Rico), 11% from Venezuela, and 8% from Ecuador. Only 57 (12%) of the English- and 2 (0.6%) of the Spanish-speakers were recruited through free advertising or postings. Amazon Mechanical Turk yielded the most English-speakers (n=347), recruited participants at the fastest rate and had the highest CER (0.78) and lowest costs/completion. Facebook yielded the most Spanish-speakers (n=173) and recruited participants at the fastest rate, although Amazon Mechanical Turk (n=156) had the highest CER (0.72) and

lowest costs/completion. As shown in the accompanying table, participants recruited across platforms differed substantially according to their age, gender, years of formal education, self-reported language proficiency, HIV testing history and health literacy skills.

	English-speaking participants				Spanish-speaking participants		
	Facebook	Amazon Mechanical Turk	Other platforms	p-value	Facebook	Amazon Mechanical Turk	p-value
	n=78	n=347	n=57	p<	n=173	n=156	p<
Demographic Characteristics	%	%	%		%	%	
Age (median, IQR)	26 (20, 36)	28 (25, 37)	25 (20, 33)	0.00	27 (21, 38)	30 (25, 36)	0.02
Gender (female)	29.5	44.1	57.9	0.00	49.7	47.4	0.00
Education				0.43			0.00
No school	0.0	0.0	0.0		0.0	0.0	
Elementary	1.3	0.3	1.8		1.2	0.0	
High school	3.8	2.4	3.5		9.8	1.3	
General equivalency diploma	6.4	8.9	14.1		16.2	8.3	
College	20.5	26.5	33.3		37.0	28.2	
Bachelor degree	48.7	45.5	31.6		27.8	49.4	
Graduate school or higher	9.2	16.4	15.8		8.1	12.8	
Self-reported language skills				0.00			0.00
Very well	59.0	82.4	93.0		91.3	78.2	
Well	34.6	17.6	7.1		8.7	18.0	
Somewhat	3.9	0.0	0.9		0.0	1.9	
Not well	2.6	0.0	0.0		0.0	1.9	
Self-reported HIV testing							
Have ever been tested for HIV	21.8	38.6	45.6		55.0	52.0	
Last HIV test				0.02			0.60
Less than 6 months ago	52.9	17.2	23.1		24.2	22.2	
Less than 1 year ago	5.9	16.4	15.4		19.0	24.7	
Less than 2 years ago	29.4	18.4	26.9		14.7	19.8	
Less than 5 years ago	0.0	20.9	26.9		28.4	19.8	
More than 5 years ago	11.8	26.1	7.7		13.7	13.6	
Health literacy level							
Confidence with completing forms				0.00			0.00
Not at all	12.8	0.9	1.8		14.5	18.0	
A litte bit	12.8	6.6	5.3		20.3	7.7	
Somewhat	14.1	17.3	21.1		30.1	23.7	
Quite a bit	28.2	32.0	43.9		27.8	32.7	
Extremely	32.0	43.2	28.1		7.5	18.0	
Difficulty reading/understanding forms				0.02			0.20
Most of the time	2.6	3.8	7.0		2.9	2.6	
Some of the time	15.4	21.0	7.0		19.1	14.1	
A little of the time	39.7	32.3	22.8		31.2	42.3	
None of the time	42.3	43.0	63.2		46.8	41.0	
Needing help with forms				0.00			0.06
Most of the time	7.7	5.8	5.3		4.6	0.0	
Some of the time	20.5	17.9	3.5		15.6	17.3	
A little of the time	29.5	32.9	21.1		25.4	26.9	
None of the time	43.5	70.2	70.1		54.3	55.8	

[Participant diversity comparison]

Conclusions: Choice of internet or social media platforms can impact the success of an internet-based research study in regards to recruitment, study costs and the characteristics of participants enrolled. This choice has important implications on study design and perhaps the external validity of these types of studies.

MOPEC427

"You care about us": exploring use of mobile phones to improve retention in care and facility delivery in Tabora, Tanzania

E.A. Bobrow[1], G. Mbita[2], G. Antelman[2], M. Gill[1], P. Njao[3], R. van de Ven[2], G. Woelk[4]
[1]Elizabeth Glaser Pediatric AIDS Foundation, Washington DC, United States, [2]Elizabeth Glaser Pediatric AIDS Foundation, Dar es Salaam, Tanzania, United Republic of, [3]Ministry of Health and Social Welfare, Dar es Salaam, Tanzania, United Republic of, [4]Elizabeth Glaser Pediatric AIDS Foundation, Research, Washington DC, United States
Presenting author email: gwoelk@pedaids.org

Background: The Supporting Attendance for Facility Delivery and Infant Health (SAFI) Study, launched in November 2014 by EGPAF, was designed to test interventions to increase adherence to clinic visits, the rates of facility-based delivery, the proportion of HIV-exposed infants (HEI) receiving nevirapine after birth, and the proportion of HEI tested for HIV within 8 weeks of age. Formative research explored the feasibility and acceptability of two interventions: mobile communication using HIV-neutral SMS appointment reminders, and mobile banking systems for transport reimbursement through cell networks in a rural, low-literacy population.
Methods: Semi-structured in-depth interviews were conducted in 13 health facilities in Tabora, Tanzania. Participants included HIV-positive (n=16) and HIV-negative (n=19) women, and health care workers (n=23) purposively selected from antenatal and postnatal clinics. Audio recordings were transcribed and translated into English. Data were analyzed using MAXqda with comparisons made between groups.
Results: Sharing mobile phones is common, often within families. Sample SMS reminders were perceived as helpful and indications of "caring" sentiments from the health facility, which respondents felt would prompt women to attend clinic appointments. Local language styles were verified as appropriate. Confidentiality was not identified as being compromised by reminders. Although health care workers expressed concern about low literacy, illiterate women indicated that they would manage by providing the mobile number of a trusted person to receive and read the reminders. All respondents felt that multiple reminders are needed - a few days before a scheduled visit, on the day of the appointment, and again a few days later. Lack of transport money meant women walked to the clinic or waited until they had money. Even small amounts of money to cover transport costs or to buy food to eat while at the facility could incentivize attendance. Most women reported having their own mobile banking accounts or access to one to receive and send money.
Conclusions: Results suggest that SMS appointment reminders would be received well and read by most women. Additionally, mobile banking is commonly used, and would be feasible for reimbursing transport costs. These interventions, demonstrating promise in promoting visit adherence, are well-suited for implementation and evaluation in larger-scale operations research.

MOPEC428

How effective are innovative strategies that use communication technology in scaling up HIV testing and engaging MSM in HIV awareness? A case study from Thailand

T. Anand[1,2], C. Nitpolprasert[1,2], J. Ananworanich[2,3,4], J. Jantarapakde[1], D. Colby[1,2], P. Phanuphak[1], C. Pakam[1,5], N. Phanuphak[1,2]
[1]The Thai Red Cross AIDS Research Centre, Bangkok, Thailand, [2]SEARCH, The Thai Red Cross AIDS Research Centre, Bangkok, Thailand, [3]U.S. Military HIV Research Program, Walter Reed Army Institute of Research, Silver Spring, United States, [4]Henry M. Jackson Foundation for the Advancement of Military Medicine, Bethesda, United States, [5]The MSM Sexual Health Clinic, The Thai Red Cross AIDS Research Centre, Bangkok, Thailand
Presenting author email: tarandeepsinghanand@gmail.com

Background: Thailand has faced a rapidly growing proportion of new HIV cases among men who have sex with men (MSM) over the past decade. The HIV testing rate among the MSM population, estimated to contribute 40% of the country's new HIV cases during 2012-2016, is very low at 29%. Only 7% of MSM reached through traditional outreach under Thailand's Global Fund Round 8 Program received HIV testing. In 2011, The Thai Red Cross AIDS Research Centre launched 'Adam's Love', Thailand's official MSM health project.
Methods: An innovative model, adamslove.org offers 60% HIV/STI education and 40% entertainment in English and Thai. The campaign features over 300 expert advice videos, a comprehensive HIV prevention package, a membership program offering designer incentives for HIV testing, fashion photography and integrated social media and web message boards for health advice. Video coverage of celebrities getting tested are posted on Adam's Love social media networks that have gone viral among the MSM community. Billboards are placed in strategic locations promoting safe sex and HIV testing messages. The campaign is linked with The Thai Red Cross AIDS Research Centre, community drop-in centres like RSAT and SWING, and 5 private hospitals in Bangkok to make HIV/STI testing easily accessible.
Results: Between Sep 2011 - Dec 2014, Adam's Love website received 147 million hits, engaged 1,703,818 total visitors (21% repeat visitors), with 8,263,071 page views with an average visit duration of 4.58 minutes per visitor. YouTube videos gained over 1 million views (82% male viewers). The three top-rated videos included symptoms of HIV infection, oral sex advice, and three simple steps for HIV testing. An average of 420 MSM per month received online counseling. 40% of MSM clients of the Men's Health Clinic at the Thai Red Cross AIDS Research Centre reported being aware of the website. 1181 MSM received HIV testing through direct referral from Adam's Love and an HIV prevalence of 15.5% was reported.
Conclusions: Adam's Love has demonstrated its feasibility in engaging MSM in HIV awareness and testing. Online outreach and innovative strategies can initiate the interest and uptake of HIV/STI testing among MSM in Thailand.

MOPEC429

M-Health, e-Health innovations and social media innovations to optimize HIV/STI test and treat strategies: what is the evidence?

R. Vijh[1], M. Diaconescu[1], J. Daher[1], N. Pant Pai[2]
[1]McGill University Health Centre, Division of Clinical Epidemiology, Montreal, Canada, [2]McGill University, Medicine, Montreal, Canada

Background: In the field of HIV/STI, innovative Mobile health (m-Health), internet-based (e-Health) and media (i.e., social media, soap operas) based intervention strategies offer novel, creative, out of the box solutions to access, engage, inform, educate, test, treat and link hard to reach at risk populations to care. However, evidence to inform their scale up is limited. A systematic review was conducted to evaluate all innovations to fill this gap.
Methods: Two reviewers independently retrieved 1640 citations from databases (i.e., MEDLINE, EMBASE, Cochrane Central, Web of Science). From 40 studies, data on study design, and metrics (patient-centered-acceptability, preference and adherence) and implementation centered-feasibility and impact) were abstracted.
Results: About 75% (30/40) studies reported data on HIV, 18% on chlamydia and 3% for each HPV, Hep A/B and Syphilis. About 34 studies evaluated m-Health, 3 evaluated e-Health, and 3 a combination of the two. Within m-health 83% (33/40) evaluated a short mes-

sage service (SMS) whereas others (2/40) explored phone-based counselling, or soap-operas. Within SMS, about 81% studies improved adherence to treatment and, 66% improved testing rates(i.e., re-attendance,, time-to-diagnosis or time-to-treat). However, SMS strategies failed to instil preventive HIV behaviours despite being feasible.

E-health innovations improved HIV/Chlamydia testing, or HIV adherence via online emails/ discussion boards. Facebook based innovations, improved, HIV testing rates, and healthy behaviors and decreased incidence of Chlamydia.

Overall, a high feasibility (9/10) and acceptability (13/13) metrics and a positive impact (10/16) on prevention, testing and treatment outcomes were reported, specifically, in at-risk populations.

Heterogeneity across strategies, implementation metrics and study designs was observed, that prevented statistical pooling. Additionally, weaker study designs, inconsistent metrics, poor statistical methods, limited a subgroup analyses. Furthermore, small and convenient sample sizes, lack of comparators, and evaluation for brief time periods reduced study quality.

Conclusions: For a majority of mobile, internet/online and social media interventions, the current evidence from feasibility studies, was overwhelmingly positive, yet limited by study quality. Future research with stronger design methods, clearer metrics and statistics, is urgently needed to guide an informed scale-up of these promising innovative solutions for at-risk populations worldwide.

MOPEC430

Structures, users, benefits, and barriers of social media for communication about HIV prevention and care: a systematic review

T. Taggart[1], M.E. Grewe[2], D.F. Conserve[1], C. Gliwa[2], M.R. Isler[2]
[1]*University of North Carolina at Chapel Hill, Health Behavior, Chapel Hill, United States,* [2]*University of North Carolina at Chapel Hill, Social Medicine, Chapel Hill, United States*
Presenting author email: ttaggart@email.unc.edu

Background: Conventional public health interventions for HIV prevention are limited in their ability to educate, link to care, and reach the public, particularly members of vulnerable groups who are most affected by HIV and have greater needs for services. Social media has the potential to address these limitations and extend the reach of HIV prevention and care. Lacking in the literature is an examination of the various structures, users, and approaches to using social media to communicate about HIV. The objective of this study was to conduct a systematic review exploring the use of social media to communicate about HIV prevention and care.

Methods: We searched seven databases to locate peer-reviewed studies; additional studies were identified by searching references of systematic reviews. PRISMA guidelines were followed. Study quality was assessed using a tool recommended by the Cochrane Collaboration.

[Figure 1: PRISMA Diagram]

Results: Thirty-five studies met inclusion criteria (figure 1). The majority of studies analyzed the use of pre-existing social media platforms, rather than creating new platforms (83%). Most studies engaged users in high-income countries (79%), the remaining in middle and low-income countries. Most studies included users age 18-40 (88%). Users included people living with HIV/AIDS and individuals from vulnerable groups, including racial and ethnic minorities, men who have sex with men, and low socioeconomic groups. Social media was used to discuss a diverse range of topics related to HIV including information on prevention and treatment, HIV testing, medication adherence, patient notification, and experiences living with HIV. Benefits of using social media to communicate about HIV included greater access to medical information and healthcare providers, increased social and emotional support, and a high level of anonymity, which may promote disclosure and discourse about stigmatized behaviors. Barriers included technology issues, costs, lack of physical interaction and privacy concerns. Studies reported high user satisfaction—platforms were easy to use, useful, and provided access to a diverse group of users.

Conclusions: Growing evidence supports the use of social media as a tool for engaging a range of diverse individuals in a collaborative discourse about HIV prevention and care. More research is needed to understand how social media affects outcomes related to HIV.

MOPEC431

Active and interactive advertising: social media as a recruitment tool for an HIV vaccine trial in Philadelphia, Pennsylvania

L. Buckingham[1], J. Becher[2], C. Voytek[3], D. Fiore[3], D. Dunbar[3], A. Davis-Vogel[3], I. Frank[3], D.S. Metzger[3]
[1]*Pennsylvania Hospital, OB-GYN, Philadelphia, United States,* [2]*University of Pennsylvania, HIV Prevention Research, Bala Cynwyd, United States,* [3]*University of Pennsylvania, Philadelphia, United States*
Presenting author email: dsm@mail.med.upenn.edu

Background: Online and mobile phone based social networking applications have been shown to be valuable tools for recruitment of subjects to interventional clinical trials. During a 3-year recruitment period we utilized multiple online modalities including "active" (email and interactive directed marketing), and "passive" (static side bar ads and online billboards) recruitment. We report more success with active rather than passive methods when recruiting MSM to a phase 2b HIV vaccine trial.

Methods: The University of Pennsylvania HIV Vaccine Trials Unit has utilized passive online recruitment methods including Facebook and Craigslist since July 2010. In December 2011 and October 2012 we began active recruitment with a Web Based Marketing Company (WBMC) and the mobile phone app GRINDR respectively. To analyze the ability of online recruitment methods to engage eligible participants we compare active and passive strategies employed during recruitment for HVTN 505.

Results: Online recruitment strategies successfully populated approximately 37% (71/191) of this HIV vaccine trial. While Facebook and Craigslist were employed for 33 months each, WBMC ran for 6 months and GRINDR for 17 24-hour periods. Passive recruitment via Facebook generated 11.1 (365/33) and Craigslist 6.5 (214/33) phone screens per month of use. Active recruitment using WBMC garnered 18 (108/6), and GRINDR produced 130.5 (233/0.56) phone screens per month. Differences in enrollment by recruitment method followed a similar pattern. Number of enrolls per month of use for Facebook and Craigslist were 0.97 (32/33) and 0.36 (12/33) respectively. Active recruitment through WBMC resulted in 1.8 (11/6) while GRINDR returned 8.96 (16/0.56) enrolls per month. All online recruitment methods produced recruits who were not significantly different by demographics or risk.

Conclusions: Recruitment via online venues and mobile phone apps is likely to continue to grow. We found that active online recruitment in the form of email and interactive directed marketing through the mobile phone app GRINDR was more successful at engaging MSM than passive recruitment via Facebook and Craigslist. Similarly, more enrollees resulted from active recruitment than passive recruitment strategies.

MOPEC432

Utilization of biometric and mobile technology in a community-based combination HIV prevention study

F. Njiri[1], P. Macharia[2], M. Anam[3], S. Rao[3], K. Agot[3], J. Buttolph[4], A. Kurth[5], I. Inwani[1], MP3 Youth Study Group
[1]*University of Nairobi, Nairobi, Kenya,* [2]*Kenya Ministry of Health, NASCOP, Nairobi, Kenya,* [3]*Impact Research and Development Organization, Kisumu, Kenya,* [4]*New York University, NYUCN Global, New York, United States,* [5]*New York University, New York, United States*
Presenting author email: jb3436@nyu.edu

Background: Various methods exist to recruit and uniquely identify study participants, particularly during follow-up periods. In a low-resource study setting the technological options are limited. Our study, *Gender-Specific Combination HIV Prevention for youth in high burden settings (MP3 Youth)*, in rural western Kenya utilizes biometric technology to uniquely identify participants (youth aged 15-24). We assess the feasibility of using biometric technology for

participant recruitment in a multi-service rural setting in a low-income country.
Methods: MP3 Youth is piloting a gender-specific combination HIV Prevention package for youth aged 15-24 in Homabay county, Kenya. Six tents are erected as service delivery points: Tent1 - registration and screening; Tent2 - consenting and enrollment; Tent3 - HIV testing and counseling; Tent4A - CCT and PrEP for girls; Tent4B - VMMC for boys; and Tent5 - Exit. After screening, study participants are enrolled by scanning their index finger using Mobiotrics® biometric data capture system on a tablet. This biometric data is associated with a unique ID. Participants are escorted to the next tent depending on gender and choice of services. Participant identification at service points occurs over Wi-Fi network biometric data synchronization. Demographic, behavioral, and intervention procedures data are entered onto the tablets using Open Data Kit (ODK) and are linked biometrically to the participant ID.
Results: Of 275 screened, 215 participants were enrolled using the Mobiotrics® biometric data capture technology, 126(59%) of whom were female, 24(11%) were HIV positive, all HIV+ participants were linked to care. All participants agreed to biometric registration. It takes approximately 30-seconds to scan a participant›s finger and electronically enter their details. Using a Wi-Fi connection, we were able to accurately identify enrolled study participants in all consecutive service delivery tents. The use of the Wi-Fi network for data synchronization was successful throughout mobile event.
Conclusions: Biometric data capture for study participant registration and unique identification is an accurate and feasible method of identifying youth in a rural low-resource setting. Smart phones/tablets are appropriate for mobile settings since they retain power for longer periods than laptops. However, adequate training of personnel and proper maintenance of equipment is critical to ensure seamless flow of data.

MOPEC433

Effectiveness of text messaging to increase adolescent engagement in prevention

M. Lightfoot[1], A. Bennett[2], J. Jackson-Morgan[2], L. Pollack[1]
[1]University of California, San Francisco, Medicine, San Francisco, United States, [2]3rd Street Youth Center and Clinic, San Francisco, United States
Presenting author email: mal@ucsf.edu

Background: Many adolescents with asymptomatic STIs do not seek treatment and those who do access the health care system may not be screened for HIV. Despite the need for attention from the health care system, adolescents are among the most medically underserved. We implemented an innovative strategy for increasing adolescents' STI/HIV testing. The strategy was a peer-driven, text message HIV-testing campaign diffused through social networks. We examined the efficacy of the intervention to increase the number of high-risk youth seeking health services and testing for HIV.
Methods: Utilizing an interrupted time series design, 100 patients at an urban adolescent health clinic were recruited to disseminate a text message to 5 friends they believed to be sexually active. The self-generated messages aimed to connect youth to the healthcare system to seek testing for HIV. We examined the feasibility and acceptability of the strategy as well as efficacy. We measured patient level data collected from a brief sexual risk behavior survey and results from HIV/STI tests completed by all clinic patients. Clinic level data assessed the number and changes in the rate of patient volume at the clinic.
Results: A total of 413 new patients at an adolescent health clinic completed an electronic intake of their risk behaviors, including sexual behavior, condom use, pregnancy, and STI/HIV diagnosis. Patients were a mean age of 18 years (range: 12 - 24 years), ethnic minority (78%), and female (78%). Adolescents reported vaginal (88%), anal (21%) and oral sex (74%), with only 27% reporting the use of a condom at last sexual intercourse. The strategy was found to be both feasible and highly acceptable, with patients reporting few concerns with texting peers, relatively low refusal rate and few negative responses. Clinic volume increased from 11 new patients per month to 13 new patients. Reports of patient risk behaviors also suggest the intervention was effective in engaging new patients who engaged in sexual risk.
Conclusions: Results of the text messaging strategy through adolescent social networks supports the approach as a potential avenue for accessing youth networks and mobilizing youth who might not otherwise seek care to connect to a clinical setting.

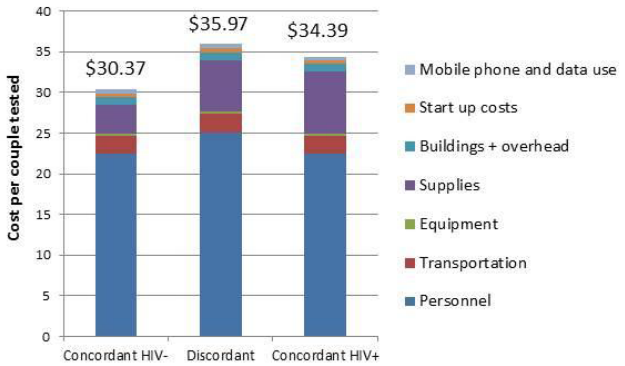
Integration of HIV prevention services (into reproductive health and STI / care and treatment / other programmes)

MOPEC434

Cost of home HIV testing and education for male partners of pregnant women in Kenya

M. Sharma[1], C. Farquhar[1,2], J. Kinuthia[3], A. Osoti[1,4], V. Asila[4], S. Parikh[5], A. Gone[4], D. Krakowiak[1], R. Barnabas[1,2]
[1]University of Washington, Epidemiology, Seattle, United States, [2]University of Washington, Global Health, Seattle, United States, [3]Kenyatta National Hospital, Department of Research and Programs, Nairobi, Kenya, [4]University of Nairobi, Nairobi, Kenya, [5]University of Washington, Seattle, United States
Presenting author email: msharma04@gmail.com

Background: Women in sub-Saharan Africa face 2-3 fold higher risk of HIV acquisition during pregnancy/post-partum than non-pregnant women. Home-based HIV testing of their male partners has potential to reduce HIV transmission to women and infants. Evaluating costs of such programs could inform policy-makers as they implement interventions within budget constraints.
Methods: We estimated incremental annual costs of providing home-based partner education and HIV testing (HOPE) to couples as part of routine antenatal care in Kisumu, Kenya. Costs were collected from the HOPE Study, a randomized controlled trial where couples received HOPE intervention or standard of care. Couples also received information on facility delivery, exclusive breastfeeding, family planning, and male circumcision. We conducted time and motion studies to estimate number of staff needed for efficient scale-up and to separate research time from program services. Costs and utilization were collected from budgets, government price lists, and staff interviews. Costs (2012 US dollars) collected from a payer perspective were divided into: staff, transportation, equipment, supplies, buildings and overhead, and startup. Capital items were assumed to have 5 years of useful life with 3% discount rate.
Results: Costing was conducted onsite in June 2014. Average time to administer the HOPE intervention was 1 hour per couple. Accounting for travel time and home location, we estimated 7,740 couples can be tested annually assuming a program of 12 health advisors and 3 clinic nurses. The incremental cost of adding the HOPE intervention to antenatal care was $30.37, $34.39, and 35.97 for couples testing concordant HIV-negative, HIV-discordant, and concordant HIV-positive, respectively. Staff salaries represented the bulk of costs (65-75%). Under a task shifting scenario, using community health workers reduced costs to $16.89, $21.00, or $20.91 depending on couple status.
Conclusions: Home-based testing and education of couples during pregnancy has potential to decrease HIV-associated morbidity and mortality and improve maternal and child health indicators at a cost of $30-36 per couple tested. Task shifting reduces costs to $17-21 per couple tested. These estimates can inform mathematical models evaluating cost-effectiveness of the HOPE program. Our costs are similar other community-based (home and mobile) HIV testing programs found to be affordable in sub-Saharan Africa.



[HOPE intervention costs per couple tested]

MOPEC435

Partner notification services to identify and refer people living with HIV for care and treatment in Cameroon 2007-14

P.T. Muffih[1], T. Welty[2], M. Golden[3], R. Shields[4], W. Wainfen[1], F. Honore[1]
[1]Cameroon Baptist Convention Health Services, Bamenda, Cameroon, [2]Cameroon Baptist Convention Health Services, AIDS Care and Prevention, McCall, United States, [3]University of Washington, Seattle, United States, [4]Cameroon Baptist Convention Health Services, Bellingham, United States
Presenting author email: piustih@cbchealthservices.org

Background: Since 2007, the Cameroon Baptist Convention Health Board (CBCHB) has assisted health facilities and community-based HIV testing programs in development of HIV partner notification (PN) services in the Northwest and Southwest Regions of Cameroon with the support of the minister of health as a public health intervention.
Methods: From 2007-14, CBCHB trained 63 health advisors (HA) (nurses, laboratory technicians, social workers, and chaplains) from 16 CBCHB facilities and 53 HA from 26 non-CBCHB facilities (governmental, faith-based and private facilities). HA interview consenting HIV-positive persons (index cases) on their sexual partners in the last two years, to find their sexual partners and inform them of their HIV-exposure. HA collect data on all consenting index cases and their partners which are entered into an Epi-info database for evaluation. HA contact partners, ask about risk of infection, provide pre-test counseling and offer HIV testing in their home or at any agreed upon location. HA educate both index cases and partners on HIV prevention and risk reduction, and refer HIV-positive partners to HIV care and treatment.
Results: From 2007-14, HA interviewed 16,537 consenting HIV-positive persons who provided information on 18,685 sexual partners. HA notified 11,762 (63%) of these partners, of whom 8421 (72%) were tested for HIV. Of partners tested, 4365 (52%) were HIV-positive, of whom 2713 (62%) enrolled into HIV care (Table 1). Of 2483 persons newly diagnosed with HIV in eight CBCHS facilities, 790 (31.8%) received PN services.

	2007	2008	2009	2010	2011	2012	2013	2014	Total
Index Persons	227	1610	2174	2587	2061	2409	2439	3030	16537
Contact Persons (CP)	278	1701	2384	2812	2476	3041	2710	3283	18685
CPs Notified	167	1309	1742	2184	1416	1627	1336	1981	11762
CP Tested for HIV	110	1004	1477	1681	808	1139	863	1339	8421
CP HIV positive	55	557	688	969	446	588	470	592	4365
CPs linked to HIV Care	0	37	90	633	302	587	473	591	2713

[Entire Program Summary]

Conclusions: PN HIV prevention in resource-limited settings identifies many partners of HIV-positive persons who otherwise may not be traced, tested, and referred for care and treatment. Significant challenges in PN include HA availability to interview index persons and to contact partners and the inaccurate contact information provided by index cases for their partners.

MOPEC436

Validation of the Denver HIV risk score for targeting HIV screening in Vancouver, British Columbia

T. Falasinnu[1], P. Gustafson[2], S. Wong[3], D. Haag[3], J. Wong[3], G. Ogilvie[3], M. Gilbert[4], J. Shoveller[1]
[1]University of British Columbia, School of Population and Public Health, Vancouver, Canada, [2]University of British Columbia, Department of Statistics, Vancouver, Canada, [3]British Columbia Centre for Disease Control, Clinical Prevention Services, Vancouver, Canada, [4]Ontario HIV Treatment Network, Toronto, Canada
Presenting author email: lola.falasinnu@ubc.ca

Background: Clinical prediction rules (CPRs) have been shown to potentially reduce the number of individuals who receive unnecessary testing. The Denver HIV risk score is a CPR developed for targeting HIV testing and validated in U.S. clinical settings (Haukoos et al, 2012; PMID: 22431561). The final logistic regression model of the Denver HIV risk score included age, gender, race/ethnicity, sex with a male, vaginal intercourse, receptive anal intercourse, injection drug use, and past HIV testing, and values ranged from -14 to 81. We aimed to validate the risk score in patients attending two publicly funded STD clinics in Vancouver, British Columbia.
Methods: We conducted a multisite, observational, cross-sectional study. Applying the same inclusion criteria and methods used in the derivation of the Denver HIV risk score, we examined electronic records (2000-2012) from 47,175 clinic visits at two sexual health clinics in Vancouver. Each clinic visit was assigned a score based on the variables included in the Denver HIV risk score. Patient visits were stratified into 5 risk groups according to their score: very low (<20), low risk (20-29), moderate risk (30-39), high risk (40-49), and very high risk (≥50). The model's calibration and discrimination for predicting an HIV diagnosis were examined by the area under the receiver operating characteristic curve (AUC) and the Hosmer-Lemeshow (H-L) statistic. We examined the sensitivity and proportion of patients that would need to be screened at different cutoffs of the risk score.
Results: The prevalence of HIV infection was 0.46% in these clinics. Validation demonstrated good performance: the AUC was 0.80 (95% CI: 0.79-0.81) and the H-L χ^2=8.8, 8 df, p=0.36. HIV prevalence within each risk groups was: 0% (very low risk), 0.05% (low risk), 0.25% (moderate risk), 0.86% (high risk) and 1.23% (very high risk). HIV testing is recommended for scores of ≥40. The risk score identified HIV cases with a sensitivity of 96% and a fraction screened of 41%.
Conclusions: The Denver HIV risk score performed well in these STD clinic settings in Vancouver, accurately identifying individuals at increased HIV risk, and may be useful for providing individualized estimates of risk as part of routine HIV screening.

MOPEC437

Provider's role in comprehensive sexual health screening and education for YBMSM aged 15-19

R. Arrington-Sanders[1], A. Morgan[1], J. Oidtman[1], D. Fortenberry[2]
[1]Johns Hopkins School of Medicine, Department of Pediatrics, Division of General Pediatrics & Adolescent Medicine, Baltimore, United States, [2]Indiana University, Department of Pediatrics, Section of Adolescent Medicine, Indianapolis, United States
Presenting author email: amorga28@jhu.edu

Background: Young Black men who have sex with men (YBMSM) in the US and abroad are most impacted by high STI/HIV rates. Access to and utilization of accurate comprehensive sexual health information may be limited for YBMSM due to stigma associated with race/ethnicity and gay identity during key milestones of sexual development. Health care providers are uniquely poised to provide sexual health information for YBMSM. We sought to examine experiences of provider-related sexual health care in a sample of YBMSM.
Methods: 50 YBMSM recruited via snowball sampling, venue-based outreach, Adolescent/STD clinics, and Internet social network advertisements (≥18y) participated in brief ACASI and 90-minute in-depth interviews about first same-sex sexual experiences/sexual health. Interviews were transcribed verbatim and double coded. Data was analyzed using categorical and contextualizing analytic methods.
Results: Mean age was 17.6 years (SD=1.3). Most (62%, N=31) self-identified as gay or bisexual (34%, N=17). Mean number of lifetime partners 13.3(SD=2.0, Median=8.5). Mean age at first sex 13.9(SD=2.6). Most (N=42(84%) had prior HIV test. Nine (18%) reported prior STI diagnosis and three (6%) were HIV-positive.
Talking About Sex - Participants were more comfortable talking about sexual orientation (92%) than first same-sex (86%) and more comfortable sharing sexual health information in research interviews than with medical providers (96%).
Sexual Identity - Participants had mean Outness Inventory (OI) of 37.2(SD=16.1, (range=0-77)) and high OI-score (≥75th %tile) was associated with positive feelings about sharing information about first same-sex.
Sexual Health Care - Most (76%, N=38) saw a provider within 6 months. Only 46% (N=23) reported receiving HPV vaccination, 28% (N=14) described anal douching before sex. None described discussing anatomy or sexual health with provider. YBMSM described three needs for comprehensive sexual health - targeted clinical services incorporating mental, minority and sexual health; developmentally appropriate sexual education (regarding anatomy, sexual position, relationships); and support services that connect YBMSM with other gay/bisexual men.
Conclusions: This work suggests providers may be missing opportunities to provide YBMSM with adequate sexual health information. Comprehensive sexual health that addresses clinical care, sexual education and support services for YBMSM and administered by providers is needed.

Efficacy of structural interventions and social protection

MOPEC438

Social, socio-economic and associated clinical benefits of ART exposure among HIV-infected people who use illicit drugs in Vancouver, Canada

L. Richardson[1,2], T. Kerr[1,3], B. Hogg[1,4], S. Guillemi[1], J. Montaner[1,3], E. Wood[1,3], M.-J. Milloy[1,3]
[1]B.C. Centre for Excellence in HIV/AIDS, Vancouver, Canada, [2]University of British Columbia, Sociology, Vancouver, Canada, [3]University of British Columbia, Faculty of Medicine, Division of AIDS, Vancouver, Canada, [4]Simon Fraser University, Faculty of Health Sciences, Burnaby, Canada
Presenting author email: lrichardson@cfenet.ubc.ca

Background: Among people living with HIV/AIDS (PHA), there is extensive documentation of the direct clinical benefits of engagement in HIV care.
However, very little is known about the possible social, socio-economic and associated clinical benefits of engagement in HIV care, particularly for people who use illicit drugs (PWUD), and whether these benefits are relevant at different stages of the HIV cascade of care, such as initiation of antiretroviral therapy (ART).
Methods: We used longitudinal data from a prospective cohort of community-recruited HIV-positive PWUD, in Vancouver, Canada, a setting of free and universal access to all HIV treatment and care. Participant data were linked to comprehensive HIV clinical monitoring and ART dispensation records. We developed a series of generalized linear mixed effects models, adjusting for potential confounders, to examine whether initial exposure to ART was associated with social, socio-economic and ancillary clinical benefits, including relationship initiation, transitioning out of homelessness, entering employment, ceasing involvement in high-risk income generation (e.g., street-based income generation, sex work, drug dealing or other illegal activities), and enrolling in addiction treatment.
Results: Between December 2005 and November 2013, of the 755 eligible study participants, 247 (32.7%) self-reported as women and 421 (55.8%) as Caucasian, with 128 (17.0%) initiating ART for the first time during the study period. In final multivariate models, newly initiating ART was positively and significantly associated with transitioning out of homelessness (adjusted odds ratio [AOR]: 2.24; 95% confidence interval [CI]: 1.50-3.35); initiating a romantic relationship (AOR: 2.19, 95% CI: 1.23-3.89) and enrolling in addiction treatment (AOR: 3.59; 95% CI: 1.90-6.75).
Conclusions: These findings demonstrate that initiating ART is associated with initiating other transitions whose benefits could support both the clinical management of HIV and improved quality of life across social, socio-economic and drug use dimensions. These results point to the potentially critical role that engagement in HIV care can have in clinical and non-clinical domains of the lives of PHA who use illicit drugs, and supports the scale-up of early initiation of ART among this population.

Combination prevention approaches

MOPEC439

The role of male circumcision and antiretroviral drugs in the evolution of the HIV and HSV-2 epidemics in Orange Farm (South Africa) between 2002 and 2012 (ANRS-12126 -12285)

K. Jean[1], A. Puren[2], E. Cutler[2], B. Singh[2], V. Masseko[2], J. Bouscaillou[1], R. Rain-Taljaard[3], D. Taljjard[4], P. Lissouba[1], D. Lewis[5], G. Peytavin[6], B. Auvert[1,7,8]
[1]INSERM, Villejuif, France, [2]NICD-NHLS, Johannesburg, South Africa, [3]Progressus, Johannesburg, South Africa, [4]CHAPS, Johannesburg, South Africa, [5]Sydney Medical School, Sydney, Australia, [6]APHP Bichat-Cl Bernard, Paris, France, [7]University of Versailles, Versailles - Saint Quentin en Yvelines, France, [8]APHP - Hopital Ambroise Pare, Boulogne, France
Presenting author email: bertran.auvert@uvsq.fr

Background: Over the past several years, antiretroviral drugs (ARVs) have been used to prevent AIDS, and male circumcision (MC) has been used to prevent HIV among men in Eastern and Southern Africa. We aimed to quantify whether MC and ARVs have impacted the HIV and HSV-2 epidemics, between 2002 and 2012 in Orange Farm, a typical township of South Africa where ARVs are available since 2005 and where MC roll-out has been conducted since 2008.
Methods: Data were collected in four independent cross-sectional surveys conducted in 2002, 2007, 2010 and 2012 from a total of 10,941 participants aged 18-49y. Age at first sexual intercourse, condom use and number of sexual partners were self-reported. Blood samples were tested for HIV, ARVs and HSV-2. Untreated HIV was defined as the prevalence of HIV-positive and ARV-negative participants.
Time trends of factors extrapolated over a 10-year period, and contribution of MC to changes in HSV-2 and untreated HIV were computed using age-adjusted linear regression models.
The preventive effect of ARVs on the HIV epidemic was estimated by comparing trends in untreated HIV prevalence and in HIV prevalence after excluding all those testing ARV-positive, a proxy of what would have been the HIV prevalence without ARVs in the community.
Results: We observed limited relative changes in sexual behaviors (< ±15%). There was a relative increase in MC prevalence of +89% (95%CI; +78% to +94%). There was a relative increase in ARVs prevalence of +78% (+55% to +102%) among HIV-positive men, and of +123% (+106% to +139%) among HIV-positive women.
Among men, MC contributed to a decrease in untreated HIV prevalence of -24% (-29% to -18%) and a decrease in HSV-2 prevalence of -8% (-11% to -5%). ARVs contributed to a decrease in untreated HIV prevalence among men of -7% (-9% to -5%) and a decrease among women of -13% (-16% to -11%).
Conclusions: Over the past years in Orange Farm, MC has had a substantial impact on the HIV epidemic among men. The impact of MC on the HSV-2 epidemic among men and the impact of ARVs on the HIV epidemic among men and women were more limited.

MOPEC440

Mixed HIV testimonies, enabling access to information, debate and above all prevention in the younger generation. 30 minutes-English subtitle

E. Carbonnel
Medical University of Lyon, Infectious Disease, Lyon, France
Presenting author email: elisabeth.carbonnel@gmail.com

Background: Thirty years ago,HIV filled the newspaper front pages, against a stigmatizing backdrop.Today, the silence is back, creating disinformation and unease among patients. This has led to two dermatologists (active in HIV since 1980s) wanting to tackle the subject outside of traditional protocols.
Methods: As figures and statistics can hide a more complex and nuanced reality, we have chosen a film building on different words, with the desire to bring to life unexpected links, and ways of thinking.
In order to look into the similarities and differences , we selected diametrically opposed subject groups:
HIV-positive and HIV-negative subjects, aged between 18 and 30 from different social backgrounds and medical players who are active participants within the historical context of HIV in France.
Results: A 30 year old director has therefore structured a film that highlights , in the younger generation, a historic ignorance of the facts and preventive shortcoming that could be at the root of risk-taking.
As for senior doctors, who have been dealing with the epidemic since the beginning and are filled with emotions and memory, they are looking to hand over the baton.Their desire to handover is also echoed by some doctors from the new generation, who must take their place on the starting line, between therapeutic effectiveness and humanity ,building on this story's foundations.
In 2014, this film received the "general public film" prize, in France and was honored with the testimony of Professor Barret-Sinoussi, Nobel Prize (Medecine).
Conclusions: This film confronts HIV' past and present, alluding to the different points of view between doctors and patients, but also revealing the ignorance of young people who do not feel affected by this subject and the failure of those who are disengaged from the fight against HIV.
A particular aspiration of the film is for prevention action in higher education to take place, and a starting point, suggests opening up debate (e.g screening, prevention and preconceived ideas) facilitated freedom of speech and open mind.

MOPEC441

Combination prevention intervention: a tool for increasing access to safer sex products and services and improved safer sex negotiation among non-brothel based female sex workers in rural North Eastern Nigeria

A. Okafor[1], N. Ndulue[2]
[1]Management Sciences for Health, HIV Prevention, Abuja, Nigeria, [2]Management Sciences for Health, Clinical, Abuja, Nigeria
Presenting author email: aokafor@msh.org

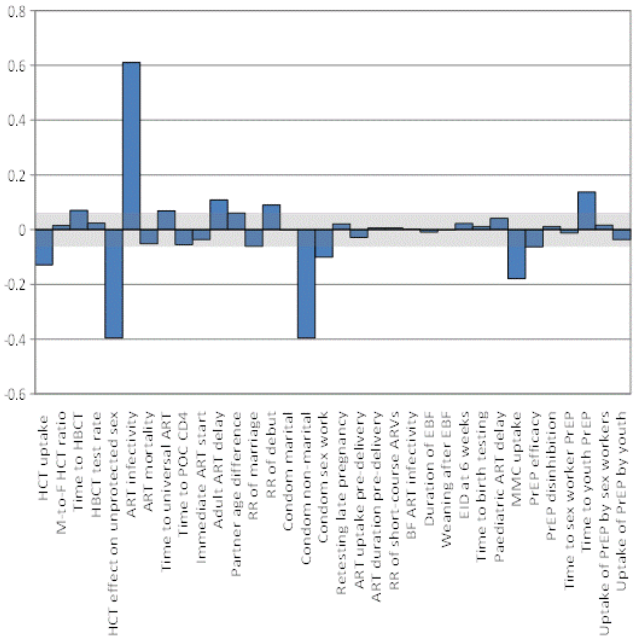
Background: Non- brothel based female sex workers operating in the difficult to reach terrains of rural North Eastern Nigeria are most vulnerable to exposure to sexually transmitted infections and unplanned pregnancies. Due to their remote and difficult to reach locations, most implementing partners and agencies often neglect them in their interventions. Information gathered from Focused Group Discussions among these groups revealed a very low level of knowledge of safer sex practices, products and services, very high level of myths and misconceptions around condom use and inability to negotiate safer sex due to socio- cultural factors.
Methods: With funding from USAID, MSH's Pro ACT project provided small grants to Community Based Organizations to conduct combination prevention interventions targeting non-brothel based female sex workers in difficult to reach rural areas. These interventions were conducted in the rural communities of Iornem, Ikyalar and Uhurrah in Donga Local Government Area of Taraba state, North East Nigeria. A total of 45 non brothels based FSWs were reached with a minimum of three HIV prevention services selected from a combination of behavioral, structural and biomedical interventions using peer education approach over a period of 12 months. These services include advocacy, condom service outlets, free HTC, referrals to comprehensive care and treatment centers and training of 9 FSWs on peer education.
Results: After twelve months, average monthly reported cases of unplanned pregnancy declined from 1 pre interventions to 0 post interventions, reported cases of new STI infections decreased from 7 pre interventions to 2 post interventions, FSWs voluntarily demanding for safer sex commodities increased from 9 pre interventions to 37 post interventions.
Conclusions: Combination Prevention Intervention when strategically tailored to address the HIV prevention needs of FSWs operating in hard to reach rural areas leads to multi-dimensional positive results. Thus, there is need to strategically design HIV prevention interventions targeting FSWs operating in difficult to reach areas using combination prevention intervention.

MOPEC442

What will it take to achieve virtual elimination of HIV transmission in South Africa?

L.F. Johnson[1], C. Chiu[2], L.-G. Bekker[3], L. Myer[1], M.-A. Davies[1], R.E. Dorrington[4], K. Stinson[1], A. Boulle[1], G. Meyer-Rath[2]
[1]University of Cape Town, Centre for Infectious Disease Epidemiology and Research, Cape Town, South Africa, [2]University of Witwatersrand, Health Economics and Epidemiology Research Office, Johannesburg, South Africa, [3]University of Cape Town, Desmond Tutu HIV Centre, Cape Town, South Africa, [4]University of Cape Town, Centre for Actuarial Research, Cape Town, South Africa
Presenting author email: leigh.johnson@uct.ac.za

Background: Virtual elimination of horizontal and mother-to-child HIV transmission in South Africa (SA) has been suggested, but there have been few systematic investigations of which interventions are likely to be most critical to reducing HIV incidence up to 2035.
Methods: A mathematical model was developed to simulate the population-level impact of different HIV interventions in SA. Probability distributions were specified to represent uncertainty around 34 intervention parameters, and a set of 1000 parameter combinations was randomly generated by sampling from these distributions. For each of the 1000 parameter combinations, the model calculated expected incidence up to 2035. Correlation coefficients (r) were calculated to assess the sensitivity of the model outputs to each intervention parameter.
Results: HIV incidence in SA adults (ages 15-49) is expected to decline from 1.4% in 2011-12 to 0.23% by 2035, though with wide ranges of uncertainty (95% CI: 0.08-0.50%). The intervention parameters most strongly correlated with future adult HIV incidence are the relative risk of HIV transmission after initiating ART (r=0.61), the level of condom use in non-marital relationships (r=-0.40), the reduction in unprotected sex following HIV diagnosis (r=-0.40), the uptake of medical male circumcision (r=-0.18) and the year of pre-exposure prophylaxis introduction among youth (r=0.14) (Figure).
Mother-to-child transmission rates (including postnatal transmission and transmission from mothers who seroconvert during breastfeeding) are expected to decline from a baseline of 9.4% in 2011-12 to 4.7% (95% CI: 3.4-6.1%) in 2035. The paediatric intervention parameters most strongly associated with modelled mother-to-child transmission rates are the relative risk of transmission through breastfeeding when the mother is receiving ART (r=0.53) and the rate of ART initiation during pregnancy (r=-0.16).
Conclusions: The virtual elimination target of a 0.1% incidence rate in adults will be difficult to achieve, but the 5% target for mother-to-child transmission is more achievable. Interventions that address the infectiousness of patients after ART initiation (e.g. adherence support and tracing of patients who do not return to care) and the sexual risk behaviour of individuals who have been diagnosed HIV-positive will be particularly critical to achieving long-term HIV incidence declines in South Africa.



[Figure: Correlation coefficients between intervention parameters and average HIV incidence in adults (15-49) over the 2015-35 period.
Grey shaded area represents correlation coefficients that are not significantly different from zero. ART = antiretroviral treatment, BF = breastfeeding, EBF = exclusive breastfeeding, EID = early infant diagnosis, HBCT = home-based counselling and testing, HCT = HIV counselling and testing, MMC = medical male circumcision, POC = point-of-care, PrEP = pre-exposure prophylaxis, RR = relative rate]

Reducing pre-partum and intra-partum transmission to infants

MOPEC443

Prevalence and correlates of *Mycoplasma genitalium* among HIV-infected pregnant African women and implications for MTCT

A. Roxby[1], K. Yuhas[1], C. Farquhar[1], J. Kiarie[1,2,3], S. Graham[1], G. John-Stewart[1], P. Totten[1]
[1]University of Washington, Seattle, United States, [2]University of Nairobi, Nairobi, Kenya, [3]Kenyatta National Hospital, Nairobi, Kenya
Presenting author email: cfarq@uw.edu

Background: Many sexually transmitted infections (STIs) increase risk of mother-to-child transmission (MTCT) of HIV, but the role of *Mycoplasma genitalium* (MG) is not known. We determined prevalence and correlates of MG infection in a cohort of HIV-infected pregnant women and determined whether MG infection was associated with MTCT.
Methods: Between 1999 and 2005, 510 HIV-infected Kenyan women were enrolled and followed in a perinatal MTCT cohort and received short-course zidovudine for PMTCT. Infant perinatal infection was determined at birth and 4 weeks of age by HIV DNA PCR. In this case-cohort design, prevalence and correlates of MG were evaluated in a random sub-cohort. The MG-MTCT association was evaluated in the sub-cohort plus all additional perinatal MTCT cases from the parent cohort. Cryopreserved cervical swabs collected at 32 weeks gestation were tested for MG infection using a transcription-mediated amplification assay. We calculated 80% power to detect a 2.5-fold increased odds of MTCT with exposure to MG (alpha=0.05, 2-sided test). Correlates of maternal MG infection were assessed with chi-squared and t-test; predictors of infant outcomes were analyzed using logistic regression.
Results: In our random sample of 220 women, 47 women (21.4%) had detectable MG during the third trimester. Antenatal MG infection was associated with higher HIV RNA levels in plasma (5.0 vs. 4.6 log copies/ml in MG-positive vs. MG-negative women, p=0.02) at 32 weeks, however vaginal HIV RNA levels at delivery did not differ between these groups. There was a trend for less detection of MG among women reporting prior STIs and genital ulcers (both p=0.05). In our larger sample including all perinatal HIV transmission cases, there was no evidence for an association between MG and MTCT (OR=0.72, 95% CI [0.35, 1.51], p=0.39).

Conclusions: Genital MG infection was frequently detected among HIV infected women, was associated with higher plasma but not vaginal HIV levels, and was not associated with perinatal transmission of HIV.

MOPEC444

Higher than expected HIV prevalence and risk factors for newly diagnosed versus known HIV infection in an antenatal clinic in Western Kenya

A. Osoti[1,2,3], J. Kinuthia[4], D. Krakowiak[2], B. Betz[2], J. Mark[2], S. Parikh[2], A. Gone[4], V. Asila[4], J. Kiarie[1], C. Farquhar[5], HOPE Study Group
[1]University of Nairobi, Obstetrics and Gynaecology, Nairobi, Kenya, [2]University of Washington, Epidemiology, Seattle, United States, [3]AIC Kijabe Hospital, Obstetrics and Gynaecology, Kijabe, Kenya, [4]Kenyatta National Hospital, Research Department, Nairobi, Kenya, [5]University of Washington, Global Health Epidemiology Internal Medicine, Seattle, United States
Presenting author email: jmark55@uw.edu

Background: In generalized epidemics, high HIV testing and counseling (HTC) rates, decreasing HIV prevalence and increased antiretroviral coverage may accelerate progress towards elimination of mother-to-child HIV transmission (EMTCT). Understanding the current prevalence and risk factors for HIV infection among women at the first antenatal care (ANC) visit may inform EMTCT strategies.
Methods: This was a nested cross-sectional study conducted among pregnant women at first ANC visit participating in a randomized trial comparing home-based versus clinic-based couple education and HTC. Women were interviewed and then offered HTC if they were not known to be HIV infected. HIV infected women were categorized as "known HIV positive" if they knew their status prior to pregnancy; and "newly diagnosed HIV positive" if they had no prior HTC or their previous test was negative. Proportions of newly diagnosed, known, and overall HIV positive women were determined and compared to regional and national HIV prevalence. Using logistic regression we determined risk factors for overall, new and known HIV diagnoses.
Results: Of 600 women, 107 (17.8%) were HIV infected. This is greater than twice the national and regional HIV prevalence, which are 5.6% and 15% respectively. Majority of HIV infected women were newly diagnosed (n=60, 56%) compared to known HIV positive (n=47, 44%). HIV negative women had a median age of 24 (interquartile range 21, 28) years. Compared to HIV negative women, HIV infection during the first ANC visit was higher if maternal age was > 25 years (Odds ratio [OR] 2.5; 95% confidence interval [CI] 1.61-3.87), if partners age was >30 years (OR 1.92; 95% CI 1.24-2.97) and parity higher (OR 1.20; 95% CI 1.05-1.37). Risk was lower among those with > secondary education (OR 0.38; 95% CI 0.18-0.79). Newly diagnosed HIV positive women were less likely to report previous HIV testing (OR 0.28; CI 0.12-0.63) while known HIV positive women were more likely to report more lifetime sexual partners (OR 1.48 95% 1.21-1.80).
Conclusions: In this high-HIV burden, low-resource setting, HIV prevalence including new diagnoses remain higher than the national or regional prevalence. To achieve EMTCT, novel strategies aimed at increasing individual and couple HTC before pregnancy are needed.

MOPEC445

Successes and failures of vertical HIV transmission prevention efforts in Canada: evidence from the Canadian Perinatal HIV Surveillance Program (CPHSP)

A. Bitnun[1], T. Lee[2], L. Samson[3], J. Brophy[3], J. Singer[2], D. Money[4], A. Alimenti[4], W. Vaudry[5], F. Kakkar[6], N. Lapointe[6], L. Sauve[7], for the Canadian Pediatric & Perinatal AIDS Research Group (CPARG)
[1]Hospital for Sick Children, Department of Paediatrics, University of Toronto, Toronto, Canada, [2]CIHR Canadian HIV Clinical Trials Network, Vancouver, Canada, [3]Children's Hospital of Eastern Ontario, University of Ottawa, Ottawa, Canada, [4]Women's Hospital and Health Centre, University of British Columbia, Vancouver, Canada, [5]Stollery Children's Hospital, University of Alberta, Edmonton, Canada, [6]Hopital Ste-Justine, University of Montreal, Montreal, Canada, [7]BC Women's Hospital and Health Centre & BC Children's Hospital, University of British Columbia, Vancouver, Canada
Presenting author email: ari.bitnun@sickkids.ca

Background: The CPHSP collects data annually on HIV infected mothers and their infants from 22 Canadian pediatric and HIV centres across the country. The objective of this report was to describe factors associated with VT in Canada since 2004, post-implementation of routine prenatal HIV testing programs in all provinces/territories.
Methods: All children born in Canada to HIV-infected mothers from 2004-2013 in the CPHSP database were reviewed. VT rates are based on data of MIP delivered in Canada and identified within 3 months after birth; infants identified beyond 3 months of birth are tracked separately.
Results: Among 1996 MIPs, 1984 (99%) were identified antenatally or within 3 months of the child's birth. Of these, 93% were prescribed antenatal combination antiretroviral therapy (acART), 85% >4 weeks before delivery, and 8.5% ≤4 weeks before delivery. Intrapartum intravenous zidovudine was administered to 88% of mothers and ≥4 weeks of antiretroviral prophylaxis was given to 96.4% of neonates. The VT rate for this cohort was 1.7% (33 infants); the rate was 14.6% with no acART, 6.6% with ≤4 weeks of acART before delivery and 0.12% with >4 weeks of acART before delivery. Of two VT cases that occurred despite >4 weeks of acART, one was associated with poor maternal adherence, the other with incomplete virologic suppression despite good adherence. An additional 12 infected infants were identified after 3 months of age. Eight of these 12 mothers were Canadian born (4 white, 4 Aboriginal) and 11/12 delivered in provinces with opt-out antenatal screening programs. On multivariate analysis of all 1996 MIP, receipt of no/≤4 weeks versus >4 weeks of acART was significantly associated with earlier year of birth, province/territory of birth and maternal risk acquisition category (28.4% IDU; 11.6% sex; 12.3% other) (all p< 0.01).
Conclusions: VT continues to occur in Canada despite a free universal access health-care system. The observations that 12/45 infected infants were identified after 3 months of age and that 11/12 of those were in provinces with opt-out prenatal screening programs suggest that lack of access to routine prenatal care is a major issue contributing to ongoing VT in Canada.

MOPEC446

HIV positivity among HIV exposed infants and turnaround time (TAT) for EID results in Iringa and Njombe regions: analysis of results from DNA-PCR laboratory and follow-up on ART initiation

R. Kisanga[1], P. Ndayanga[1], J. Ng'weshemi[2], P. Swai[3], O. Were[1]
[1]Christian Social Services Commission, Health Department, Dar es Salaam, Tanzania, United Republic of, [2]Deloitte Consulting Tanzania LTD, Health Department, Dar es Salaam, Tanzania, United Republic of, [3]USAID Tanzania Mission, Health Department, Dar es Salaam, Tanzania, United Republic of
Presenting author email: kisangarf@gmail.com

Background: Njombe and Iringa regions have the highest HIV prevalence in Tanzania. Effective and quality pediatric HIV treatment requires early diagnosis, prompt initiation of ART, and frequent monitoring to ensure retention in care. According to UNAIDS 2013 Global Report, the percentage of infants born to HIV infected mothers who becomes HIV infected is 15%. Further studies report that without ART, 52% of perinatally HIV-infected infants and 26% of postnatally HIV-infected infants will die within 12 months.[1] The main objective of this analysis was to ascertain effectiveness of PMTCT interventions as well as TAT at various health delivery and testing points.
Methods: Data for all EID samples received between June 2013 and February 2014 were obtained from zonal DNA-PCR laboratory. The collected data had all information from when the sample was collected, age of the infant at sample collection, date of birth of the infant, date at which the results were out at the DNA-PCR laboratory and HIV test outcome, Further more follow-up was made to the facility level for those infants diagnosed HIV+ to determine if and when they were started ART.
Results: Between June 2013 and February 2014 a total of 1357 samples were tested at Mbeya DNA PCR laboratory of which 70 samples (5%) tested positive for HIV. Follow up of those tested positive for HIV revealed that 31 infants (44%) were already initiated on ART, 12 infants (17%) had already died before the results while 27(39%) infants were still being tracked by volunteers for ART initiation. Turnaround time calculations revealed an average of 41 days between DBS collection to when results reached health facilities.
Conclusions: Mother to child HIV transmission is showing decline in Tanzania as shown by this analysis, 5% against 15% reported by UNAIDS global report 2013. This decline could be attributed by increase in ART coverage among pregnant and lactating mothers but also efforts by health care workers in ensuring mothers have knowledge on optimal infant feeding practices. ART initiation for HIV diagnosed infants is still a challenge. To increase enrolment of infants' into ART, special strategies to strengthen mother-baby pair facility/community linkage need to be instituted.

Reducing post-partum transmission in infants

MOPEC447

Systematic review of perinatal HIV transmission from breastfeeding for up to twelve months when the mother has viral suppression with combination antiretroviral therapy

M. Loutfy[1], J. Brophy[2], M. Aden[1], W. Wu[1], L. Serghides[3], S. Greene[4], V.L. Kennedy[1], M. Ringlein[5], W. Tharao[6], S. Seigel[4], L. Chambers[4], C.K. Beaver[1], D. McLay[7], S. Ka Hon Chu[8], M. Yudin[9], P. Rochon[1]
[1]Women's College Research Institute, Toronto, Canada, [2]Children's Hospital of Eastern Ontario, Ottawa, Canada, [3]Sandra Rotman Centre for Global Health, Toronto, Canada, [4]McMaster University, Hamilton, Canada, [5]Teresa Group, Toronto, Canada, [6]Women's Health in Women's Hands Community Health Centre, Toronto, Canada, [7]CATIE, Toronto, Canada, [8]Canadian HIV/AIDS Legal Network, Toronto, Canada, [9]St. Michael's Hospital, Toronto, Canada
Presenting author email: mona.loutfy@wchospital.ca

Background: The reduction of perinatal HIV transmission to < 1% when pregnant women are given antiretroviral therapy (ART) in the absence of breastfeeding and birthing complications has been a key breakthrough of modern infectious disease prevention. However, there remains limited comprehensive knowledge of the current risk associated with breastfeeding. We undertook a systematic review to determine the risk of perinatal transmission through breast milk among women on combination ART (cART). Understanding this risk is paramount given the discrepancies in global guidelines, and heightened concerns of breastfeeding in high-income countries among communities where formula feeding may not be acceptable, feasible, affordable, sustainable or safe.
Methods: We searched electronic databases for relevant observational studies and randomized controlled trials (RCTs) without restriction to publication date, language or study jurisdiction. To increase sensitivity, we reviewed reference lists of identified studies and review articles, and hand-searched selected journals to ascertain recently published articles. Included studies reported cART use among HIV-positive pregnant women prior to delivery with stated viral load responses, who then breastfeed for any length of time with reported perinatal HIV transmission rates to the infants. Two reviewers independently extracted methodological characteristics and outcomes and assessed risk of bias. Meta-analytic techniques calculated rates of HIV transmission among breastfed infants in included studies.
Results: Of 5270 citations, 10 studies met the eligibility criteria (three RCTs and seven observational studies) of which five were included in the meta-analysis, with a sample size of 2059. The transmission rates were 2.9%, 95% CI [2.2-3.8] at one month; 3.6%, 95% CI [2.7-4.0] at three months; 4.0%, 95% CI [3.1-5.2] at six months; and 5.1%, 95% CI [4.0-6.5] at twelve months. Transmission rates increased by 1.1% in the early perinatal breastfeeding period (one to six months). Late transmissions increased by 1.1% from six to twelve months.
Conclusions: Though limited by a predominance of observational studies, our findings suggest an overall HIV transmission risk attributable to breastfeeding of at least 2.2% during the early perinatal period with heightened risk during the first year when the mother is on cART. This data can facilitate counseling for mothers experiencing difficulty adhering to formula-only guidelines in high-income settings.

Strategies to increase HIV testing in pregnant women and their partners

MOPEC449

Invitation cards during pregnancy enhance male partner involvement in prevention of mother to child transmission (PMTCT) of human immunodeficiency virus (HIV) in Blantyre, Malawi: a randomized controlled open label trial

A.L. Nyondo[1], A.T. Choko[2], A.F. Chimwaza[3], A.S. Muula[4]
[1]Unversity of Malawi, College of Medicine, School of Public Health and Family Medicine, Blantyre, Malawi, [2]Malawi Liverpool Wellcome Trust Clinical Research Programme, Blantyre, Malawi, [3]Univeristy of Malawi, Kamuzu College of Nursing, Blantyre, Malawi, [4]University of Malawi, College of Medicine, School of Public Health and Family Medicine, Blantyre, Malawi
Presenting author email: lindaalinane@gmail.com

Background: Male involvement (MI) is vital for the uptake of Prevention of Mother to child transmission (PMTCT) of Human Immunodeficiency Virus (HIV) interventions. Partner notification (PN) is among the strategies identified for MI in PMTCT services. The purpose of this randomized controlled trial was to evaluate the efficacy of an invitation card to the male partners as a strategy for MI in PMTCT services by comparing the proportion of pregnant women that were accompanied by their partners between intervention and the non-intervention study groups.
Methods: Pregnant women attending antenatal care without a male partner at South Lunzu and Mpemba health centres were enrolled in the study from June to December 2013. In an intention-to-treat analysis, we compared all participants that were randomized in the invitation card group with the standard of care (SoC) group. Risk ratios (RR) with 95% confidence intervals (CI) were computed to assess the efficacy of the invitation card.
Results: Of the 462 randomized women, 65/230 (28.26%) of the women in the invitation card group reported to the antenatal care clinic with their partners compared to 44/232 (18.97%) women in the SoC group. In an unadjusted intention to treat analysis women in the invitation card group were 50% more likely to be accompanied by their male partners than those in the SoC group RR: 1.49
(95% CI: 1.06-2.09); p = 0.02. Our random effects analysis showed that there was no clustering by site of recruitment with an inter cluster correlation coefficient (ICC) of 1.98x 10^{-3},
(95% CI: 1.78 x10^{-7} - 0.96 x 10^{-1}); p =0.403.
Conclusions: An invitation card significantly increased the proportion of women who were accompanied by their male partners for the PMTCT services. An invitation card is a feasible strategy for MI in PMTCT.

MOPEC450

Improving PMTCT service uptake through integration into maternal, neonatal and child health week in a high prevalence setting

O. Akinleye[1], G. Dura[2], D. Chamla[3], A. De Wagt[4]
[1]UNICEF, Children and AIDS, Enugu, Nigeria, [2]Benue State Ministry of Health, Public Health, Benin, Nigeria, [3]UNICEF, Health Department, New York, United States, [4]UNICEF, Children and AIDS, Abuja, Nigeria
Presenting author email: oakinleye@unicef.org

Background: In Nigeria, PMTCT coverage was 27% in 2013. A key challenge is low ANC coverage which limits the potential reach of HCT among pregnant women. Biannual 1-week campaigns are conducted to increase uptake of maternal, neonatal and child health (MNCH) services and these are known to be well utilized.
We hypothesize that integrating HCT for pregnant women into MNCH week will boost PMTCT coverage.
Methods: MNCH campaign was conducted in Benue State (highest HIV prevalence State) on 8-12 December 2014 and the integration was implemented in 288 health facilities in 13 of 23 Local Government Areas (LGAs). Strategies for mobilizing pregnant women for ANC were developed for the period. About 600 volunteers were trained to collect basic data from respondents with the aid of questionnaires and support health workers in providing HCT in accordance with national guidelines. All pregnant women accessing ANC were offered HCT, using the opt-out approach. Those testing positive were enrolled in PMTCT and linked with volunteers to follow them up to ensure retention. The feasibility of integration of HCT was measured by the number of pregnant women receiving HCT and those enrolled in PMTCT services. The results were also compared with 2013 PMTCT programme data.
Results: 50,271 pregnant women (median age 25 years) had ANC during the MNCH week; this represented 135% and 86% respectively of the population seen in the selected LGAs and the State in 2013. Of these, 50,269 had HCT; this represented 129% and 82% respectively of those tested in the selected LGAs and the State in 2013. 1,063 of the tests were positive, 54% of these were new positives and enrolled in PMTCT. All enrolled in PMTCT will be tracked for retention in care till delivery. 31% of pregnant women seen were first time ANC clients in their current pregnancy with 59% of these beyond first trimester.
Conclusions: Service uptake in 13 LGAs in 5 days (70% pregnant women population) exceeded 80% uptake for the entire State in a year. This suggests that integrating HCT into MNCH campaigns is feasible as an additional strategy to improve access to PMTCT and move Nigeria towards eMTCT earlier.

MOPEC451

A rapid structured assessment of health facilities for PMTCT scale up in four states in Nigeria with high prevalence

A.C. Ajibola[1], B. Oyeledun[2], A. Inedu[2], C. Imarhiagbe[2], B. Uguge[2], P. Jwanle[3], E. Madina[3]
[1]Center for Integrated Health Programs, Clinical Services Unit, Abuja, Nigeria, [2]Center for Integrated Health Programs, Abuja, Nigeria, [3]CIHP, Abuja, Nigeria
Presenting author email: aajibola@cihpng.org

Background: Access to PMTCT services in Nigeria remains low at less than 18% despite the presence of many Health Facilities (HF)across Kaduna, Benue, Gombe and Kogi States, where HIV prevalence is higher than National prevalence of 4.1 %. The aim of this study was to assess HF in these states for scale up of PMTCT program. Center for Integrated Health Programs(CIHP) with funding from CDC implemented a Health Care Facility Assessment in four (4) Nigerian states.

Methods: The health facility assessment was conducted within a four day period in all the states concurrently from February 10 to 13 2013. The exercise was jointly conducted by the State Ministry of Health, Local Government and CIHP. A total of 4661 health facilities were listed in all the states, 815 (17%) were said to be providing PMTCT pre assessment. 3, 846 health facility were included in the study including private health facilities and mission centers. Prior to the assessment, a structured health facility assessment tool was designed to document available information; identify gaps that might hinder effective PMTCT scale up. A one day training on the tools was conducted across the states. A total of 128 health care providers and 32 supervising officers were trained on the administration of tools and monitoring.
Results: 3616 (94%) of the 3846 HF were assessed for possible PMTCT scale up and 473 were identified and activated for PMTCT services 1006(27.8%) health facilities were not offering ANC thus pregnant women could not have access to antenatal care and PMTCT services. All the private facilities in one state provide HIV testing for pregnant women with a fee. More than one- quarter of the PHCs record very low volume of ANC uptake (2-5 in a month). A half of the health facility assessed need facility upgrade.
Conclusions: The assessment revealed a huge number of HF with MNCH services without PMTCT services. The assessment using LGA structures was innovative and cost effective, as over a thousand health facilities were assessed within four days with an opportunity to have evidence based listing of facilities and status, while institutionalizing ownership to promote sustainability of the PMTCT program.

MOPEC452

Partner antenatal attendance associated with partner HIV testing among pregnant women in Kisumu, Kenya

D. Krakowiak[1], J. Kinuthia[2,3], A. Osoti[4], V. Asila[2], M.A. Gone[2], B. Betz[5], S. Parikh[6], C. Farquhar[1,5,7]
[1]University of Washington, Epidemiology, Seattle, United States, [2]Kenyatta National Hospital, Research and Programs, Nairobi, Kenya, [3]Kenyatta National Hospital, Obstetrics and Gynecology, Nairobi, United States, [4]University of Nairobi, Nairobi, Kenya, [5]University of Washington, Global Health, Seattle, United States, [6]University of Washington, Public Health, Computer Science and Engineering, Seattle, United States, [7]University of Washington, Medicine, Seattle, United States
Presenting author email: daisykr@uw.edu

Background: HIV testing among couples prevents horizontal and vertical transmission and facilitates linking individuals to care. Evidence suggests that male involvement in antenatal care facilitates HIV testing; however, male antenatal clinic attendance is low in Kenya and elsewhere. In this study, we identify factors associated with male partner HIV testing.
Methods: The Home-based Partner Education and Testing (HOPE) study is a randomized clinical trial of pregnant women and their partners, determining whether home visits result in higher HIV testing uptake among partners than invitations to attend the antenatal clinic. Results presented here come from a screening questionnaire completed at enrollment. All pregnant women attending the Kisumu District Hospital Antenatal Clinic from October 2012 to May 2013 were verbally consented, screened for eligibility and asked about previous pregnancies as well as HIV testing. Correlates of partner HIV testing, including past partner antenatal attendance, female and partner age, female education, household income, individual income, gravidity, number of living children with partner, and duration living together, were examined using multiple logistic regression with α-level of 0.05.
Results: In total, 1105 women were screened, 85 (7.7%) of whom were accompanied by their partner. Overall, 673 (61%) women reported their partner had been HIV tested, 617 (91.7%) were aware of their partner's status, and 73 (13.9%) partners were positive. Among 511 women reporting a previous pregnancy with their current partner, 131 (25.6%) partners attended at least one antenatal visit during the preceding pregnancy. In a multiple logistic regression model, partners who attended any antenatal clinic visits during the preceding pregnancy were 4.11 times as likely to have been HIV tested compared to those did not (95% CI: 2.24-7.55). Additionally, household monthly income level (OR=1.42; 95% CI: 1.11-1.83) and female education level (OR=1.27; 95% CI: 1.02-1.57) were significantly associated with partner HIV testing. There were no other significant correlates of partner testing.
Conclusions: While partner antenatal attendance was low, it was positively associated with HIV testing in previous pregnancies. Strategies to increase partner attendance could boost HIV testing during the antenatal period and need to be considered for pregnant couples in areas with high HIV prevalence.

MOPEC453

Where are pregnant women who were not tested for HIV? The use of IQSMS in identifying pregnant women for HIV testing, Tanga experience, Tanzania

T.S. Tulli[1], D. Mwikali[2], A. Mourad[2], S. Jongo[1], G. Binde[1], A. Madhehebi[1]
[1]Futures Group International, Dar es Salaam, Tanzania, United Republic of, [2]Catholic Relief Services, Dar es Salaam, Tanzania, United Republic of
Presenting author email: ttulli@futuresgroup.com

Background: The Local Partners Excel in Comprehensive HIV & AIDS Service Delivery (LEAD) project, funded by the Centers for Disease Control under PEPFAR, supports prevention of mother-to-child transmission (PMTCT) services at 293 facilities in Tanga region, Tanzania. HIV testing and counselling of pregnant women is a major initiative to reduce transmission of HIV from mother to child. Lack of HIV testing kits caused some of the women not to be tested on time which resulted in missed opportunity for early identification of infected babies. LEAD project used International Quality Short Message Software (IQSMS) to identify pregnant women from all facilities in Tanga who were not tested for HIV.
Methods: The IQSMS software uses health providers' mobile phones to send monthly reports of HIV test kits stock status and number of pregnant women tested and not tested from each facility to a server via SMS. The monthly reports submitted to the server are analysed and women not tested identified. A call-back campaign, jointly implemented by program officers, nurses and clinicians based on reports retrieved from the IQSMS, encouraged women who were not tested to return to facilities to be tested.
Results: Between January and March 2013, a total of 18,663 pregnant women attended antenatal clinics from 293 facilities for the first time, among them 15,677(84%) were tested for HIV while 2986 (16%) were not tested due to lack of HIV test kits. Between April and September 2013, the test kits stock improved and by the use of IQSMS, Out of 2986 women who were not tested 2752(92%) were identified and tested for HIV and 234(8%) were not traced. There was improvement in testing when data collected among pregnant women who attended for the first time in the clinic between April and September 2013, a total of 36,118 pregnant women attended clinic and all of them 100% were tested for HIV.
Conclusions: Through the use of IQSMS, stakeholders at the facility- district-, regional-, and national-levels obtained up-to-date information that can quickly identify pregnant women who have not yet been tested for HIV to be tested when HIV test kits become available.

MOPEC454

Systematic HIV-testing in delivery rooms is feasible: a pilot program through 8624 consecutive deliveries in Burundi, East Africa

H. Leroy[1], S. Manyundo-Risase[2], B. Ninyibutse[2], J. Biziragusenyuka[3], N. Cartier[4], C. Arvieux[1]
[1]University of Rennes, Infectious Diseases, Rennes, France, [2]Hopital Prince Regent Charles, Bujumbura, Burundi, [3]ESTHER-Burundi, Bujumbura, Burundi, [4]ESTHER-France, Paris, France
Presenting author email: leroy_bidoune@yahoo.fr

Background: Burundi associates high HIV prevalence (1,3% in 15-49 years old) and limited resources in a post conflict area. In 2012, according UNAIDS, 54% of HIV-infected pregnant women will receive antiretrovirals during pregnancy, but access to HIV- testing is poor. Testing for HIV during pregnancy is recommended by national guidelines, free of charge.
Methods: As HIV testing was poorly proposed in public healthcare settings, we have implemented a systematic testing in the delivery room of Bujumbura's main hospital. Testing is systematically proposed by community workers, who perform a rapid pre-test counseling. If a woman is diagnosed previously unknown HIV-positive, with no prior access to the PMTCT program, she's proposed immediate lamivudine/tenofovir/efavirenz intake and a free 72H hospitalization to perform active counseling, a doctor's visit, and to schedule protected breast-feeding.
Results: From April 2012 to June 2014, there were 8624 deliveries, and 76% of women were tested for HIV: before intervention, less than 10% of mothers were tested during delivery; one month after the onset of the intervention, 65% of women were tested, and 98% in june 2014. 105 women were tested newly positive (1.8% of women with previous unknown status). Four hundred and fifty seven women were previously diagnosed for HIV, thus the global prevalence at delivery was 6.5%. Among previously unknown HIV- infected women, there was a high prevalence of unemployed, singles with unknown father or unmarried, and women who had no medical follow-up during pregnancy. In these late-diagnosed women, lost to follow-up after delivery was very high, with 28% of women never returning to the healthcare setting; three babies and 2 mothers died, among those who were not lost for follow-up.
Conclusions: Systematic testing in delivery rooms is feasible and should be encouraged if we want to be on the path of ETME. Special care must be emphasized for the women who are diagnosed during delivery, because of their high risk of lost to follow-up. Delivery is their unique occasion to be in touch with healthcare workers. Community and healthcare support for adherence, juridical or psychological assistance is critical to lower lost to follow-up, infant and mother mortality and mother-to-child-transmission.

MOPEC455

Infant HIV outcomes and timing of presention to prenatal care: contribution of HIV seroconversion during pregnancy

M. Melo[1], J. Raney[2], K. Nielsen-Saines[3], T. Rocha[4], B. Santos[4], I. Varella[4]
[1]Hospital Nossa Senhora da Conceicao, Porto Alegre, Brazil, [2]Yale Medical School, New Haven, United States, [3]David Geffen UCLA School of Medicine, Los Angeles, United States, [4]Hospital Conceicao, Porto Alegre, Brazil
Presenting author email: knielsen@mednet.ucla.edu

Background: Mother to Child HIV-1 Transmission (MTCT) is rare in women who receive combination antiretroviral therapy (cART) throughout pregnancy but women who undergo primary HIV-1 infection during gestation or are undiagnosed until delivery are at high risk of HIV transmission.
Methods: HIV MTCT rates at a tertiary HIV referral institution in southern Brazil were evaluated over 7.5 years. Infant outcomes were determined for mothers who received antiretrovirals throughout pregnancy and mothers identified with HIV only at delivery. Rapid HIV testing was performed during labor in women with negative HIV results ≥ 1 month prior to admission or with unknown HIV-1 diagnosis. Neonatal infection was ascertained using RNA PCR over several time points.
Results: Between 1/2006 to 7/2013, 48,560 deliveries occurred at our institution, 1,673 (3.4%) in HIV- infected women. Data was available for 1,132 HIV+ pregnant women who continued postnatal follow-up at our hospital. Infant outcomes were available for children of 949 women (83.8%) who were accompanied for HIV exposure. Women either received prenatal care and cART during pregnancy (n=761) or were only identified as HIV-infected at delivery (n=371). As seen in the table, HIV MTCT was over 10 times more frequent among women identified during labor as compared to women receiving cART ($p < 0.001$). Rates of miscarriage were two-fold higher in women not on cART during pregnancy (p =0.02), while rates of early infant death and loss to follow-up were similar in both groups. Forty-two women identified at delivery (11.3% of late presenters) had documented HIV seroconversion during pregnancy, HIV MTCT rate 19%. None of the women followed postpartum at our institution breastfed. The incidence of HIV-1 seroconversion in pregnancy was 0.9/1,000 (CI 95% 0.6-1.2/1,000).

	HIV-uninfected infant	HIV-infected infant	Infants w/ HIV status confirmed	Miscarriage	Infant death prior to HIV status	Lost-to-follow-up	Total
Pre-natal care with cART	602 (99.2%)	5 (0.8%)	607 (83.4%)	11 (1.4%)	22 (2.9%)	121 (15.9%)	761
HIV identified in labor:No cART	263 (91.3%)	25 (8.7%)	288 (77.6%)	10 (2.7%)	11 (3.0%)	62 (16.7%)	371
Total	865	30	895	21	33	183	1132

[Outcomes by time of maternal presentation to care]

Conclusions: In southern Brazil, an area of high HIV-1 prevalence, seroconversion during pregnancy is not unusual, and carries a high MTCT risk. Women not on cART have higher rates of miscarriage as compared to treated patients. Early infant death among HIV-exposed children was higher than in the general population (3% vs.1.9%). Loss to follow-up of HIV-affected mother-infant pairs is still a significant problem in our setting.

Increasing coverage and quality of PMTCT programmes

MOPEC457

Characteristics and outcomes of women initiating ART during pregnancy versus breastfeeding in Option B+ in Malawi

M. Landes[1,2], S. Sodhi[1,2], A. Matengeni[2], C. Meaney[1], M. van Lettow[2], A.K. Chan[2,3], J. van Oosterhout[2]
[1]University of Toronto, Department of Family and Community Medicine, Toronto, Canada, [2]Dignitas International, Malawi, Malawi, [3]University of Toronto, Department of Medicine, Toronto, Canada
Presenting author email: mclandes@gmail.com

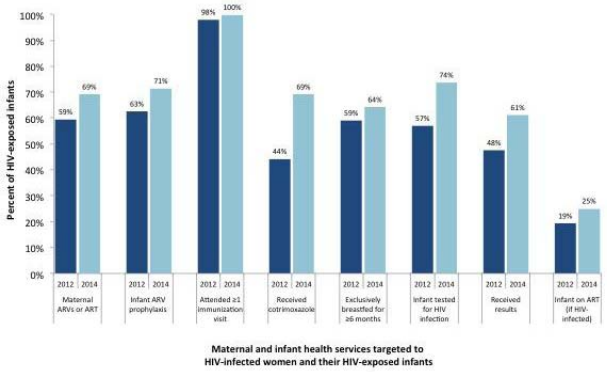
Background: Malawi adopted the PMTCT strategy 'Option B+' in 2011, providing lifelong ART for all HIV-infected pregnant and breastfeeding women. We explore differences in characteristics and outcomes of women initiating ART during pregnancy versus breastfeeding.
Methods: We conducted a retrospective cohort analysis of women initiating ART during pregnancy or breastfeeding in Zomba District, southern Malawi, from January 2012 to September 2013. Data were extracted from the Zomba District Observational Cohort Study database, a surveillance project collecting information from standard Ministry of Health ART monitoring tools.
Results: 2965 women were included: 1993 (67.2%) initiated ART during pregnancy, 972 during breastfeeding.
54.4% of women were between 21-30 years old. Younger women (< 30 years) were 1.3 times more likely to initiate in pregnancy (vs. breastfeeding) than older women (aOR 1.32, 95%-CI 1.1-1.6; p=0.00).
WHO clinical staging was recorded in 2162 (72%) women: 92.1% were either Stage 1 or 2. Women initiating during breastfeeding were more likely to have advanced HIV disease (Stage 3 or 4: aOR 2.8, 95%CI 2.0-3.9; p=0.00) than women initiating in pregnancy.
Overall, 25 (0.84%) women died: 15 initiated ART in pregnancy and 10 in breastfeeding (p=0.16). 786 (26.5%) women defaulted with the majority defaulting either immediately after the first visit (30.5%) or within three months (21.1%). Those defaulting immediately or within three months were more likely to have initiated ART in pregnancy than during breastfeeding compared to those defaulting after one year (aOR 3.5; 95%CI 2.1-5.7; p=0.00 and aOR 2.7, 95% CI1.6-4.6; p=0.00, respectively).
Conclusions: Many women in Malawi started ART during breastfeeding within Option B+. These women were older, more often in WHO Clinical Stage 3 or 4 and defaulted later compared to those starting during pregnancy. They represent missed PMTCT opportunities during the antenatal phase. Further studies are required to identify why they fail to access care during pregnancy, based upon which targeted interventions can be designed.

MOPEC458

Dramatic improvements in uptake of prevention of mother to child HIV transmission services in Zimbabwe, 2012-2014

S.I. McCoy[1], R. Buzdugan[1], M. Kang Dufour[2], R. Musarandega[3], A. Mushavi[4], A. Mahomva[3], B. Engelsmann[5], N.S. Padian[1], F.M. Cowan[6,7]
[1]University of California, Division of Epidemiology, Berkeley, United States, [2]University of California, San Francisco, United States, [3]Elizabeth Glaser Pediatric AIDS Foundation, Harare, Zimbabwe, [4]Ministry of Health and Child Welfare, Harare, Zimbabwe, [5]Organization for Public Health Interventions and Development, Harare, Zimbabwe, [6]Centre for Sexual Health, HIV & AIDS Research, Harare, Zimbabwe, [7]University College London, London, United Kingdom
Presenting author email: smccoy@berkeley.edu

Background: Prevention of mother-to-child HIV transmission (PMTCT) requires an integrated cascade of services for pregnant and breastfeeding women and their infants. We compared uptake of maternal PMTCT services among women with a recent birth in Zimbabwe in 2012 and 2014 using community-based data.
Methods: We analyzed serial cross-sectional data from the evaluation of Zimbabwe's accelerated implementation of the 2010 WHO PMTCT guidelines. Using multi-stage cluster sampling, eligible women were randomly sampled in 2012 and 2014 from the catchment areas of 157 facilities offering PMTCT services in Harare, Manicaland, Mashonaland Central, Matabeleland South, and Mashonaland West. Eligible women were ≥16 years old and biological mothers of infants (alive or deceased) born 9 to 18 months before the survey. Participants were tested for HIV infection and interviewed about health service utilization during pregnancy and breastfeeding.



[Figure. Utilization of services in the PMTCT cascade among HIV-infected women and their HIV-exposed infants, Zimbabwe, 2012 and 2014]

Results: Overall, 8,800 and 10,225 mother-infant pairs were interviewed in 2012 and 2014, respectively. The uptake of reproductive health services increased significantly among all pregnant and postpartum women, including attendance at ≥1 antenatal care (ANC) visit during pregnancy (94% to 96%), ≥4 ANC visits (64% to 71%), receiving HIV test results (92% to 96%), institutional delivery (77% to 84%), postnatal visit attendance (92% to 95%), and use of

a modern contraceptive method (77% to 84%). Among women who were HIV-infected (2012: 12.7%, 2014: 12.1%), the proportion reporting initiation of antiretroviral therapy (ART) before pregnancy or an antiretroviral prophylactic regimen increased significantly from 59% to 69% (p< 0.01, see Figure), as did the proportion reporting antiretroviral prophylaxis for their HIV-exposed infant (63% to 71%, p< 0.01). Coverage of cotrimoxazole increased 25 percentage points and early infant diagnosis increased 13 percentage points. Among infants with complete testing data, the proportion who were HIV-infected (2012: n=97 (8.9%); 2014: n=59 (5.1%)) and on ART did not change significantly (19% to 25%, p=0.31).
Conclusions: Zimbabwe's accelerated PMTCT program had large and positive impacts on service uptake in a two-year period. Nevertheless, these data from women in the community indicate gaps in the PMTCT cascade where further efforts are needed to increase engagement and retention in PMTCT services as Zimbabwe approaches virtual elimination of MTCT.

MOPEC459

Acceptability of prevention of mother to child transmission of HIV Option B+ among HIV-infected pregnant and breastfeeding women in Chiradzulu District, Malawi

T. Mwapasa, A. Muula
University of Malawi, College of Medicine, School of Public Health, Blantyre, Malawi
Presenting author email: tmwapasa@gmail.com

Background: In 2011, Malawi became of of the the first countries in the world to adopt the Option B+ Prevention of Mother-to-Child Transmission of HIV (PMTCT) antiretroviral treatment (ART) programme, which entails lifelong ART for all Human Immunodeficiency Virus (HIV) infected pregnant and breastfeeding women. However, the acceptability of lifelong treatment, especially to healthy women, has not been examined. Therefore the objective of this study was to assess the acceptability of PMTCT Option B+ among HIV infected pregnant and breastfeeding women in Chiradzulu District.
Methods: We conducted a cross sectional qualitative study using in-depth interviews (IDIs) with 32 pregnant and breastfeeding women at Chiradzulu District Hospital in Malawi. Eligible study participants were women who had just been initiated on Option B+ regimen (n=10), those that had been on the regimen for 3 to 6 months (n=12) and postnatal women transitioning from the PMTCT programme to the adult ART programme (n=10). IDIs were recorded and then transcribed in verbatim. Data was analyzed manually using thematic content analyses.
Results: We found that Option B+ PMTCT regimen was highly acceptable among pregnant and breastfeeding women regardless of their health status or duration of treatment. Most women were in favor of Option B+, mainly because they viewed the regimen as being beneficial in preventing frequent illnesses, prolonging life, and enabling a longer period of breastfeeding. However, a few women were not in favor of Option B+ because of the need to take daily medications for the rest of their lives.
Conclusions: Option B+ regimen was highly acceptable to HIV+ women due to expectation of improved health status for themselves and their infants. These benefits seem to outweigh concerns about long duration of treatment and ART side-effects.

MOPEC460

Same day integration of HIV diagnosis and treatment with antenatal care affects retention in Option b+ prevention of mother to child transmission services in Zomba District, Malawi

A.K. Chan[1,2,3], E. Kanike[1], R. Bedell[1], I. Mayuni[1], R. Manyera[1], W. Mlotha[4], A.D. Harries[5,6], M. van Lettow[1,3]
[1]Dignitas International, Medical and Research, Zomba, Malawi, [2]University of Toronto, Sunny Brook Health Science Centre, Toronto, Canada, [3]University of Toronto, Dalla Lana School of Public Health, Toronto, Canada, [4]Malawi Ministry of Health, District Health Office, Zomba, Malawi, [5]International Union Against Tuberculosis and Lung Disease, Paris, France, [6]London School of Hygiene and Tropical Medicine, London, United Kingdom
Presenting author email: a.chan@dignitasinternational.org

Background: Early programmatic data from Malawi show considerable variation between health facilities in retention on ART of Option B+ women. We studied whether full integration of HIV testing and counseling (HTC) and ART initiation on the same day during antenatal care (ANC) impacted on retention on ART compared with partial integration: HTC at ANC with referral for ART initiation. We also investigated whether any difference in retention was due to the impact of having diagnosis and ART initiation on the same day.
Methods: A retrospective cohort study of pregnant women seeking ANC at all rural primary health facilities in Zomba District, Malawi was conducted using data extracted from standardized national ANC and ART registers, and ART master cards and linked by patient identifiers. Descriptive information on the organization of Option B+ service delivery at each health facility, accounting for the degree of integration of ANC, HTC and ART, was identified by the Zomba District Health Office.
Results: Between October 2011 and March 2012 a total of 10,168 women were newly registered at ANC, in 23 rural health facilities. Twelve health facilities provided HTC and ART on the same day at ANC (Model 1) to 3,842 women and 11 provided only HTC at ANC and referred to an ART clinic for treatment (Model 2) to 6,686 women. There was no difference in uptake of HTC or ART between the models. For those who started ART, there was a significantly higher loss-to-follow-up in Model 1 (22%) vs. Model 2 (8%), p< 0.001. Multivariable analysis (adjusted for mothers age, gravida and model of care applied) showed that initiation of ART at ANC on the same day was associated with reduced retention on treatment both 3 months [aOR1.82 (95% CI:1.04-3.18)] and 6 months after starting ART [aOR1.94
(95% CI:1.15-3.29).
Conclusions: Retention on ART was higher in those who are referred to start ART from ANC vs. starting ART in ANC. HIV diagnosis and treatment on the same day appears to be associated with reduced retention on treatment. Reduced retention related to implementing test and treat on the same day needs further evaluation.

MOPEC461

Predictors and outcomes of perinatal HIV transmission at regional referral hospitals implementing Option B plus in Uganda

C. Katureebe[1,2], I. Lukabwe[2], M. Kwikiriza[3], E. Namagala[2], N. Tumwesigye[4]
[1]University Research Co, PMTCT/EID and Peadiatric HIV, Kampala, Uganda, [2]Ministry of Health, Uganda STD/AIDS Control Program, Kampala, Uganda, [3]University Research Co, LLB, SUSTAIN Project, PMTCT/Peadiatric HIV, Kampala, Uganda, [4]UNICEF, HIV, Kampala, Uganda
Presenting author email: cordeliamboijana@yahoo.com

Background: Mother-to-child transmission of HIV (MTCT) accounts for more than 90% of pediatric HIV cases. Prevention of mother to child transmission (PMTCT) programs are effective if a continuum of care is provided for HIV infected pregnant women and their exposed infants.
This study assessed predictors of HIV transmission and clinical outcomes among HIV-exposed infants in care at ten regional referral hospitals in Uganda.
Methods: Retrospective chart review for exposed infants enrolled at Early infant diagnosis care points at ten Regional referral hospitals was conducted. All records of HIV-exposed infants enrolled between October 2012 and September 2013 were included. Trained midwives and data personnel collected data using a structured data extraction format. Data were then entered in to EPI DATA Version 3.5.1 statistical software and analyzed by STATA version 12.0. Both bivariate and multivariate analyses were carried out to identify associations.
Results: A total of 2,657 infant records were included in the analysis. The median age of infants at enrolment was 2.8 months. A total of 207(7.8%) were HIV infected and 82% initiated on ART. Not breast feeding status at enrolment (AOR=2.75, 95% CI: 2.34, 10.9), lower health facility delivery (AOR=2.83, 95% CI: 1.53, 5.23), not receiving infant Nevirapine at birth (AOR=2.57, 95% CI: 1.29, 5.09), and mother not in care (AOR=4.08, 95% CI: 1.09, 14.8) were significantly and independently associated with maternal to child transmission of HIV in this study. Sixteen percent of the exposed infants had stopped breast feeding with median duration 8 months IQR (5-8) and 56% of these received a second HIV test. Mother-baby pairs active in care were 75%.
Conclusions: Perinatal HIV transmission is high.Predictors were: None- breast/feeding status by first PCR test,No Nevirapine receipt, mother not being in care and delivery at a health facility other than the RRH.
Only half of the children that have stop breastfeeding received a 2nd DNA-PCR test indicating losses in care. Three quarters of HIV exposed infants and their mothers are still active in care.

MOPEC462

Male partner involvement improves uptake of prevention of mother to child HIV transmission services in Kenya

B.M.O. Odeny[1], C. Mcgrath[1,2], J. Kinuthuia[3], B. Singa[4], A. Langat[5], J. Pintye[1], A. Katana[5], L. Nganga[5], G. John-Stewart[1]
[1]University of Washington, Seattle, United States, [2]University of Texas Medical Branch, Galveston, United States, [3]Kenyatta National Hospital, Nairobi, Kenya, [4]Kenya Medical Research Institute, Nairobi, Kenya, [5]United States Centers for Disease Control and Prevention (CDC), Nairobi, Kenya

Background: Male partner involvement, such as antenatal clinic (ANC) attendance, may increase uptake of prevention of mother-to-child transmission of HIV (PMTCT) services. We assessed the prevalence and correlates of male ANC attendance and the effect of male involvement on PMTCT-related outcomes in Kenya.
Methods: We conducted a cross-sectional survey of mother-infant pairs in 141 maternal child health (MCH) clinics throughout Kenya between July and December 2013. Structured questionnaires and MCH booklets were used to gather information on maternal and partner ANC attendance, antiretroviral drug (ARV) use, skilled delivery, contraceptive use, infant HIV testing, ARV prophylaxis, and infant HIV-1 status. Multivariable logistic regression models ad-

justed for clustering effect at the clinic level, geographic region, maternal and partner characteristics were used to compare maternal and infant outcomes by male ANC attendance, and to identify correlates of male ANC attendance.

Results: Among 2730 women attending MCH, 960 (33.7%) reported male ANC attendance. Male ANC attendance was similar among HIV infected (55 male partners of 460 women) and uninfected (786 male partners of 2270 women) women [aOR (95%CI)=1.08 (0.65-1.74)]. Maternal HIV disclosure [aOR=4.2 (2.2-7.8)], shorter relationship duration [aOR=1.39 (1.10-1.77)], higher maternal education [aOR=1.8 (1.6-2.1)], earlier gestational age at first ANC [aOR=1.32 (1.05-1.66)], and absence of intimate partner violence [aOR=1.64 (1.12-2.42)] were significantly associated with higher male ANC attendance. Male ANC attendance varied significantly by geographic region with higher rates in Central compared to Western Kenya [aOR= 3.30 (1.78-6.10)]. Among HIV+ women, male ANC attendance was significantly associated with higher maternal uptake of ARVs for PMTCT [aOR=4.36 (1.51-12.05)], ≥4 maternal ANC visits [aOR=1.68 (1.41-1.99)], skilled delivery [aOR=1.54 (1.21-4.58)], and contraceptive use [aOR=1.55 (1.16-2.08)]. Among HIV infected women, partner attendance had no discernable effect on infant HIV status [aOR=0.96 (0.35-2.65)], likelihood of infant HIV testing [aOR=1.08 (0.72-1.65)], or infant nevirapine use [aOR=0.74 (0.20-2.74)], although power to detect associations in HIV exposed infants was low.

Conclusions: Male partner ANC attendance was associated with increased maternal uptake of MCH and PMTCT services. Further efforts to increase male ANC attendance such as national awareness campaigns or incentives for men may be useful.

MOPEC463

Male partner participation in antenatal clinic services Is associated with improved mortality and HIV-free survival among infants of HIV-positive women in Nairobi, Kenya: a prospective cohort study

A. Aluisio[1], R. Bosire[2], B. Betz[3], C. Farquhar[4]
[1]*State University of New York at Downstate Medical Center, Department of Emergency Medicine, Division of International Emergency Medicine, Brooklyn, United States,* [2]*Kenya Medical Research Institute, Nairobi, Kenya,* [3]*University of Washington, Epidemiology, Seattle, United States,* [4]*University of Washington, Epidemiology, Medicine, Global Health, Seattle, United States*
Presenting author email: adam.aluisio@gmail.com

Background: Male involvement in PMTCT in sub-Saharan Africa is recommended however evidence supporting improved outcomes with participation is limited. This prospective study investigated the relationship between male ANC/PMTCT involvement and infant HIV-free survival.

Methods: From 2009-2013, HIV-infected pregnant women were enrolled from six clinics in Nairobi, Kenya and followed with their infants until six weeks postpartum. Women were screened for consent for partner involvement. If females consented, men were encouraged to attend through invitation letters. Standardized questionnaires were used to survey all participants. Males who failed to attend antenatally had questionnaires provided for self-completion postnatally. Informed consent was obtained from all subjects.

Results: Among 830 enrolled women, 519 (62.5%) consented to male participation and 136 partners (26.2%) attended the ANC. For the 383 (73.8%) women whose partners failed to attend, 63 (16.4%) were surveyed via outreach. Partner attendance was more likely among couples in monogamous relationships that had previously discussed PMTCT interventions and if men reported prior HIV testing, awareness that vertical transmission was possible and that their partner was HIV-positive. In multivariate analysis only male report of prior HIV testing was associated with attendance (aOR=3.7; 95%CI:1.5-8.9, p=0.003). Thirty-three (6.6%) of 499 infants acquired HIV or died by six weeks of life. Infants born to women with male attendance had an incidence of vertical transmission or death of 20.2/100-person-years (95%CI:6.5-62.6), and those born to mothers without partner attendance had an incidence of 76.4/100-person-years (95%CI:53.4-109.2). Infant lacking male ANC engagement had reduced HIV-free survival with a 3.7-fold higher risk as compared to those born to women with partner attendance (HR=3.70 (95%CI:1.12-12.50, p=0.031). Adjusting for ARV treatment the risk of survival failure remained significantly greater among those born to females without male participation (aHR=3.57 95%CI:1.10-11.11, p=0.037).

Conclusions: Male ANC attendance was greater among couples in which men had previously undergone HIV testing and partner involvement was associated with improved infant HIV-free survival. Promotion of male HIV testing and engagement in ANC/PMTCT services may improve infant outcomes in similar settings and warrants further study.

MOPEC464

An innovative approach to triple elimination of mother to child transmission of HIV, syphilis and hepatitis B in Viet Nam

V.T.T. Nguyen[1], Q.T. Ho[2], L.A. Nguyen[3], K.A. Le Ai[2], B.M. Truong[2], D.V. Nguyen[4], Y.-R. Lo[5], M. Kato[1]
[1]*World Health Organization, Country Office in Viet Nam, HIV, Hanoi, Vietnam,* [2]*Thai Nguyen Provincial AIDS Centre, Thai Nguyen, Vietnam,* [3]*National Institute for Hygiene and Epidemiology, Hanoi, Vietnam,* [4]*Pho Yen District Health Centre, Thai Nguyen, Vietnam,* [5]*World Health Organization, Office of Western Pacific Region, Manila, Philippines*
Presenting author email: nguyenva@wpro.who.int

Background: Elimination of mother-to-child transmission (EMTCT) is a global target. Vietnam has a concentrated HIV epidemic and high prevalence of hepatitis B virus (HBV) infection. Prevention of mother-to child-transmission (PMTCT) has focused only on HIV. This operational research aims to demonstrate an innovative model of integrated PMTCT of HIV, HBV and syphilis to inform policy change toward more comprehensive approach to eliminate new infection of HIV, HBV and syphilis among infants.

Methods: This study was implemented in all 18 communes in Pho Yen district, Thai Nguyen province between October 2012 to December 2014. Pregnant women (PW) were offered HIV, HBV and syphilis testing during antenatal visits. PW diagnosed with HIV, HBV and syphilis and their infants were offered interventions, including antiretrovirals (ARV), syphilis treatment, and HBV immunoglobulin (HBIG) for infants in addition to HBV vaccine. Infants were tested for HIV, HBV and syphilis at age 7 and 12 months.

Results: Among a total of 3,498 PW, 98.6% were tested for HIV, HBV and syphilis. Prevalence of HIV, HBV and syphilis were 0.17%, 8% and 0.03%, respectively. Five out of six HIV positive women received ARV. All HIV exposed infants underwent early infant diagnosis of HIV had negative results. One woman diagnosed with syphilis infection in week 24 of gestation received treatment and her infant was uninfected. Among PW infected with HBV, 45.5% were HBeAg and 52% HBeAb positive. Overall, 76% HBV-exposed infants received the birth-dose immunization (within 24 hours) which was higher than the overall birth-dose coverage (33.5%) in the same district during the same period. Among 143 HBV-exposed infants born in 2013, 28 were HBsAg positive (19.6%). The multivariate analysis showed that not receiving HBIG was strongly associated with increased risk of infant HBV infection (AOR 4; 95%CI:1.6-12; P=0.004).

Conclusions: This study suggested triple EMTCT is feasible. However, PMTCT of HBV needs further effort and investment. Our findings suggest that investment in HBV screening for PW could increase uptake of hepatitis B birth-dose among exposed infants and HBIG could reduce the risk of HBV infection for infants.

MOPEC465

National estimates of mother to child transmission of HIV-1 at 6 weeks and 9 months in Kenya

C. McGrath[1], B. Singa[2], A. Langat[3], J. Kinuthia[4], K. Ronen[5], D. Omolo[2], B. Elly Odongo[3], R. Wafula[6], P. Muange[6], A. Katana[3], L. Nganga[3], G. John-Stewart[7]
[1]*University of Texas Medical Branch, Galveston, United States,* [2]*Kenya Medical Research Institute, Nairobi, Kenya,* [3]*United States Centers for Disease Control and Prevention, Nairobi, Kenya,* [4]*Kenyatta National Hospital, Nairobi, Kenya,* [5]*Fred Hutchinson Cancer Research Center, Seattle, United States,* [6]*Kenya Ministry of Health, National AIDS and STI Control Programme, Nairobi, Kenya,* [7]*University of Washington, Seattle, United States*
Presenting author email: chmcgrat@utmb.edu

Background: To reach targets for elimination of perinatal HIV infection, Kenya has expanded prevention of mother-to-child transmission of HIV (PMTCT) coverage. We evaluated PMTCT program effectiveness and factors influencing MTCT in a nationwide survey

Methods: We conducted probability-proportional-to-size sampling of 120 clinics in Kenya, July-December 2013. Staff surveyed mother-infant pairs attending 6-week and 9-month immunizations, offered HIV retesting to HIV-uninfected mothers, and collected blood spots from infants of HIV-infected mothers for HIV DNA testing. Transmission risk (TR) was calculated by dividing number of DNA-positive infants by infants at risk at each time point. Multivariable regression models weighted for survey design and clinic-level clustering compared exposures between HIV-infected and uninfected infants.

Results: Among 2521 mother-infant pairs surveyed, 1502 attended 6-week and 1019 attended 9-month visits. Overall, 2423 (94.7%) reported HIV test in pregnancy or prior HIV diagnosis, of whom 200 (7.4%) were HIV-infected, 86 (40.7%) diagnosed in pregnancy. Of 200 infants born to mothers with known HIV, 188 underwent HIV-testing, of whom 7.2% (95% CI: 3.7-13.5%) were HIV-infected. HIV-TR was 8.8% (CI: 4.0-18.3%) in the 6-week cohort and 4.8% (CI: 1.3-15.6%) in the 9-month cohort. Including mothers with incident HIV since pregnancy, 9-month postpartum HIV-TR was 8.7% (3.1-22.0%). Mothers of HIV-infected infants were less likely to know their CD4 count (18.6% vs 58.5%, p=0.02) or disclosed their status to male partners (24.5% vs 80.6%, p< 0.001) than mothers of uninfected infants. Infected infants were more likely to be female (82.3% vs 17.8%, p=0.03). Overall, 69% of HIV-infected mothers received antiretroviral drugs (ARVs) during pregnancy, 65% at delivery, 64% postpartum; 93% of

infants. HIV-TR was higher in mothers reporting no ARVs compared to mothers receiving ARVs during pregnancy (aOR=6.4; CI: 1.2-34.4), at delivery (aOR=10.9; CI: 1.9-62.4), or postpartum (aOR=6.7; CI: 1.2-37.4). Infant ARVs were associated with lower TR (aOR=0.1; 0.01-0.4).
Conclusions: MTCT was appreciable despite high coverage of pregnancy HIV testing, likely due to incomplete ARV coverage. Evaluation at 6-weeks and 9-months postpartum yielded differences in TR estimates potentially due to loss and mortality; precision of estimates was limited by sample size. Efforts to improve maternal and infant ARV use remain critical to attain PMTCT goals.

MOPEC466

The action birth card: evaluation of an innovative goal-setting tool to increase demand and uptake of underutilized services along the PMTCT cascade

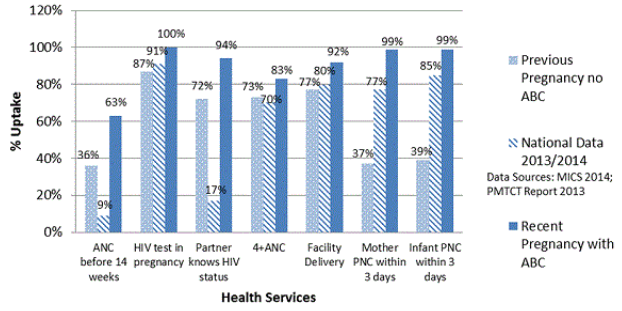
K. Webb[1], V. Chitiyo[1], D. Patel[1], A. Chari[1], A. Dhlana[2], M.-A. Nicholas[3], E. Kennedy[3], B. Engelsmann[1]
[1]Organisation for Public Health Interventions and Development (OPHID) Trust, Harare, Zimbabwe, [2]Ministry of Health and Child Care, Rushinga District, Rushinga, Zimbabwe, [3]Burnet Institute, Melbourne, Australia
Presenting author email: kwebb@ophid.co.zw

Background: Reducing morbidity and mortality during pregnancy and preventing vertical transmission of HIV requires demand and uptake of services along the PMTCT cascade. The Action Birth Card (ABC) is an innovative goal-setting tool for use by pregnant women to plan uptake of underutilized services across the PMTCT cascade in Zimbabwe. The ABC prompts women to identify barriers to service uptake, problem solve using existing community resources, record and reflect on their performance. Objective of our evaluation was to assess service utilization rates of women who received the ABC in their most recent pregnancy.
Methods: In November 2014, a cross-sectional survey of women who received the ABC during their most recent pregnancy in Rushinga District was conducted. Service uptake related to each ABC Goal during recent (with ABC) and previous (without ABC) pregnancies was documented using a structured, pre-tested questionnaire.

ABC Goal	Specific Indicator
1. Early Antenatal Care (ANC) Booking	1a. Uptake of ANC < 14wks gestation; 1b. Male partner accompanies to 1st ANC visit
2. HIV Test in Pregnancy	2a. Pregnant woman HIV tests in pregnancy; 2b. Male partner knows HIV status
3. 4+ ANC Visits	3a. Number ANC visits attended;
4. Develop a Birth Plan	4a. Birth plan developed; 4b. Birth plan followed at time of labour
5. Facility Based Delivery	5a. Use of maternity waiting home 5b. Facility-based delivery
6. Prompt Postnatal Care	6a. Postnatal care for mother < 3 days after delivery; 6b. Postnatal care for infant < 3 days after delivery

[Service utilization indicators for ABC]

Proportion of women who made use of services in pregnancies with and without Action Birth Card were compared by Chi-square analysis. To explore potential influence of temporal bias upon service uptake between pregnancies, utilization during the recent pregnancy was compared with national data over a similar period.
Results: Among 174 women interviewed, average age was 26.9yrs (range 16-40yrs) and average number of pregnancies 2.5. Women demonstrated significantly higher service uptake during their recent pregnancy using the ABC planning tool compared to previous pregnancy without ABC for all ABC utilization indicators (p< 0.005), with the exception of 4+ ANC (p=0.07). Women who used ABCs during their recent pregnancy also demonstrated higher uptake rates than national figures over the same time period.



[Service utilization during pregnancy]

Conclusions: Rural women who received the Action Birth Card and planned for service use in their recent pregnancy demonstrated higher reported uptake of services along the PMTCT cascade compared to both previous pregnancies and national data. Implementation of this low-cost, effective intervention should be expanded to enhance existing efforts by the Ministry of Health and Child Care to increase demand and uptake for services along the PMTCT Cascade. Service goals in the ABC should be extended to postnatal services in the PMTCT cascade and the impact upon health and development outcomes of mother-baby pairs explored.

MOPEC467

Awareness, utilization and access to HIV and maternal health care services for pregnant women in two high HIV prevalence districts of India: a baseline evaluation

J. Behara[1], A. Sarkar[1], G. Mburu[2], P. Sharma[1], S.K. Mishra[1], S. Mehra[1]
[1]MAMTA Health Institute for Mother and Child, Research Department, New Delhi, India, [2]International HIV/AIDS Alliance, Brighton, United Kingdom
Presenting author email: jagannath@mamtahimc.org

Background: Mother-to-child transmission is the single most important source of HIV infection in children. However, utilisation of antenatal care (ANC), which is an important entry point for preventing Mother-to-Child Transmission of HIV, remains low in India. A baseline survey was carried out to understand knowledge, perceptions, practices and barriers related to early HIV testing, care and support among pregnant women, and their community members.
Methods: Cross-sectional and mixed methods were used. Quantitative data were collected from 1108 pregnant or recently delivered women in Nagpur and Adilabad districts through structured questionnaires. These included 19 women living with HIV. Qualitative data were gathered through in-depth interviews (IDIs) and focus group discussions (FGDs) with identified stakeholders including ASHAs, ANMs, Doctors, Integrated Counselling Testing Centre (ICTC) counsellors and Panchayat members. Data were collected between March and April 2014.
Results: Awareness of complete antenatal care (ANCs) package was only 28% in Adilabad whereas it was 53% in Nagpur. Only 38% of women in Nagpur and 33% in Adilabad went for HIV testing in the second trimester of pregnancy. Around 28% women were not aware of any place where HIV testing could be done. Notably, 12 out of 19 women living with HIV reported that they had late ANC registration and came to know about their "positive status" as late as six months of their pregnancy. Five HIV positive women reported that they were not currently under ART. Qualitative data on barriers revealed that local norms and traditional beliefs did restrict many women to visit health facility for HIV screening during first ANC. Further, frontline functionaries reported limited availability of HIV rapid testing in remote areas, notion of stigma and lack of motivation by community health workers also acted as barriers for uptake of services.
Conclusions: Poor uptake of ANC services and HIV testing during pregnancy results from both community and facility level barriers in the intervention districts. The study indicates that there is a need to motivate frontline community health workers, and to support pregnant women to access ANC and early HIV testing.

MOPEC468

Timing of maternal HIV diagnosis and uptake of PMTCT in Kenya

A. Langat[1], A. Katana[1], C. McGrath[2], J. Kinuthia[3], B. Odongo[1], B. Singa[4], R. Wafula[5], M. Sirengo[5], G. John-Stewart[6], L. Nganga[1]
[1]Centers for Disease Control and Prevention, Nairobi, Kenya, [2]University of Texas Medical Branch, Galveston, United States, [3]Kenyatta National Hospital, Nairobi, Kenya, [4]Kenya Medical Research Institute, Nairobi, Kenya, [5]Kenya Ministry of Health, National AIDS and STI Control Programme, Nairobi, Kenya, [6]University of Washington, Seattle, United States
Presenting author email: vpl4@cdc.gov

Background: Prevention of mother-to-child transmission (PMTCT) services/coverage has been scaled up in Kenya over the last decade aiming at eliminating perinatal infection. With expanded PMTCT and HIV care programs, more women are diagnosed with HIV prior to pregnancy. We compared characteristics of mothers diagnosed with HIV prior to pregnancy to those diagnosed in pregnancy and examined uptake of PMTCT interventions in these groups in a national survey.
Methods: We conducted a cross-sectional study enrolling mother-infant pairs at week 6 and month 9 immunizations from 140 maternal child health clinics selected by probability-proportionate-to-size sampling in Kenya, between July and December 2013. Maternal socio-demographics, HIV status, uptake of PMTCT services, and maternal and infant clinical data were collected by standardized questionnaire. Blood spots were collected for infant HIV DNA testing and maternal HIV rapid testing. Chi-square tests were used to compare uptake of PMTCT services between mothers diagnosed before and during pregnancy. All analyses account for clustering at the clinic level.
Results: Among 2891 mother-infant pairs surveyed, 498 HIV-positive mothers were enrolled, of whom, 306 (61.4%) had HIV diagnosis before pregnancy and 192 (38.6%) had HIV diagnosis during pregnancy. Mothers diagnosed during pregnancy were younger (median, 26.2

versus 29.5 years, p< 0.001), more likely to be unemployed (67.5% vs. 52%, p=0.002), more likely to be primigravida (23% vs. 5.2%,
p< 0.001) and to have attended less than the recommended 4 ANC visits (51.6% vs. 60.4%, p=0.03) than women diagnosed with HIV before pregnancy. Women who were first diagnosed with HIV during pregnancy were less likely to receive "complete PMTCT" defined as receipt of maternal and infant antiretroviral prophylaxis (75.5% vs. 84.3%, p=0.04) and had higher risk of vertical HIV transmission (8.3% vs. 2.5%, p=0.006) than women diagnosed before pregnancy.
Conclusions: As PMTCT and HIV services expand, there are distinct groups of previously diagnosed and newly diagnosed mothers with different characteristics and programmatic needs. Mothers who are newly diagnosed during pregnancy have lower PMTCT antiretroviral uptake and further efforts to increase early identification of the mothers will be useful in the PMTCT programs.

MOPEC469

Why did I stop? Barriers and facilitators to acceptance of and retention in the Option B+ program in Lilongwe, Malawi

M. Kim[1,2], A. Zhou[3], A. Mazenga[2], S. Ahmed[1,2], C. Markham[4], G. Zomba[5], P.N. Kazembe[2], E.J. Abrams[6]
[1]Baylor International Pediatric AIDS Initiative at Texas Children's Hospital, Houston, United States, [2]Baylor College of Medicine-Abbott Fund Children's Clinical Centre of Excellence - Malawi, Baylor Children's Foundation, Lilongwe, Malawi, [3]University of California Los Angeles, Sociology, Los Angeles, United States, [4]The University of Texas School of Public Health, Health Promotion and Behavioral Sciences, Houston, United States, [5]Ministry of Health, HIV Unit, Lilongwe, Malawi, [6]ICAP, Mailman School of Public Health and College of Physicians & Surgeons, Columbia University, New York, United States
Presenting author email: amy.yuan.zhou@gmail.com

Background: Despite the early success of Malawi's Option B+ program, early loss-to-follow up remains a challenge. Few studies address how women make treatment decisions and their reasons for dropping out of care. This study compares the experiences of women in care and those not in care and examines how women decide whether to start and stay on ART. We aim to identify the key factors that lead to ART refusal, default, and retention.
Methods: We conducted in-depth qualitative interviews with HIV-positive women who initiated ART through Option B+ in Lilongwe, Malawi (N=62). We included those successfully retained in care (N=27) and those who refused/defaulted ART (N= refuse14; default 21). Open-ended interviews were used to understand women's experience through the PMTCT cascade. We explored potential barriers and facilitators to acceptance/retention in Option B+. Data was analyzed in Atlas.ti using an inductive approach based on grounded theory methodology.
Results: Women who refused ART were concerned with immediate initiation. Half of the women who refused felt healthy and wanted to wait until their health declined or try alternate forms of healing first (7/14). Others expressed that they wanted to wait because they needed time to process their newfound status (4/14). The main reasons women gave for defaulting includes side effects and lack of partner support. 43% of women expressed that the severity of efavirenz related side effects were too much to bear (9/21). 29% expressed that their husbands were not supportive and was preventing them from taking their treatment (6/21). The most common reason women gave for accepting ART was to protect their child and future health (16/27). Several women felt sick when tested positive and saw ART as the way to become healthy again (7/27). In general, we found that treatment decisions were considered an individual's own decision (44/62). Partners, family, community, and church members' opinions were noted but did not determine a woman's choice to start or stop ART.
Conclusions: Successful retention is related to how women conceptualize early ART initiation in light of their perceived health. Interventions that provide early support for patients experiencing side effects may be helpful.

PMTCT services for marginalized groups

MOPEC470

Mother to child transmission of HIV amongst adolescents: findings from three national surveys, South Africa, 2010, 2011-12 and 2012-13

T. Ramraj[1], D. Jackson[2], T.-H. Dinh[3], S. Olorunju[4], C. Lombard[4,5], G. Sherman[6,7], A. Puren[6,8], V. Ramokolo[1], N. Noveve[1], Y. Singh[1], V. Magasana[1], S. Bhardwaj[9], Y. Pillay[10], A.E. Goga[1,11]
[1]South African Medical Research Council, Health Systems Research Unit, Cape Town, South Africa, [2]University of Western Cape, School of Public Health, Western Cape, South Africa, [3]Centers for Disease Control and Prevention (CDC), Center for Global Health, Division of Global HIV/AIDS, Atlanta, United States, [4]South African Medical Research Council, Biostatistics Unit, Cape Town, South Africa, [5]University of Cape Town, School of Public Health and Family Medicine, Cape Town, South Africa, [6]National Institute for Communicable Diseases, Centre for HIV and STI, Pretoria, South Africa, [7]University of the Witwatersrand, Department of Paediatrics and Child Health,Faculty of Health Sciences, Johannesburg, South Africa, [8]University of the Witwatersrand Medical School, Division of Virology and Communicable Diseases, School of Pathology, Johannesburg, South Africa, [9]UNICEF, Health and Nutrition, Pretoria, South Africa, [10]National Department of Health, South Africa, South Africa, [11]University of Pretoria, Department of Paediatrics and Child Health, Pretoria, South Africa
Presenting author email: trisha.ramraj@mrc.ac.za

Background: Globally, nearly 16 million births occur annually to adolescents (15 to 19 years), mostly in developing countries. These contribute to higher maternal or infant morbidity/mortality. Noting the new global call for better adolescent health, we sought to quantify access to HIV-related care and risk of early mother-to-child transmission of HIV (MTCT) amongst adolescents in South Africa where HIV prevalence is high and 30% of teenage girls report ever being pregnant.
Methods: Data from three national, cross-sectional, facility-based surveys, conducted in 2010, 2011-12 and 2012-13, were analysed. Stratified, multi-stage, probability proportional to size sampling methodology, with random sampling of facilities and consecutive or systematic sampling of participants (caregivers with infants aged 4-8 weeks receiving their 1st DTP immunization) was conducted. Interviews gathered data on maternal socio-demographics, ante- and postnatal care and uptake of prevention of MTCT (PMTCT) services. Infant dried blood samples were tested for HIV antibodies and total nucleic acid to determine HIV exposure and infection, respectively. During analysis mothers were categorised into adolescents (< 20 years) or adults (≥20 years); data were weighted for sample realisation and population live births
Results: Data from 4704 adolescents (1646 from 2010, 1680 from 2011-12 and 1388 from 2012-13) and 25253 adults (8536 from 2010, 8426 from 2011-12 and 8291 from 2012-13) were analysed. Overall, adults utilized PMTCT interventions 3 times more than adolescents (unadjusted odd ratio, OR, 3.36; 95% confidence interval, CI, 2.95-3.83). This did not differ significantly by survey. Early MTCT amongst adolescents compared with adults was 7.2% (CI:4.2-12.1%) versus 3.2% (CI:2.6-4.0%) in 2010, 5.8% (CI:3.1-10.5%) versus 2.5% (CI:1.9-3.2%) in 2011-12 and 6.7% (CI:3.4-12.9%) versus 2.4% (CI:1.8-3.1%) in 2012-13. The OR for MTCT in adolescents compared with adults, across all surveys was 2.99 (CI:1.12-7.98), adjusted for PMTCT intervention, maternal education, knowledge of partner's HIV status, CD4 cell count conducted, maternal income source, survey year and infant birth weight. Between 2010 and 2012-13 early MTCT reduced significantly in adults but not in adolescents.
Conclusions: Adolescents have lower coverage of PMTCT services and significantly higher early MTCT compared with adults. Adolescent-focused services are urgently needed to improve PMTCT service coverage for adolescents and reduce adolescent MTCT.

Integration of family planning and HIV services

MOPEC471

Unplanned pregnancies and unmet family planning needs among HIV-1-discordant couples in Nairobi, Kenya

K. Hancuch[1], C. Farquhar[1], R. Bosire[2], J. Kiarie[3], B. Guthrie[1]
[1]University of Washington, Seattle, United States, [2]Kenya Medical Research Institute, Nairobi, Kenya, [3]University of Nairobi, Nairobi, Kenya
Presenting author email: khancuch@uw.edu

Background: HIV-1-discordant couples face a complex set of decisions surrounding fertility desires and contraceptive practices. The vertical and horizontal transmission risks associated with conception and pregnancy can be substantially mitigated if pregnancies are planned

and couples are aware of their options. We sought to describe unplanned pregnancies among a cohort of HIV-1-discordant couples and identify factors associated with these pregnancies.

Methods: HIV-1-discordant couples in Nairobi, Kenya were followed quarterly for up to 2 years. In 64.2% of the couples, the woman was the HIV-positive partner. Pregnancy status was assessed via self-report at study exit and risk factors were assessed via questionnaires given at multiple time points during the study. Logistic regression was used to determine associations between risk factors and unplanned pregnancy.

Results: Of 402 women in stable heterosexual HIV-1-discordant relationships, 75(18.7%) reported having been pregnant during the study, and of the 70 women who responded to the question, 39 (55.7%) reported that the pregnancy was unplanned. Contraceptive use (excluding condoms) was low; current usage at baseline was reported by 7 (17.9%) women with unplanned pregnancies, 4 (12.9%) women with planned pregnancies, and 67 (20.5%) women who did not become pregnant. Among those who reported a planned pregnancy, only 3 (9.7%) reported taking action to reduce the risk of HIV-1 transmission. The likelihood of an unplanned pregnancy was not significantly different between HIV-1-infected women (51.1%) and uninfected women (66.7%) (p=0.23).

Women who reported planned pregnancies were also more likely to report unprotected sex (OR=4.7; 95% CI 1.6 to 13.6; p=0.004), and HIV-infected women were almost twice as likely as uninfected women to report any unprotected sex during the study period (30.6% vs. 15.9%, p=0.001). Baseline desire for additional children (p=0.61), number of living children (p=0.45), any reported unprotected sex at baseline (p=0.87), and baseline contraceptive use (p=0.28) were not associated with the likelihood of an unplanned pregnancy.

Conclusions: Unplanned pregnancies were common among HIV-1-discordant couples, while usage of hormonal or other modern contraceptives was low. The results stress a need to consider fertility desires of discordant couples and take action to provide both highly effective contraception and safer conception counseling.

MOPEC472

Uptake of highly effective contraception among HIV-infected postpartum women in Kenya: results from a national survey

A. Drake[1], J. Pintye[2], B. Odongo[3], J. Unger[4], J. Kinuthia[5], C. McGrath[6], N. Obudho[3], A. Langat[3], G. John-Stewart[7]
[1]University of Washington, Global Health, Seattle, United States, [2]University of Washington, Nursing and Global Health, Seattle, United States, [3]Centers for Disease Control and Prevention, Nairobi, Kenya, [4]University of Washington, Obstetrics and Gynecology, Seattle, United States, [5]Kenyatta National Hospital, Nairobi, Kenya, [6]University of Tex Medical Branch, Galveston, United States, [7]University of Washington, Seattle, United States
Presenting author email: jpintye@uw.edu

Background: Uptake of postpartum contraception is critical to prevent unintended pregnancies and promote healthy birth spacing. Moreover, pregnancy prevention is an important component of preventing mother-to-child HIV transmission. We measured contraceptive use and correlates of highly effective contraception (HEC) among HIV-infected postpartum Kenyan women.

Methods: We conducted a nationally representative cross-sectional survey of women attending 9-month infant immunization visits at 120 MCH clinics in Kenya between July and December 2013, with a secondary survey oversampling HIV-positive mothers at 30 clinics. Study staff administered questionnaire assessing self-reported contraceptive practices and maternal characteristics. Maternal HIV positive status was confirmed with clinic records, or determined through rapid testing for women with unknown status.

Factors associated with HEC were analyzed using logistic regression accounting for clinic-level clustering. HEC was defined as using injectables, oral contraceptives (OCs), implants, tubal ligations, or intrauterine devices (IUDs).

Results: Among 238 HIV-infected women surveyed, median age was 28 years, 194 (81.5%) were married, median relationship duration was 6 years and 156 (65.6%) reported using contraception at 9-months postpartum. The majority (73.9%) of women were breastfeeding. Most (90.3%) women did not want children in the next 1-2 years. Among these women 141 (66.5%) reported contraceptive use: 32 (22.7%) used condoms alone while 109 (77.3%) used HEC [67 (61.5%) injectables, 8 (7.3%) OCs, 21 (19.2%) implants, 4 (3.7%) tubal ligations, 2 (1.8%) IUDs, and 7 (6.5%) dual methods (condoms plus HEC)]. Women who were married, more educated (≥12 years), received contraceptive counseling earlier, and delivered at a facility were more likely to use HEC (Table 1). HEC use during the prior pregnancy was significantly associated with current postpartum HEC use p=0.02).

Conclusions: In this national survey, 65.6% of HIV-infected postpartum women who did not desire pregnancy in the next 1-2 years were using HEC and use of dual methods was rare. Unmarried and less educated women, and women who had not recently received contraceptive counseling were less likely to use HEC, which suggests these women need tailored contraceptive counseling.

However, effective strategies to improve contraceptive counseling and uptake, including long-acting reversible contraception and dual methods, are needed for all HIV-infected postpartum women.

	Median (IQR) or N (percentage)			Univariate analyses	
		Currently using highly effective contraception			
	Total (n=215)	No (n=106)	Yes (n=109)	Crude OR (95% CI)	p-value
Maternal demographic characteristics					
Age (years)	28 (25-33)	28 (25-33)	29 (24-33)	0.99 (0.94-1.04)	0.70
Married	176 (81.8%)	78 (73.6%)	98 (89.9%)	2.37 (1.23-4.58)	0.01
>12 years of completed education	51 (23.7%)	17 (16.0%)	34 (31.2%)	3.20 (1.50-6.82)	0.003
Age difference with partner (years)[1]	6 (3-10)	5 (3-9)	7 (3-10)	1.03 (0.97-1.08)	0.32
Gravidity	3 (2-4)	3 (2-4)	3 (2-4)	1.05 (0.86-1.29)	0.62
Delivered at facility	178 (82.8%)	81 (76.4%)	97 (89.0%)	2.49 (1.18-5.28)	0.02
Number of ANC visits	4 (3-5)	4 (3-5)	4 (3-5)	0.98 (0.84-1.15)	0.84
Duration of breastfeeding (months)	9 (9-9)	9 (8-9)	9 (9-9)	1.15 (0.98-1.36)	0.09
Received contraceptive counseling ≥6 months ago[2]	68 (37%)	23 (25%)	45 (48%)	2.72 (1.46-5.06)	0.002
Used highly effective contraception to prevent last pregnancy[3]	26 (55.3%)	7 (35.0%)	19 (70.4%)	4.41 (1.28-15.17)	0.02
Intimate partner violence	57 (26.5%)	30 (28.3%)	27 (24.8%)	0.83 (0.45-1.53)	0.56

OR=odds ratio; CI= confidence interval, ANC=antenatal care
[1]Among women who reported having a current partner; 37 (17%) women reported not currently having a partner
[2]Among women who reported receiving contraceptive counseling; 28 women (13%) reported not having contraceptive counseling
[3]Among 47 women that reported using contraception to prevent the prior pregnancy

[Table 1. Correlates of highly effective contraceptive use among HIV-infected postpartum women not desiring children in the next 2 years]

Promoting health and reducing maternal mortality in HIV positive women

MOPEC473

Loneliness and perceived social support in mothers living with HIV in Ontario

S. Khan[1], A. Ion[2], R. Keshmiri[1], S. Greene[2], S. Walmsley[1,3], L. Kennedy[4], M. Loutfy[1,4,5]
[1]University of Toronto, Toronto, Canada, [2]McMaster University, Hamilton, Canada, [3]Toronto General Hospital, Toronto, Canada, [4]Women's College Research Institute, Toronto, Canada, [5]Maple Leaf Medical Clinic, Toronto, Canada
Presenting author email: sarahz.khan@sickkids.ca

Background: HIV-related stigma results in isolation, poor perceived social support and barriers to healthcare. The perinatal period adds challenges, potentially increasing the sense of isolation experienced by women living with HIV (WLWH). Correlations between loneliness, depression, and poor coping styles amongst WLWH have been described, but not in the context of motherhood. The analysis identified correlates of lower perceived social support and loneliness in mothers living with HIV (MLWH).

Methods: The HIV Mothering Study is an observational study that explored the psychosocial experiences of MLWH. Data collected at 12 months postpartum (n=62) measuring depression, HIV stigma, race and gender-based discrimination, loneliness and perceived social support were analyzed. Univariable and multivariable linear regression were used to determine the correlates of loneliness and perceived social support at 12 months postpartum, with a priori correlates of interest being stigma, depression, discrimination, number of children, age, and race. Covariates with p values < 0.1 were included in the multivariable model and backward stepwise elimination was carried out until a best-fit model was reached.

Results: The median age of the cohort was 33 years, consisting mainly of African/Black women (65%); 42% of participants were not in a relationship, and 25% had no previous children. All psychosocial variables (HIV stigma, depression, racism, and gender discrimination) were highly correlated to perceived social support and loneliness (r=0.39 to 0.774), and were significant covariates in univariate analysis (p< 0.10). In multivariable analyses, depression was a significant covariate of perceived social support (β=-0.359, p< 0.05); and depression (β=0.599) and HIV stigma (β=0.241) were significant covariates of loneliness (p< 0.05). Loneliness and perceived social support were highly negatively correlated (r=-0.736, p< 0.0005).

Conclusions: Understanding the relationship between depression, isolation and low social support in the context of HIV and motherhood is essential for optimal maternal and child health. Multivariable regression revealed that depression was a significant factor in low perceived social support whereas depression and stigma were significant factors of loneliness. Screening and treating depression, as well as destigmatization may be optimal ways to reduce loneliness and improve perceived social support in MLWH.

MOPEC474

Breastfeeding did not have negative impact on body mass index of HIV-infected mothers in 4 African countries

E.N. Somé[1], I.M. Engebretsen[2], N. Meda[3], N. Nagot[4], R. Vallo[5], M. Péries[5], C. Kankansa[6], J. Tumwine[7], J. Hofmeyr[8], P. Van De Perre[4], T. Tylleskar[2], ANRS 12174 Trial Group
[1]Institut de Recherche en Sciences de la Santé Burkina Faso, Department of Nutrition, Ouagadougou, Burkina Faso, [2]University of Bergen, Nutrition, Bergen, Norway, [3]Centre Muraz, Université de Ouagadougou, Bobo Dioulasso, Burkina Faso, [4]INSERM U 1058, Centre Hospitalier Universitaire, Université de Montpellier 1, Montpellier, France, [5]INSERM U 1058, University of Montpellier1, Montpellier, France, [6]University of Zambia, School of Medicine, Pediatrics and Child Health, Lusaka, Zambia, [7]Mekerere University, School of Medicine, Pediatrics and Child Health, Kampala, Uganda, [8]University of Fort Hare, Effective Care Research Unit, Cape Town, South Africa
Presenting author email: eric.nsome@gmail.com

Background: In socio-economic deprived settings breastfeeding is a key survival strategy to infants born to HIV-infected women. HIV-infection is known to cause wasting in people infected. Breastfeeding further increases energy demands. Our objective was to explore the impact of breastfeeding on changes in Body Mass Index (BMI).
Methods: The data were collected in the ANRS 12174 trial (clinical trial no NCT00640263) in Burkina Faso, South Africa, Uganda and Zambia. We ran a linear mixed model with BMI as the dependent variable and exclusive and predominant breastfeeding (EPBF) duration as the key explanatory variable.
Results: Among 1225 participants, 97% initiated BF in the first week of infant's life for a mean duration of 5.9 (95%CI 5.8- 6.0) and a median of 6.6 months (Interquartile range: 0.9). The mean (standard deviation) age, BMI, CD4 count, and HIV viral load at baseline (day 7) were respectively 27.4 (5.4) years, 24.5 (4.5) kg/m^2, 579 (198) cells/µl and 39000 (336000) copies/mm^3. The hemoglobin concentration (week 14 post-delivery) was 12.1 (1.5) g/dl.
For each additional month of EPBF, there was a non-significant decrease in BMI of -0.08 (95% CI: -0.24; 0.08) kg/m^2 (table 1), and the total mean reduction was -0.50 (95% CI: -1.42; 0.47) kg/m^2.
The mothers' HIV-1 viral load, disease stage, hemoglobin concentration, the marital and occupational status, breastfeeding initiation time child gender as well as the study treatment arm were not statistically significantly associated with the BMI change. Conversely, the mothers' age, education level, mode of delivery (vaginal versus C-section) and parity were statistically significantly and positively associated with the BMI change.
Conclusions: According to our findings breastfeeding practice did not have a negative impact in HIV-1 infected mothers' BMI. EBF should be widely advised for infants born to HIV-infected women in poor resource settings where formula is not safe.

MOPEC475

Postpartum transfer of care among HIV-infected women who initiated antiretroviral therapy during pregnancy: a cohort study

T. Phillips[1], M. McNairy[2,3], A. Zerbe[3], L. Myer[1,4], E.J. Abrams[3]
[1]Division of Epidemiology and Biostatistics, University of Cape Town, School of Public Health & Family Medicine, Cape Town, South Africa, [2]Weill Cornell Medical College, New York, United States, [3]ICAP at Columbia University, Mailman School of Public Health, New York, United States, [4]Desmond Tutu HIV Centre, University of Cape Town, Cape Town, South Africa
Presenting author email: eja1@cumc.columbia.edu

Background: The movement in prevention of mother-to-child transmission (PMTCT) programmes to integrate antiretroviral therapy (ART) provision into antenatal care has created the need to transfer women to general ART clinics after delivery for ongoing care. While there are widespread concerns around ART adherence and loss to follow-up after delivery, there are few data describing this postpartum step in the HIV care cascade for women starting ART in pregnancy.
Methods: We examined postpartum transfer between ART services in a cohort of virally suppressed women who had started ART in pregnancy and were transferred from an integrated antenatal ART clinic to general ART clinics from May 2012 - September 2013. Before transfer, women completed a brief questionnaire and post-transfer engagement in care at an ART clinic was assessed via routine laboratory records and telephonic follow-up.
Results: During the study period 279 postpartum women were transferred to ART clinics (median age, 28 years; median duration of ART use at transfer, 30 weeks). Overall, between 74% and 91% of women had evidence of attending an ART clinic after delivery, depending on the outcome definition. The median time from transfer to reported engagement in ART care and first laboratory assessment was 8 weeks and 22 weeks, respectively. In a logistic regression model adjusted for age, CD4 cell count and being diagnosed with HIV in the current pregnancy, additional weeks on ART prior to transfer improved the odds of engagement in care at an ART clinic after transfer (OR 1.04 95% CI 1.00-1.07, p=0.033).
Conclusions: Postpartum transfer of ART care is an important step in the HIV care cascade for PMTCT programmes but one that has received little attention. Even in this cohort, women who were adherent at the time of transfer, up to 26% of women had no evidence of engaging in care at an ART clinic post-transfer, suggesting this is a vulnerable step in the HIV care cascade. To ensure the benefits of ART for both maternal health and PMTCT, retention is required across all steps of the cascade, including transfer of ART care after delivery.

Prevention addressing gender inequalities

MOPEC476

Knowledge, attitudes and experiences of violence among adolescent girls: a baseline assessment in the Soweto township of South Africa

R.B. Hershow[1], B.F. Sanders[1], C.K. Barkley[1], B. Rakosa[1], T.S. Clark[1], J. DeCelles[1], M. Das[2]
[1]Grassroot Soccer, Cape Town, South Africa, [2]International Center for Research on Women (ICRW), New Delhi, India
Presenting author email: rebeccah@grassrootsoccer.org

Background: South Africa has one of the highest rates of sexual violence against girls ages 12 to 17,
with more than a third of girls experiencing sexual violence before the age of 18. There is an urgent need for effective interventions that address the intersections of violence and HIV among adolescent girls. In May 2014, Grassroot Soccer conducted a baseline assessment with 200 girls aged 11-16 to better understand the practices, attitudes, knowledge, and experiences of girls related to gender, intimate relationships and violence.
Methods: A 164-item questionnaire was administered to grade 8 female learners in 4 schools in Soweto, Guateng (n = 200; mean age = 13.61) on mobile phones using Open Data Kit (ODK) software. For the analysis, SPSS version 18 was used for simple frequency distribution and cross tabulation. Self-efficacy, gender-equitable beliefs (measured using a modified Gender Equitable Men scale), justification of violence, and HIV knowledge were analyzed by age distribution (11-13 years = 49%; 14 years = 38%;
15 -16 years = 13%).
Results: Respondents aged 11-13 had higher gender-equitable beliefs (21%) than the other age cohorts (Table 1). Respondents in the younger cohorts had higher perceived self-efficacy (11-13 years = 25%;
14 years = 32%) than the oldest cohort (15-16 years = 15%). The mean level of HIV-related knowledge decreased with age (11-13 years = 3.53; 15-16=3.22). 31% of all respondents reported intimate partner violence (IPV) as unacceptable; justification of a boyfriend's violent behavior increased with age (11-13 years = 18%; 15-16 years = 33%). 47% of all respondents identified street, 24% school, and 17% home as high-risk areas of violence. 48 respondents (42%) reported experiencing IPV, and 126 (63%) reported experiencing non-partner violence in the last 12 months. 62% of respondents who had experienced violence reported disclosure of experience to parents. 58% of respondents shared IPV experiences with mothers;
2% with fathers. 31% and 36% respectively reported to police for IPV and non-partner violence.

Age of respondents	Percent of respondents with low gender-equitable beliefs (no. of respondents)	Percent of respondents with moderate gender-equitable beliefs (no. of respondents)	Percent of respondents with high gender-equitable beliefs (no. of respondents)	Total percent of respondents (total no. of respondents)
11-13 years	18.6 (18)	60.8 (59)	20.6 (20)	100.0 (97)
14 years	21.1 (16)	60.5 (46)	18.4 (14)	100.0 (76)
15-16 years	25.9 (7)	66.7 (18)	7.4 (2)	100.0 (27)
Total	20.5 (39)	61.5 (123)	18.0 (36)	100.0 (200)

[Table 1. Level of gender-equitable beliefs by age]

Conclusions: Findings indicate that older girls reported lower gender-equitable beliefs, self-efficacy, and HIV-related knowledge, and higher justification of a boyfriend's violent behavior than younger girls. These data demonstrate high experiences of violence and absence of the father when disclosing violence among girls. Creating a safe space and integrating linkages to support services, family, and schools is important.

MOPEC477

Gender norms, masculine gender-role strain and HIV risk behaviors among men in rural South Africa

A. Gottert[1], C. Barrington[2], H.L. McNaughton-Reyes[2], S. Maman[2], C. MacPhail[3,4,5], S.A. Lippman[6], K. Kahn[4,7], R. Twine[4,7], A. Pettifor[1,4]
[1]University of North Carolina-Chapel Hill, Epidemiology, Chapel Hill, United States, [2]University of North Carolina-Chapel Hill, Health Behavior, Chapel Hill, United States, [3]University of New England, CRN for Mental Health and Wellbeing, Armidale, Australia, [4]University of the Witwatersrand, MRC/Wits Rural Public Health and Health Transitions Research Unit, Agincourt, South Africa, [5]University of the Witwatersrand, Wits Reproductive Health and HIV Institute (WHRI), Johannesburg, South Africa, [6]University of California-San Francisco, Department of Medicine, Center for AIDS Prevention Studies (CAPS), San Francisco, United States, [7]University of the Witwatersrand, School of Public Health, Johannesburg, South Africa
Presenting author email: agottert@live.unc.edu

Background: Theory suggests that gender norms and the related construct of masculine gender-role strain (MGRS) influence HIV risk behaviors among men. Evidence supports a link between inequitable gender norms and HIV risk in the African setting. MGRS, defined as the psychological strain men experience from trying or failing to live up to masculine expectations, has rarely been examined as a predictor of risk behaviors in HIV prevention research.
Methods: We examined associations between men's gender norms and MGRS and sexual partner concurrency, intimate partner violence (IPV) perpetration and alcohol abuse using data from a household survey of 579 18-35 year-old men residing in the rural Agincourt Health and Socio-demographic Surveillance Site, South Africa. To measure gender norms we used the Gender Equitable Men's Scale. To measure MGRS we used a multi-dimensional scale we developed for the South African context.
Results: Prevalence of concurrency in the last 12 months was 38.0%, 13.4% of men reported perpetrating IPV in the last 12 months, and 19.9% abused alcohol. In multivariate analyses that controlled for demographic characteristics, more inequitable gender norms was significantly associated with an increased odds of concurrency (AOR 1.31, 95% CI: 1.07-1.62, p=0.01), IPV perpetration (AOR 1.31, 95% CI: 1.03-1.65, p=0.03), and alcohol abuse (AOR 1.40, 95% CI: 1.04-1.87, p=0.02). Higher MGRS was also associated with an increased odds of concurrency (AOR 1.26, 95% CI: 1.06-1.50, p=0.008), IPV perpetration (AOR 1.48, 95% CI: 1.17-1.88, p=0.001) and alcohol abuse (AOR 1.58, 95% CI: 1.22-2.03, p< 0.001). Analyses of the specific relationships between different MGRS sub-dimensions and study outcomes found significant positive associations between concurrency and *subordination to women* (p=0.04)*;* IPV perpetration and *restrictive emotionality* (p=0.006)*;* and alcohol abuse and *success, power, competition* (p=0.008).

	Sexual partner concurrency	Intimate partner violence perpetration	Alcohol abuse
	AOR (95% CI)	AOR (95% CI)	AOR (95% CI)
Inequitable gender norms	1.31 (1.07-1.62)*	1.31 (1.03-1.65)*	1.40 (1.04-1.87)*
Masculine gender-role strain (MGRS)	1.26 (1.06-1.50)**	1.48 (1.17-1.88)**	1.58 (1.22-2.03)***
MGRS sub-dimensions			
Success, power, competition	1.16 (0.84-1.60)	1.08 (0.72-1.63)	1.56 (1.12-2.16)**
Subordination to women	1.36 (1.01-1.83)*	1.27 (0.86-1.88)	1.31 (0.85-1.71)
Restrictive emotionality	0.81 (0.63-1.02)	1.50 (1.12-2.00)**	0.87 (0.65-1.17)
Sexual prowess	1.05 (0.82-1.34)	0.84 (0.56-1.27)	1.20 (0.88-1.63)

*p<0.05 **p <0.01 ***p<0.001. AOR = odds of a 1 standard deviation (SD) increase on the independent variable of interest, controlling for age, education, employment status and marital status. All analyses incorporated sampling weights and accounted for clustering by village.

[Table 1. Multivariate logistic regression results]

Conclusions: Men with more inequitable gender norms and higher MGRS are more likely to engage in HIV risk behaviors in this setting. HIV prevention programs to transform gender norms should be coupled with strategies to reduce the strain men experience around fulfilling expectations of themselves as men. Research is needed to identify effective strategies to reduce MGRS, currently lacking worldwide.

MOPEC478

Factors associated with depression between men and women in people living with HIV/AIDS in Guangzhou, China

Z. Guo[1], W. Cai[2], Q. Zhou[3], Y. Zhu[1], Y. Guo[1,4]
[1]Sun Yat-sen University, Department of Biostatistics and Epidemiology, Guangzhou, China, [2]Guangzhou NO.8 People's Hospital, Guangzhou, China, [3]The First Affiliated Hospital of Sun Yat-sen University, Epidemiology Research Unit, Guangzhou, China, [4]Sun Yat-sen University, Sun Yat-sen Center for Migrant Health Policy, Guangzhou, China
Presenting author email: runninguoyan@163.com

Background: Previous studies have shown gender differences in factors associated with depression among the general population, but few studies have examined such differences in people living with HIV/AIDS. This study aimed to explore the rates of depression and associated factors between men and women among people living with HIV/AIDS.
Methods: We conducted a cross-sectional survey by convenient sampling from March to June, 2013 in Guangzhou, China. Center for Epidemiological Studies Depression scale (CES-D) was utilized to measure depression of 409 PLWHA, including 286 men and 123 women. 16 was the cut-off point for depression. Chi-square tests and multivariate unconditional logistic regressions were performed to explore the related factors with depression.
Results: The average age of PLWHA was 36.4 years for male and 36.0 years for female; about 60.8% female and 48.9% male PLWHA were married/cohabitation (*P*=0.027). 54.9% male and 25.0% female had middle school education or higher (*P*<0.001). The rate of depression was 48.2%, with 49.0% for male and 46.3% for female. Multivariate Logistic regressions showed that for male PLWHA, HIV-related stigma was significantly associated with depression (*OR*=3.222, *CI*: 1.880,5.522),whereas self-efficacy was negatively associated with depression (*OR*=0.188, *CI*: 0.109,0.321); for female PLWHA, HIV-related stigma (*OR*=4.103, 95% *CI*: 1.710,9.844) and having work experience outside of hometown (*OR*=2.645, *CI*: 1.033, 6.775) were significantly associated with depression, whereas social support was negatively associated with depression (*OR*=0.327, *CI*: 0.139,0.771).
Conclusions: The rates of depression were high for both male and female PLWHA in Guangzhou, China. There were gender differences in factors associated with depression. Future interventions targeting PLWHA to improve mental health need to take into account gender differences. Strategies to reduce HIV-related stigma, help improve self-efficacy for male PLWHA and strengthen social support for female PLWHA are likely to have the potential to reduce depression and improve mental health among PLWHA.

Reproductive choices and interventions for women (including discordant couples)

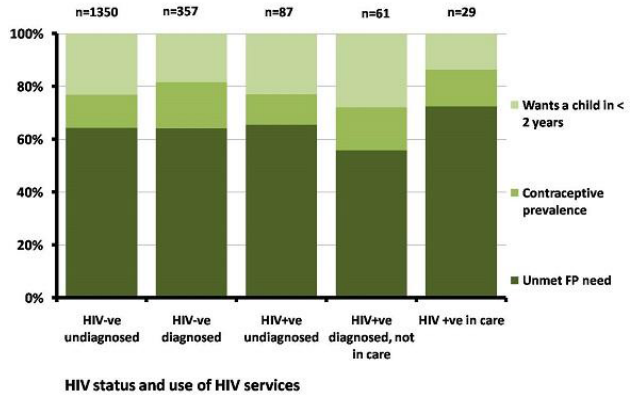
MOPEC479

High levels of unmet need for family planning among HIV-infected women participating in an open HIV community cohort study in rural Tanzania: implications for HIV prevention and service integration

A. Wringe[1], K. Church[1], A. Aveika[2], J. Todd[1], D. Michael[2], B. Zaba[1], M. Urassa[2]
[1]London School of Hygiene and Tropical Medicine, Population Studies, London, United Kingdom, [2]National Institute of Medical Research, Mwanza, Tanzania, United Republic of
Presenting author email: alison.wringe@lshtm.ac.uk

Background: Unmet family planning (FP) needs contribute to HIV transmission and unwanted pregnancies. This study investigated factors associated with unmet FP need in rural Tanzania.
Methods: Data on sexual and reproductive health needs and HIV service use were collected using structured questionnaires during the 2012 round of a community-level HIV surveillance study, covering a population of approximately 30,000 persons. HIV voluntary counselling and testing services were available during surveillance rounds, and at the local health centre from 2005. Antiretroviral therapy was also available from 2005. FP services were available at the local health centre, but were not integrated with HIV services. Women of reproductive age were defined as having unmet FP need if they were married or sexually active in the past month, not pregnant, reported not desiring a child within the next two years and were not using modern contraception. Cross-tabulations were used to describe the distribution of unmet FP need, contraceptive prevalence and fertility intentions by HIV status, and by HIV diagnosis and treatment status. Logistic regression was used to identify factors independently associated with unmet FP need.
Results: 8.8% (199/2258) of included women were HIV-infected, of whom 52% knew their status. 13% reported modern contraceptive use. Unmet FP need was 64% overall and highest among HIV-infected women receiving HIV care (figure 1). Factors independently associated with unmet FP need included age, marital status, area of residence, education, income source,

parity, and HIV and treatment status. Demand for FP (unmet FP need plus current contraceptive use) was 70% among HIV-negatives and 74% among HIV-positives, while the proportion of demand satisfied (FP use/demand) was 19% and 18% among HIV-negatives and HIV-positives respectively, reflecting low contraceptive prevalence. Among women with unmet FP need, 49% of negatives and 43% of positives reported past, or intended future FP use.



[Fig1: Unmet FP need by HIV, testing & care status]

Conclusions: Reduced fertility desires among HIV-infected women receiving HIV care did not translate into increased contraceptive use, resulting in high unmet FP needs. Those reporting past or intended FP use may be amenable to interventions promoting contraception. Reductions in HIV transmission and unwanted pregnancies may be achieved by integrating FP interventions within HIV care and treatment services.

MOPEC480

Pregnancy incidence and outcomes in women receiving tenofovir-based PrEP in the VOICE trial

K. Bunge[1], J. Balkus[2], L. Noguchi[3], J. Pan[2], J. Piper[4], S. Kabwigu[5], J. Marrazzo[6], Z. Chirenje[7], B. Richardson[2], C. Hendrix[8], M. Marzinke[9], H. Watts[10], K. Kintu[5], G. Ramjee[11], F. Mhlanga[7], G. Nair[12], M. Taljaard[13], T. Palanee-Phillips[14], R. Panchia[15], J. Rooney[16], J. Schwartz[17], K. Torjesen[18], K. Gomez[18], R. Scheckter[18], R. Beigi[19]

[1]University of Pittsburgh, Department of Obstetrics, Gynecology, and Reproductive Sciences, Pittsburgh, United States, [2]Fred Hutchinson Cancer Research Center, Vaccine and Infectious Disease Division, Seattle, United States, [3]Magee Womens Research Institute, Pittsburgh, United States, [4]National Institutes of Health, DAIDS, Bethesda, United States, [5]Makerere University-JHU Research Collaboration, Kampala, Uganda, [6]University of Washington, Division of Allergy & Infectious Diseases, Seattle, United States, [7]UZ-UCSF Collaborative Research Programme, Harare, Zimbabwe, [8]Johns Hopkins University, Division of Clinical Pharmacology, Baltimore, United States, [9]Johns Hopkins University, Department of Pathology, Baltimore, United States, [10]US Department of State, Office of the Global AIDS Coordinator, Washington D.C., United States, [11]South African Medical Research Council, Durban, South Africa, [12]CAPRISA, Durban, South Africa, [13]Aurum Institute, Klerksdorp, South Africa, [14]Wits Reproductive Health and HIV Institute, Johannesburg, South Africa, [15]Perinatal HIV Research Unit, Soweto, South Africa, [16]Gilead Sciences, Foster City, United States, [17]CONRAD, Arlington, United States, [18]FHI 360, Durham, United States, [19]University of Pittsburgh, Department of Obstetrics, Gynecology and Reproductive Sciences, Pittsburgh, United States
Presenting author email: kbunge@mail.magee.edu

Background: Reproductive aged-women are a primary target for antiretroviral preexposure prophylaxis (PrEP) for HIV prevention. Understanding exposure effects of PrEP in the periconception period is vital to assessing drug safety. While oral tenofovir disoproxil fumarate (TDF) and emtricitabine/TDF (FTC/TDF) are FDA approved PrEP medications, the efficacy of 1% tenofovir vaginal gel (TFV) is yet to be established. We assessed pregnancy incidence and outcomes among women assigned to these products in the VOICE trial.
Methods: VOICE was a five-arm, double-blinded, randomized, placebo-controlled trial evaluating the effectiveness of daily oral TDF, oral FTC/TDF and vaginal TFV for HIV prevention. Sexually active, contracepting women, aged 18-45, from Uganda, South Africa and Zimbabwe were enrolled between 2009-2011. Pregnancy tests were performed monthly and, if positive, study product was withheld. Pregnancy incidence was calculated per 100 person-years of follow-up and compared across arms using an Andersen-Gill proportional hazards models. Pregnancy outcomes were determined by participant report and medical record review and compared using generalized estimating equations with a logit link.
Results: Among 5029 enrolled women, 452 pregnancies occurred among 428 participants. Overall pregnancy incidence was 8.2 (95% confidence interval [CI] 7.4, 8.9). Pregnancy rates by arm did not differ compared to oral placebo arm. Among participants who became pregnant, the median age was 23 (interquartile range 21, 27) and 67.5% reported oral contraceptive use at enrollment. Outcomes were available for 448 (99%) pregnancies and did not differ by arm.

	All Arms	TDF	FTC/TDF	Oral Placebo	TFV	Gel Placebo
Pregnancy outcomes reported	448	65	104	100	93	86
Full term live birth	263 (59%)	43 (66%)	61 (59%)	59 (59%)	51 (55%)	49 (57%)
Premature live birth	22 (5%)	0 (0%)	3 (3%)	6 (6%)	8 (9%)	5 (6%)
Stillbirth	14 (3%)	1 (2%)	4 (4%)	5 (5%)	2 (2%)	2 (2%)
Spontaneous abortion	83 (19%)	10 (15%)	20 (19%)	20 (20%)	17 (18%)	16 (19%)
Ectopic pregnancy	3 (1%)	0 (0%)	1 (1%)	1 (1%)	1 (1%)	0 (0%)
Elective abortion	60 (13%)	11 (17%)	13 (13%)	9 (9%)	13 (14%)	14 (16%)
Other	3 (1%)	0 (0%)	2 (2%)	0 (0%)	1 (1%)	0 (0%)

[Table 1]

Conclusions: Differences in pregnancy incidence and outcomes did not differ across arms. Specifically, neither the use of tenofovir based medication nor the presence of gel in the vagina impacted early loss rates. Study product adherence was suboptimal; therefore, further analyses integrating data on drug detection in the periconception period are ongoing. However, the present analyses suggest that tenofovir-based PrEP exposure, including a vaginal formulation, is safe in the periconception period.

Population-based intervention studies

MOPEC481

Treatment as prevention (TasP) in rural Swaziland: initiating the change towards universal treatment in the public health sector

B. Kerschberger[1], A.H. Bakri[1], S. Mazibuko[2], I. Zabsonre[1], S.M. Kabore[1], R. Teck[3,4], I. Ciglenecki[3]

[1]Medecins Sans Frontieres (Operational Centre Geneva), Mbabane, Swaziland, [2]Ministry of Health, SNAP, Mbabane, Swaziland, [3]Medecins Sans Frontieres (Operational Centre Geneva), Geneva, Switzerland, [4]Medecins Sans Frontieres, Southern Africa Medical Unit (SAMU), Cape Town, South Africa
Presenting author email: msfch-nhlangano-research@geneva.msf.org

Background: Antiretroviral therapy (ART) is an effective HIV prevention tool to reduce viral load and HIV transmission in HIV+ patients. Swaziland, the country with the highest HIV prevalence globally, developed a Treatment as Prevention (TasP) framework for population HIV incidence reduction. However, evidence is scarce on the feasibility of TasP interventions under routine programmatic conditions. In 2013, the Ministry of Health and Medecins Sans Frontieres (MSF) launched TasP pilot projects in the Shiselweni region to assess feasibility of rapid ART expansion beyond current WHO treatment eligibility criteria.
Methods: ART-uptake of two consecutively implemented TasP strategies was analysed in a decentralized health zone with a network of 9 rural health facilities. The PMTCT option B+ (PMTCTB+) was scaled-up between Jan/2013 to Jun/2014, and followed by phase-in of Early Access to ART for All (EAAA) from Oct/2014 to Dec/2014. Under EAAA, all HIV+ clients aged ≥16 years are eligible for ART initiation regardless of clinical/immunological criteria. Proportions of ART-uptake within one-month of an HIV clinic visit were compared between reporting quarters (PMTCTB+), and between patients with high (>350) and low (≤350) CD4 levels (PMTCTB+/EAAA).
Results: Overall, 665 women were eligible for ART under PMTCTB+; ART-uptake at CD4>350 increased in consecutive quarters from 60% (Q1-2013) to 92% (Q2-2014) (p< 0.01), and it was higher than in CD4≤350 group (86%; p=0.03) at the end of the pilot. Six of 9 facilities had uptake levels >80%. In the first 3 months of EAAA implementation, 287 clients initiated ART of which 203 (71%) were already enrolled into pre-ART care and 84 (29%) were new HIV+ cases (p< 0.01). Among new HIV+ cases with one-month minimum follow-up time (n=90), ART-uptake was 63% for CD4≤350 and 73% for CD4>350 (p=0.17).
Conclusions: High levels of ART-uptake are needed for TasP to reduce HIV transmission at population level. Early challenges in PMTCTB+ implementation were overcome resulting in acceptable ART-uptake levels after scale-up. Early one-month treatment uptake under EAAA was acceptable and comparable with uptake levels in lower CD4 strata. Phase-in of TasP interventions appeared feasible in the public health sector but it may need time and efforts to achieve acceptable treatment uptake.

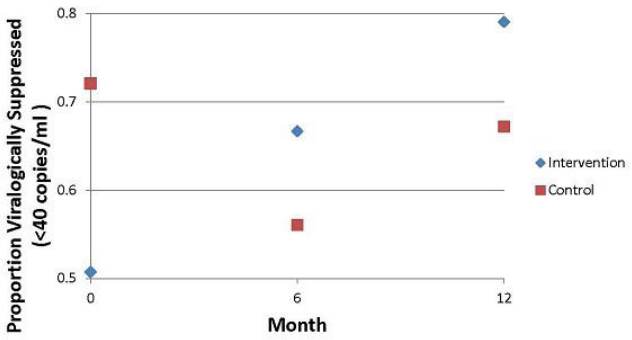
Economic-based HIV interventions (i.e., micro-capital/cash transfer/contingency management/housing/poverty reduction programmes)

MOPEC482

The impact of a multisectoral agricultural and finance intervention on nutritional and HIV health outcomes in rural Kenya

S. Weiser[1], E. Bukusi[2], R. Steinfeld[3], E. Frongillo[4], E. Weke[2], S. Dworkin[5], K. Pusateri[3], S. Shiboski[6], K. Scow[7], L. Butler[8], C. Cohen[3]
[1]University of California, Division of HIV/AIDS, San Francisco, United States, [2]Kenya Medical Research Institute, Nairobi, Kenya, [3]University of California, Obstetrics, Gynecology and Reproductive Sciences, San Francisco, United States, [4]University of South Carolina, Health Promotion, Education and Behavior, Columbia, United States, [5]University of California, Social and Behavioral Sciences, San Francisco, United States, [6]University of California, Epidemiology and Biostatistics, San Francisco, United States, [7]University of California, Department of Soil Science and Soil Microbial Biology, Davis, United States, [8]Boston's Children Hospital, Boston, United States
Presenting author email: sheri.weiser@ucsf.edu

Background: Food insecurity and HIV/AIDS outcomes are inextricably linked in sub-Saharan Africa. We report on health and nutritional outcomes of a multisectoral agricultural intervention trial aimed to improve food insecurity and health outcomes among HIV-infected rural Kenyan adults.
Methods: The intervention included:
i) a human-powered water pump,
ii) a microfinance loan (~$125) to purchase the pump and farm commodities, and
iii) education in sustainable farming practices and financial management.
Two health facilities in the Nyanza Region of Kenya were randomly assigned as intervention or control. HIV-infected adults on antiretroviral therapy (n=140) ages 18-49, with access to surface water and land were enrolled beginning in April 2012, and followed quarterly for one year. Data were collected on food security, dietary intake, anthropometry, CD4, and viral load measurements. Difference in difference fixed-effects regression models were used to test whether the patterns in nutritional and HIV health outcomes across visits differed from baseline between the intervention and control arms.
Results: We enrolled 72 and 68 participants in the intervention and control groups respectively. At baseline, participants at the two sites were similar in age, gender, education, marital status, and food security, but incomplete viral suppression and low diet diversity were more common in the intervention group. At 12 months follow-up, participants enrolled in the intervention arm had statistically significant improvements in food security (3.6 scale points higher, p< 0.001) and frequency of food consumption (9.4 times per week greater frequency, p=0.013) compared to the control arm. While body mass index improved for the intervention compared to the control group, results were not significantly different (p< 0.12). We found statistically significant improvements in CD4 cell counts (165 cells/mm3, p< 0.001) and proportion virologically suppressed in the intervention arm compared to the control arm (comparative improvement in proportion of 0.33 suppressed, OR 7.6, 95% CI: 2.2-26.8, p=0.002, Figure 1).



[Figure 1. Viral load suppression]

Conclusions: Participants in the intervention arm of this multisectoral agricultural intervention demonstrated significant improvements in nutritional and health outcomes compared to controls. Livelihood interventions may be a promising approach to tackle the intersecting problems of food insecurity and HIV/AIDS morbidity.

MOPEC483

Economic incentives to increase demand for voluntary medical male circumcision in Kenya: qualitative interviews with participants in a randomized controlled trial

E. Evens[1], M. Lanham[2], K. Murray[3], S. Rao[4], K. Agot[4], E. Omanga[4], H. Thirumurthy[3]
[1]FHI 360, Health Services Research, Durham, United States, [2]FHI360, Social and Behavioral Health Sciences, Durham, United States, [3]UNC Chapel Hill, Carolina Population Center, Chapel Hill, United States, [4]Impact Research and Development Organization, Kisumu, Kenya
Presenting author email: eevens@fhi360.org

Background: Interventions to increase demand for medical male circumcision are urgently needed in eastern and southern Africa. Despite promising evidence that economic incentives can promote uptake of health interventions, few studies have sought to identify why incentives are—or are not—effective.
Methods: As part of a randomized controlled trial in Kenya that found incentives to be effective in increasing male circumcision uptake, we conducted in-depth interviews with 45 circumcised and uncircumcised participants to explore how the incentives influenced circumcision uptake. An inductive, thematic analysis was conducted to identify patterns in decision-making.
Results: Financial concerns, particularly the prospect of lost wages, continue to be an important consideration for many adult men. Economic incentives in the form of food vouchers conditional on becoming circumcised were found to beeffective because they partially compensated participants for the transportation and opportunity costs such as lost wages associated with getting circumcised. Many circumcised participants stated the economic incentive was influential because (a) it offset associated costs and increased their willingness to get circumcised; or (b) it 'nudged' them towards doing something that they had previously been intending to do. Moreover, we found that offering even higher amounts could increase male circumcision uptake without being coercive. For the majority who chose not to get circumcised, the incentive amounts were perceived as either being inadequate relative to their expected circumcision-related costs or not addressing their non-economic barriers to VMMC uptake.
Conclusions: This study provides important insights into how economic incentives influence men's decision-making about VMMC. Men explain a detailed thought process by which they weighed the costs and benefits of becoming circumcised and assessed whether the voucher was sufficient to outweigh the costs incurred through loss of income and transportation. The vouchers offered were not effective for addressing all men's concerns and demand generation strategies other than economic incentives are needed to address the array of circumcision-related concerns men have. However, they were an important tool for increasing circumcision uptake among some adult men and warrant further consideration in future VMMC demand creation efforts.

Assessing impact/cost-effectiveness of structural interventions

MOPEC484

Evaluating the impact of health system strengthening on HIV and sexual risk behaviors in Nigeria

G.I. Eluwa[1], S. Adebajo[1], O. Idogho[2], W. Fajemisin[2], J. Anyanti[2]
[1]Population Council, HIV/AIDS, Abuja, Nigeria, [2]Society for Family Health, Garki, Nigeria

Background: Evaluating the impact of health system strengthening on disease and behavior change outcomes provides evidence of returns on investment in health. The Enhancing Nigeria's Response (ENR) to HIV/AIDS project began implementation of a health systems strengthening (HSS) program in seven states in Nigeria in 2008. We evaluated the impact of HSS on HIV prevalence and sexual risk behaviors in the project states.
Methods: Between 2007 and 2012, two rounds of HIV bio-behavioral surveys were conducted in Nigeria and evaluated in a cross sectional analysis. Contiguous states with similar socio-cultural characteristics and no presence of HSS programs (non-HSS) served as comparative groups. Chi-square was used to evaluate differences over time while logistic regression was used to assess the impact of the HSS program on HIV and risk behaviors.
Results: A total of 4,856 and 11,712 respondents were surveyed in 2007 and 2012 respectively with females accounting for 47% and 50% in 2007 and 2012. Overall, change in HIV prevalence between 2007 and 2012 was 6.3% vs. 5.3%(p=0.113) and 3% vs. 5.1% (p<0.001) in the HSS and non-HSS states respectively. Overall change between 2007 and 2012 for HSS and non-HSS states respectively was 19.5% vs. 34.2% (<0.001) and 17.1% vs. 32.8% (p<0.0001) for ever testing for HIV; 4.9% vs. 7.0%(p< 0.001) and 5.0% vs. 4.7%(p=0.545) for comprehensive HIV knowledge; 59.3% vs. 58.7%(p=0.959) and 29.4% vs. 45.2%(p=0.121) for consistent condom use with casual partners; 43.7% vs. 49.2%(p=0.064) and 38.5% vs. 39.7%(p=0.739) for consistent condom use with boy/girlfriends over 12 months. When controlled for age, gender, HSS intervention, location (rural vs. urban) and year (2007 vs. 2012),

respondents in the HSS states were more likely to have comprehensive HIV knowledge(AOR: 1.37;95%CI:1.19-1.56); ever tested for HIV (AOR:1.09;95%CI:1.01-1.17); used a condom consistently in the last 3 months with casual sex partners (AOR:2.22;95%CI:1.26-3.91) and boy/girlfriends (AOR:1.41;95%CI:1.17-1.70). There was no significant difference in HIV acquisition between HSS and non HSS states (AOR:1.11;95%CI:0.93-1.33).

Conclusions: HIV prevalence decreased in HSS states between 2007 and 2012. Respondents in HSS states were more likely to have reduced sexual risk behaviors and increased comprehensive HIV knowledge. There appears to be progress in mitigating the burden of HIV by reduction of HIV-related risk behaviors through HSS. Thus HSS intervention should be sustained to achieve more impact.

MOPEC485

Model the impact of needle and syringe program on HIV incidence: how to gain more

M. Noroozi[1], A. Mirzazadeh[2,3], A. Noroozi[4], Y. Mehrabi[1], A. Hajebi[5], S. Zamani[6], H. Soori[1]
[1]Shahid Beheshti University of Medical Science, Department of Epidemiology, School of Public Health, Tehran, Iran, Islamic Republic of, [2]University of California San Francisco, Global Health Sciences, San Francisco, United States, [3]The Regional Knowledge Hub, and WHO Collaborating Centre for HIV Surveillance, Kerman, Iran, Islamic Republic of, [4]Iranian National Center for Addiction Studies, Tehran University of Medical Sciences, Tehran, Iran, Islamic Republic of, [5]School of Behavioral Sciences and Mental Health, Iran University of Medical Sciences, Mental Health Research Center, Tehran Institute of Psychiatry, Tehran, Iran, Islamic Republic of, [6]The Global Fund to Fight AIDS, Tuberculosis and Malaria, Geneva, Switzerland
Presenting author email: ali.mirzazadeh@gmail.com

Background: Sharing syringes by people who inject drugs (PWID) is an important mode of global transmission of HIV. Since 2002, needle-syringe programs (NSPs) have been one of the core public health strategies aimed at reducing the sharing of syringes in Iran.
However, the impacts of NEPs in developing settings have not systematically studied. The objective of this study is to estimate the impact of NEPs on HIV incidence in PWID in Kermanshah, Iran.

Methods: We used Wilson et al mathematical model to forecast the incident of HIV among PWID with sufficient and insufficient client-level coverage of NSPs. We parameterized and calibrate the model using behavioral and epidemiological data collected in an empirical study of 470 active injecting drug users living in Kermanshah in 2014. Other parameters such risk of HIV transmission per injection with a shared injection, and effectiveness of syringe cleaning were obtained from literature. We applied Monte Carlo simulation (10,000 runs) to capture the uncertainty (simulation interval - SI) in the results given the uncertainty in the parameters.

Results: Given the output of the model, we found that among PWID with sufficient coverage of NSPs the HIV incidence is 1.02%, while in those with insufficient coverage it's increased to 4.04% (risk different = 3%, SI95% 2.7-3.4%). By reducing the percentage of sharing from 18% (in PWID with insufficient NSPs coverage) to 10%, the HIV incidence will be dropped to 0.9% (SI95%, 0.4-1.3%).

Conclusions: We found a large impact of NSPs on reducing the HIV incidence among active drug injectors if they have been provided sufficient needles and syringes. The coverage of NSPs needs to be increased to observe such significant impact.

Gender sensitization, empowerment and violence reduction

MOPEC486

Understanding the violence cycle and the impact of structural interventions reducing different forms of workplace violence perpetrated against female sex workers: implications for HIV prevention

E. Mountain[1], M. Pickles[1], K. Deering[2,3,4], K. Shannon[2,3,4], M.-C. Boily[1]
[1]Imperial College London, London, United Kingdom, [2]University of British Columbia, Division of AIDS, Department of Medicine, Vancouver, Canada, [3]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada, [4]University of British Columbia, School of Population and Public Health, Vancouver, Canada
Presenting author email: elisa.mountain08@imperial.ac.uk

Background: Recent and past exposure of female sex workers (SWs) to workplace violence (e.g. by police, clients) continues to be high and frequent globally, facilitated by criminalization of sex work, stigma and perspectives of SWs as transgressing gender norms. Increasing evidence suggests sexual/physical violence may be associated with lower client condom use and increased HIV risk. Understanding the violence cycle and impact of reducing violence is critical to designing structural HIV interventions to support SWs health and human rights. We assess the impact of violence prevention and influence of violence dynamics on violence outcomes among SWs in Vancouver.

Methods: A dynamical deterministic compartmental model was developed, comprehensively representing multiple violence pathways. We assumed women began sex work without prior experience of workplace violence (police harassment (PH), client physical violence (CPV) or client sexual violence (CSV)). Over time SWs could independently experience different forms of workplace violence multiple times. Data for model parameters came from a community prospective cohort (An Evaluation of Sex Workers' Health Access, 'AESHA'). The model reflected data suggesting increased risks of PH or CSV following CPV (IR_{PH} or IR_{CSV}, respectively), and of CPV following PH (IR_{CPV}) (IR_{PH}=1.3,IR_{CPV}=1.5,IR_{CSV}=5.3). Prevalence of lifetime and recent (last 6 months) PH/CPV/CSV were used for model calibration/validation. We derived relative reductions (RRs) in overall or individual violence prevalence, 3 and 20 years after eliminating different forms of workplace violence, and assessed the influence of IR_{PH}/IR_{CSV}/IR_{CPV} (range explored:1-10) on violence prevalence and intervention impact.

Results: When preventing individual violence types the maximum 3/20-year reduction in lifetime-overall violence prevalence is achieved by eliminating PH (RR=7.9%/20.4%) (Table). Elimination of PH or CPV has the most impact on other outcomes (recent-CPV and lifetime-CSV, respectively) (Table). Variations in IR have the most influence on recent-CPV prevalence at baseline (-17.5%/+120% relative to baseline, IR_{CPV} varied) and recent-CPV prevalence after eliminating PH (absolute change in 20-year RR=-17.0/+44.5, IR_{CPV} varied).

Conclusions: Structural HIV interventions e.g. decriminalizing sex work, that support safer work places for SWs by jointly addressing police harassment and client violence, are critical in reducing overall violence experienced by SWs. Understanding the causal relationship between workplace violence is important for predicting intervention impact.

	Baseline Prevalence among Female Sex Workers (%)					
Scenario	Overall violence, lifetime	Police harassment (PH), lifetime	Client physical violence (CPV), lifetime	Client sexual violence (CSV), lifetime	PH, recent (last 6 months)	CPV, recent (last 6 months)
No Intervention (observed prevalence in AESHA cohort)	70.2	59.3	48.7	42.8	38.1	17.4
	Relative Reduction in Baseline Prevalence after 3/20 years (%)					
Eliminate PH and CPV	12.4/41.4	15.0/62.2	13.4/59.5	3.4/14.1	99.8/100.0	99.8/100.0
Eliminate PH and CSV	10.4/30.6	15.0/62.2	1.2/4.4	13.0/59.0	99.8/100.0	14.4/17.0
Eliminate CPV and CSV	5.7/14.8	15.0/62.2	13.4/59.5	13.0/59.0	2.4/2.9	99.8/100.0
Eliminate PH only	7.9/20.4	15.0/62.2	1.2/4.4	0.4/1.9	99.8/100.0	14.4/17.0
Eliminate CPV only	3.4/7.9	15.0/62.2	13.4/59.5	3.4/14.1	2.4/2.9	99.8/100.0
Eliminate CSV only	5.7/14.8	0.0/0.0	0.0/0.0	13.0/59.0	0.0/0.0	0.0/0.0

[Table: Impact of violence prevention]

Research designs in epidemiology

MOPEC487

What is the effect of including online-recruited seeds within an in-person bio-behavioural study of men who have sex with men (MSM) employing respondent-driven sampling (RDS)?

A. Lal[1], N. Lachowsky[1,2], Z. Cui[1], A. Rich[1], P. Sereda[1], H. Raymond[3], W. McFarland[4], J. Forrest[5], E. Roth[6,7], R. Hogg[1,8], D. Moore[1,2,9]
[1]British Columbia Centre for Excellence in HIV/AIDS Research, Vancouver, Canada, [2]Faculty of Medicine, University of British Columbia, Vancovuer, Canada, [3]University of California San Francisco, San Francisco, United States, [4]San Francisco Department of Public Health, San Francisco, United States, [5]University of British Columbia, Vancouver, Canada, [6]Department of Anthropology, Faculty of Social Sciences, University of Victoria, Victoria, Canada, [7]Centre for Addictions Research BC, Victoria, Canada, [8]Faculty of Health Sciences, Simon Fraser University, Burnaby, Canada, [9]British Columbia Centre for Disease Control, Vancouver, Canada
Presenting author email: alal@cfenet.ubc.ca

Background: Respondent driven sampling (RDS) is an increasingly popular method for recruiting MSM in research. "Seeds" (initial participants) are purposively selected in-person or online and given a determined number of coupons to assist with study recruitment. We aimed to discover differences between:

1) being an online versus in-person recruited seed and
2) being in a recruitment chain started from an online versus in-person recruited seed.

Methods: MSM aged ≥16 years were recruited using RDS from February 2012 to February 2014 to complete a self-administered computer-based survey. Seeds were selected online (e.g., Grindr, social media) or in-person or offline (e.g., community agency, social group). All analyses used RDS weights. Manual backward-stepwise multivariate logistic regression was used to examine factors associated with 1) being an online recruited seed versus not and 2) being in a recruitment chain started from an online seed versus not.

Results: Of 119 seeds, 85 were recruited online (71.4%). Most of these seeds cited the following reasons for wanting to participate: help the community (33.6%), interested in sexual health and HIV (29.4%), and interested in gay men's issues (19.3%). Online-recruited seeds were more likely to not attend gay specific groups in the past six months (adjusted odds ratio, AOR=3.02 with [95% Confidence Intervals 1.11-8.20]), attended the pride parade versus not going (AOR=6.30[1.69-23.45]), use apps to seek sex in the past 6 months versus not (AOR=4.29[1.53-12.05]), to not find it important to be involved in the gay community versus finding it very important (AOR=6.13[1.07-34.48]), and asking a partner's HIV status 100% of the time versus less than 50% of the time (AOR=5.21[1.17-23.23]). Of 600 non-seeds that were recruited, 283 were recruited from an online seed (47.2%). Online seed chains were more likely to be negative versus positive (AOR=4.00[2.53-6.33]), have been out for 11-21 versus 1-4 years (AOR=2.22[1.27-3.88]), have 201-500 Facebook friends versus >500 (AOR=1.69[1.02-2.80]), prefer to bottom versus being versatile (AOR=1.80[1.14-2.84]), and to be in a relationship lasting >1 year versus being single (AOR=1.65[1.06-2.56]).

Conclusions: While offline seeds were more productive recruiters, electronic innovations in RDS produce a diverse set of seeds that recruit chains that differ from in-person and offline recruited seeds.

Research designs in prevention research

MOPEC488

Implementing electronic coupons within respondent-driven sampling (RDS) to improve recruitment of men who have sex with men (MSM) in Vancouver, British Columbia

R.S. Sankey[1], A. Lal[1], N. Lachowsky[1,2], Z. Cui[1], A. Rich[1], P. Sereda[1], H. Raymond[3], W. McFarland[4], J. Forrest[5], E. Roth[6], R. Hogg[1,7], D. Moore[1]
[1]British Columbia Centre for Excellence in HIV/AIDS Research, Vancouver, Canada, [2]Faculty of Medicine, University of British Columbia, Vancouver, Canada, [3]University of California, San Francisco, United States, [4]San Francisco Department of Public Health, San Francisco, United States, [5]University of British Columbia, Vancouver, Canada, [6]Department of Anthropology, Faculty of Social Sciences, University of Victoria, Victoria, Canada, [7]Faculty of Health Sciences, Simon Fraser University, Burnaby, Canada
Presenting author email: alal@cfenet.ubc.ca

Background: Respondent driven sampling (RDS) has been utilized in HIV research for selecting and connecting with under-represented communities like men who have sex with men (MSM). Conventionally, "seeds", primary participants, are elected in-person and equipped with a selected number of vouchers via email or paper to continue recruitment. The objective of this study was to explore the impact of online and electronic RDS innovations on differences between MSM who redeemed electronic versus paper coupons.

Methods: Participants were MSM aged ≥16 years, recruited using RDS from February 2012 to February 2014 to complete a self-administered computer-based survey. Seeds were selected online (e.g., Grindr, social media) or offline (e.g., community agency, social group) and recruitment coupons were electronic or paper. All analyses used RDS weights. Manual backward-stepwise multivariate logistic regression was used to examine factors associated with redeeming an electronic versus paper coupon.

Results: Of 596 participants recruited from seeds into the study, 93 redeemed electronic coupons (15.6%) and the remaining 503 redeemed paper coupons. Men who redeemed online coupons were more likely to be within a recruitment chain started by an online seed (91.4%) compared with men who redeemed paper coupons (84.4%; odds ratio (OR)=1.97 95% Confidence Interval: 1.18, 3.27). MSM who redeemed an electronic coupon were more likely to be currently employed versus not (adjusted odds ratio, AOR=3.10 with [95% Confidence Interval 1.46-6.59]), to be homeless versus stably housed (AOR=6.48[1.39-30.25]), to have come out as gay more recently (e.g., within 1-4 years versus 11-21 years, AOR=2.53[1.10-5.81]), to be out at work versus not (AOR=3.88[1.44-10.45]), to be out to their male guardian versus not (AOR=2.53[1.14-5.62]), to prefer not to have anal sex versus receptive anal sex (AOR=4.97[1.37-18.01]), to be in a relationship ≥1 year versus < 1 year (AOR=3.00[1.12-8.00]), to ask partner's HIV status < 50% of time versus >50% of time (AOR=2.11[1.03-4.33]).

Conclusions: Participants recruited through electronic vouchers vary on some socio-demographic factors and appear to have different connections to gay identities and communities than those recruited in person. This electronic recruitment innovation parallels changes in online gay communities and MSM networking, and allows for a more diverse sample.

MOPEC489

Effect of antiretroviral therapy on diarrhoea incidence and stool pathogens among HIV-infected individuals in rural Uganda: a prospective population-based cohort study

L. Disan
Community AIDS Care, Outreach, Masulita, Uganda
Presenting author email: lubwamadisan@gmail.com

Background: Diarrhoea is a common problem in people with untreated HIV infection, especially with increasing immunosuppression. We examined the effect of ART on diarrhea and stool pathogens among HIV-infected individuals in rural Uganda.

Methods: In a cohort of HIV-infected and uninfected participants followed from 2005-09, stool microscopy (modified Ziehl Neelsen stain) was done at quarterly visits and whenever participants presented with diarrhoea, and diarrhoea samples were cultured. HIV-infected participants had regular CD4 cell count measurements.
We identified pathogens and compared diarrhoea incidence in three groups of participants; HIV-uninfected, HIV-infected not yet on ART, and those on ART. Random effects Poisson regression models were used to account for repeated events and adjustment: made for covariates (HIV and ART status).

Results: 282 diarrhoea events occurred: 28 among 205 HIV-uninfected, 127 among 262 HIV-infected not yet on ART and 97 among 283 HIV-infected on ART. 44 events (15.6%) yielded pathogens and 95 (33.7%) yielded non-pathogenic organisms. The proportions of participants with pathogenic and non-pathogenic organisms were highest among HIV-infected individuals not on ART. The commonest pathogens (number of isolates) were: Giardia lamblia (22), Shigella (13) and cryptosporidiosis (4).
Pathogens (number of isolates) isolated from HIV-infected individuals not yet on ART were G. lamblia (13) and Shigella (9), and among individuals on ART were G. lamblia (8) and Shigella (2).
Compared with an incidence of 0.50 per 100 pyr [95%CI 0.20,1.40] among HIV-uninfected participants, diarrhoea incidence was modestly increased among HIV-infected individuals on ART for upto 2 years (aRR 2.37 [95%CI 0.68, 8.24]) and much higher among not yet on ART (adjusted rate ratio [aRR] 8.51[95%CI 2.89, 25.07]). Diarrhoea incidence was higher at CD4 cell counts less than 250 (p< 0.001).

Conclusions: Pathogenic and non-pathogenic organisms were most commonly isolated from HIV-infected individuals not yet on ART. ART reduced the risk of HIV-related diarrhea.

MOPEC490

A comparison of strategies to recruit Black men who have sex with men with undiagnosed HIV infection and/or unsuppressed viral load

J. Franks[1], S. Mannheimer[1,2,3], Y. Hirsch-Moverman[3,4], E. Hayes-Larson[3,4], P.W. Colson[1,3], W.M. El-Sadr[3,4]
[1]ICAP at Columbia University, Harlem Prevention Center, New York, United States, [2]Harlem Hospital Center, New York, United States, [3]Columbia University Mailman School of Public Health, Department of Epidemiology, New York, United States, [4]ICAP at Columbia University, New York, United States
Presenting author email: jf642@cumc.columbia.edu

Background: HIV prevalence among US Black men who have sex with men (BMSM) is nearly 4-fold higher than among White MSM and evidence suggests that BMSM are less likely to be aware of HIV infection and to be in care. Identifying effective strategies to find such individuals are a national priority. We compared the effectiveness of respondent-driven sampling (RDS), community-based (CB), web-based (WB), and hybrid (HYB) recruitment methods to identify BMSM with undiagnosed HIV and/or unsuppressed HIV infection.

Methods: From July 2012 to December 2014, RDS (a chain referral sampling method in which participants receive incentives for recruiting members of their social networks) was used to enroll BMSM at risk for HIV infection in a study of testing, linkage, and retention in care. RDS was supplemented with CB outreach and WB recruitment beginning in August 2013. All participants enrolled through CB and WB methods were offered incentives to recruit their associates via RDS; these enrolled associates are referred to as HYB-CB and HYB-WB, respectively. Rapid HIV testing was done; participants with reactive tests had confirmatory testing and HIV RNA viral load measured. Participants with viral load < 200 copies/mL were considered virally suppressed (VS). Associations were tested using Chi-square, Fisher's exact, and Wilcoxon rank-sum tests.

Results: 1552 eligible BMSM were enrolled and tested for HIV over 29 months. Median age was 43 years; 27% of participants were Latino, 3% transgender and 63% identified as bisexual. Overall, 7% were HIV-infected. HIV infection was associated with recruitment method, with highest prevalence among those recruited via HYB-WB, albeit with low yield (p=< .001), younger age (p=.041), being transgender (p=.002), homosexual/gay identity (p=< .001), and more than high school education (p=.019). Of HIV-infected participants, 48% were VS at enrollment. There was no significant difference in VS by recruitment method (p=0.369) (see table).

Variable, n (%)	Total (N=1,552)	RDS (N=641)	CB (N=261)	HYB-CB (N=608)	WB (N=31)	HYB-WB (N=11)
Positive HIV rapid test*	107 (6.9%)	24 (3.7 %)	23 (8.8%)	48 (7.9%)	6 (19.4%)	6 (54.5%)
Virally suppressed (among HIV+)†‡	46 (48.4%)	6 (33.3%)	9 (39.1%)	25 (56.8%)	3 (60.0%)	3 (60.0%)
Age, median (IQR)	43 (29-49)	42 (30-49)	34 (23-46)	45 (35-51)	30 (26-46)	29 (24-40)
Latino‡	414 (26.7%)	185 (28.9%)	70 (26.8%)	153 (25.2%)	5 (16.1%)	1 (9.1%)
Transgender	50 (3.2%)	18 (2.8%)	19 (7.3%)	13 (2.1%)	0 (0.0%)	0 (0.0%)
Bisexual Identity‡	938 (62.8%)	414 (67.3%)	147 (58.8%)	364 (62.0%)	9 (29.0%)	4 (36.4%)
Homosexual Identity‡	354 (23.7%)	111 (18.0%)	77 (30.8%)	142 (24.2%)	17 (54.8%)	7 (63.6%)
Heterosexual Identity‡	202 (13.5%)	90 (14.6%)	26 (10.4%)	81 (13.8%)	5 (16.1%)	0 (0.0%)

*p<0.001; †p=0.369; ‡ percentages exclude participants with missing data (viral suppression n=12, Latino n=1, and sexual identity n=58).

[HIV Status and Characteristics of Participants]

Conclusions: CB and HYB-CB identified more BMSM with HIV infection than RDS or WB. VS at enrollment was high across recruitment strategies, suggesting need for additional approaches to find BMSM with undiagnosed HIV and/or unsuppressed HIV infection, a critical group to engage in care for individual clinical benefit and to prevent further transmission of HIV.

MOPEC491

Estimating the population-level impact of methamphetamine use on HIV acquisition among men who have sex with men using population attributable risk percent: a powerful and underused planning tool

S. Buskin[1,2], J. Hood[1,2], D. Katz[1,2], R. Burt[1], J. Chipps[1], K. Gardner Toren[1], J. Dombrowski[1,2]
[1]Public Health - Seattle & King County, Seattle, United States, [2]University of Washington, Seattle, United States
Presenting author email: susan.buskin@kingcounty.gov

Background: HIV prevention funding is increasingly data driven as HIV epidemiologists help guide local prevention efforts. Informed allocation of HIV prevention funding-- assuming effective and cost-effective strategies exist - hinges on: 1) the size of the population and 2) the relative risk of HIV in that population. One epidemiology measure takes both of these factors into account: population attributable risk percent (PAR%; etiologic fraction). To illustrate its use, we calculated PAR% for methamphetamine use among men who have sex with men (MSM) in King County (KC), Washington.
Methods: We used data from multiple sources, including the National HIV Surveillance System (NHSS), National HIV Behavioral Surveillance (NHBS), Seattle Gay Pride survey, and the KC STD Clinic. We defined the number of MSM at risk of acquiring HIV as: the number of male KC residents 15 years and older times 0.054, minus the number of MSM living with HIV (Table). Data on methamphetamine use were available from NHSS and STD Clinic patients recently diagnosed with HIV. Gay Pride, STD Clinic, and NHBS data provided age-standardized estimated of the proportion of HIV-uninfected MSM who used methamphetamine in the last year. PAR% was calculated as [the estimated population incidence minus the estimated incidence in non-methamphetamine-users] divided by the estimated population incidence.

Summary of Methods to Estimate the Population Attributable Risk % Corresponding to Methamphetamine Use among MSM and Risk of HIV Acquisition

	Number	Percent
# 2013 HIV diagnoses in men who have sex with men (MSM)	179	
# Prevalent MSM with diagnosed HIV infection (PLWHA) in 2013	5,582	
# of men (15 years+) living in King County in 2013 (based on census data)	803,277	
Percent of men (15 years+) who are MSM (from Purcell et al. (2012), midpoint between 5 year and lifetime recall)	5.4%	
Estimated # MSM in King County (5.4% × 803,277)	43,377	
Estimated # MSM in King County without an HIV diagnosis	37,795	
Estimated Population MSM HIV incidence 2013 {(179/37,795)× 100,000}	**474**	
Age-Standardized percent of HIV-negative MSM reporting methamphetamine use (last 12 months), by data source:		
2014 Pride Survey		3%
STD Clinic patient intake form		6%
National HIV Behavioral Surveillance		10%
Percent of MSM recently diagnosed with HIV reporting methamphetamine use in the past 12 months, by data source and assumptions:		
HIV Surveillance with missing values set to 'No Meth Use'		23%
STD Clinic patients with incident HIV infection		25%
HIV Surveillance with missing values excluded		28%
Percentages Simulated through Latin Hypercube Sampling		
% of newly diagnosed HIV cases NOT reporting recent methamphetamine use		75%
% of HIV-negative MSM NOT using methamphetamine in prior 12 mos		94%
Estimated HIV Incidence among MSM not using methamphetamine =(179 × .75)/(37795 × .94)	**377**	
PAR% for MSM [$PAR\% = \{[474 - 377]/474\} \times 100$]		**20%**
PAR% Overall [PAR% for MSM × % of new cases that are MSM]		**17%**

[Methods for Population Attributable Risk Percent]

Results: The overall 2013 incidence of HIV among MSM was 474 per 100,000 people at risk. The estimated incidence of HIV for methamphetamine users (25% of recent HIV infections) was 1,984 per 100,000. Among MSM who did not report using methamphetamines in the last year, HIV incidence was estimated as 377 per 100,000 (relative risk = 5.3; 95% CI = 3.7 - 7.3). Estimates of methamphetamine use among HIV negative MSM ranged from 3% (Gay Pride) to 10% (NHBS). These led to an estimated PAR% of 20%. With 87% of KC HIV diagnoses occurring among MSM, we estimate that methamphetamine use among MSM might be associated with 17% of HIV infections.
Conclusions: Methamphetamine use contributes substantially to ongoing HIV transmission among MSM in KC. HIV prevention programs might consider incorporating PAR% for prevention decisions. KC HIV prevention will benefit from methamphetamine prevention and harm reduction interventions.

MOPEC492

Cohort study as a comprehensive approach to evaluate the impact of HIV prevention interventions on risk behavior change and HIV seroconversion among PWIDs in Ukraine

M. Samko[1], K. Dumchev[2], J. Barska[1]
[1]International HIV/AIDS Alliance in Ukraine, Kiev, Ukraine, [2]Ukrainian Institute on Public Health Policy, Kiev, Ukraine
Presenting author email: mariya.samko@gmail.com

Background: HIV prevention program among PWIDs has been implemented in Ukraine since 2004. 60% PWIDs of 310,000 estimated are covered annually with prevention services. The comprehensive HIV prevention package includes condoms and syringes provision, medical/social specialist counseling, informational-educational activities, HIV, HCV and STI testing. So far, no study on impact of available prevention activities on HIV incidence among PWIDs has been done in Ukraine.
Methods: The study is a 2-year research which implies a combination of retrospective analysis of programmatic data and prospective multi-center cohort study conducted in 11 randomly chosen cities, which represent regions with all levels of HIV prevalence among PWIDs. A cohort of 2,200 PWIDs HIV-negative, who are clients of HIV prevention program, was recruited by using respondent-driven sampling.
HIV incidence and risk behavior change are the main study outcomes, measured at baseline and every 6-month follow-ups by using interviews and HIV rapid tests which will be confirmed with additional lab assays on dry blood spot samples.
Data, collected within the cohort study, is linked to programmatic data collected with a help of SYREX database which tracks each client and services s/he received for the analysis.
The impact will be assessed in both retrospective and prospective part using time-to-event statistical methods bases on frequency of services utilization by clients.
Results: The preliminary analysis of the prospective data showed that out of 2143 PWIDs covered with HIV prevention packages, 28 PWIDs seroconverted within first 6-months and additional 16 new HIV cases were detected in the 12-months follow-up. All new cases are associated with risky injection behavior during the last injection 3.6% vs 1.9% (p< 0.001) and during last 30 days 6.5% vs 10.7% (p< 0.01).
Retrospective data analysis identified five main patterns of services utilization: occasional clients, minimal package clients, regular testers, regular clients and secondary exchangers.
Conclusions: The study documents the impact of available prevention services on risk behavior change and HIV incidence in the prospective cohort of PWIDs in Ukraine. This will, for the first time, enable to make an evidence-based decision with regard to the most effective activities to be included into the National AIDS Programme.

Ethical and human rights issues in prevention research

MOPEC493

Barriers to and strategies for reducing the length of informed consent forms in HIV prevention research

A. Corneli[1], E. Namey[1], M. Mueller[1], T. Grey[1], J. Tharaldson[1], K. Mckenna[1], J. Sugarman[2]
[1]FHI 360, Durham, United States, [2]Johns Hopkins University, Baltimore, United States
Presenting author email: acorneli@fhi360.org

Background: Sufficient understanding of a research study is necessary for potential research participants to make informed decisions about enrolling. Yet, long informed consent forms (ICFs), which are commonplace in HIV-related research, are a barrier to understanding research and place an unnecessary burden on both potential participants and study staff. Limited data are available on barriers to and strategies for reducing the length of ICFs in HIV prevention research.

Methods: We partnered with two active HIV prevention studies within the HIV Prevention Trials Network (HPTN) to identify barriers to and strategies for reducing ICF length. We conducted 100 in-depth interviews with a variety of key stakeholders: HPTN research participants (n=42); HPTN study chairs, core staff, site investigators, and site staff (n=20); community representatives (n=11); representatives of the Division of AIDS at the National Institutes of Health (n=9); officials at institutions where HPTN research is conducted (n=6); and members of institutional review boards that review HPTN research (n=12). The data were analyzed using qualitative thematic analysis.
Results: Legal concerns were the most common barrier mentioned, followed by habit or reluctance to challenge the status quo, and then by a sense of duty to provide sufficient information. Stakeholders also described how multiple groups — institutions, agencies, and institutional review boards — must review, come to consensus on, and approve the language included in ICFs, while ensuring that their separate ICF template language remains intact. Several strategies were identified to reduce ICF length, such as reducing repetition, removing superfluous information, grouping study procedures by visits, simplifying the listing of risks, and placing reference-type information in appendices.
Conclusions: Multiple barriers limit the use of shorter ICFs in HIV prevention research. Identifying these barriers and building awareness of them among key stakeholders should facilitate dialogue on implementing the suggested strategies to reduce ICF length. In the next phase of the research, stakeholders will review findings from the initial in-depth interviews and reach consensus on recommendations for reducing ICF length through a series of online surveys. Findings from this research will be used to advance the use of shorter ICFs in HIV-related research.

Estimation of the size of HIV-infected and key populations

MOPEC494

Adjustment of HIV prevalence in men who have sex with men to account for changes in networking pattern following diagnosis

C.M. Poon[1], N.S. Wong[2], S.S. Lee[2]
[1]Chinese University of Hong Kong, Jockey Club School of Public Health and Primary Care, Hong Kong, Hong Kong, [2]Chinese University of Hong Kong, Stanley Ho Centre for Emerging Infectious Diseases, Hong Kong, Hong Kong
Presenting author email: steven_poon@cuhk.edu.hk

Background: HIV prevalence of men who have sex with men (MSM) at community level is often determined by surveys conducted at specific venues. This approach is based on the assumption that MSM's frequency of visiting social venues for sex-networking is independent of one's HIV status. The validity of such assumption is questionable as sex-networking behaviours may change following HIV diagnosis. This study aims to assess the changes of sex-networking patterns among MSM following HIV diagnosis and assess its impact on estimating the HIV prevalence of MSM population.
Methods: A venue-based survey in 2011 gave an HIV prevalence of 4.08% among MSM in Hong Kong. Separately, data on the use of local bars, saunas and beaches for sex-networking among HIV-infected MSM were collected from a cross-sectional questionnaire survey, which was conducted at the largest HIV specialist clinic in Hong Kong between October and December 2014. The post-diagnosis sex-networking patterns were used to estimate the relative size of MSM populations in different social venues and adjust the result of the previous prevalence study.
Results: Out of 345 recruited MSM, 153 were diagnosed in or before 2010. Of these, 62.1%, 76.4% and 54.2% had visited local bars, saunas and beaches for sex-networking respectively before their HIV infection status was known, while the corresponding figures in 2011 had fallen to 23.5%, 54.2% and 22.2%. The ratio of the size of MSM networked through local bars, saunas and beaches was estimated at 1:1.13:0.49. The adjusted HIV prevalence would be 4.56% after accounting for the differential usage of social venues for sex-networking among HIV-infected MSM.
Conclusions: Since a proportion of MSM is likely to avoid social venues after their diagnosis of HIV infection, sampling bias might be introduced in venue-based subject recruitment for HIV prevalence studies. Thus, HIV prevalence derived from venue-based surveys has to be adjusted by the degree of venue attendance among HIV-infected MSM. The ever-changing sex-networking pattern among HIV-infected MSM also deserves monitoring for assessing its long-term impacts.

MOPEC495

Estimating the population size of injection and non-injection drug users along the coast and in other regions of Tanzania 2013/2014

J.N. Joel[1], A. Msami[2], Y.I. Laurent[2], S. Mwankemwa[2], M. Makumbuli[2], A. Ngonyani[2], E. Matiko[3], J. Tiberio[4], S. Welty[4], W. Mc Farland[4]
[1]Global Programs, Dar es Salaam, Tanzania, United Republic of, [2]Drug Control Commission, Dar es Salaam, Tanzania, United Republic of, [3]CDC-Tanzania, Dar es Salaam, Tanzania, United Republic of, [4]University of California, San Francisco, United States
Presenting author email: j_ndayongeje@hotmail.com

Background: People who use (PWUD) and inject (PWID) drugs are at higher risk for acquiring and transmitting HIV through sexual and injection behaviors. Injection and non-injecting drug use is thought to be spreading in parts of sub-Saharan Africa; however, very little is known about the scope of drug use in regions of Tanzania outside Zanzibar and Dar es Salaam. From 2013-2014, we conducted a rapid assessment to identify drug-use hotspots and estimate the number of PWUD/PWID in 12 regions of Tanzania (Mtwara, Dodoma, Morogoro, Pwani, Kilimanjaro, Arusha, Tanga, Mbeya, Mwanza, Geita, Shinyanga, Kigoma).
Methods: To estimate the locations of drug use and the number of PWUD/PWID in each region, we triangulated data through:
(1) key informant interviews with PWUD, PWID, community members, government officials, and health care providers;
(2) population size estimation using Wisdom of the Crowds, mapping enumeration, and modified Delphi; and
(3) drug use hotspot location with GPS. Data collection and synthesis occurred successively within each region in a robust, iterative process.
Results: Of 436 key informants interviewed, 75% were PWUD/PWID, 9% police officers, 5% health care providers, and 11% community leaders and service providers overall. Illicit drug use occurred in all regions, with regional differences in the number of PWUD/PWID (table 1). Mtwara had the smallest number of PWUD at 65 (35 - 150), with few PWID and no females. Tanga had the largest number of PWUD and PWID, followed by Mwanza and Arusha. Mwanza, Tanga, and Arusha had the largest numbers of female PWID.
Conclusions: We found drug use in all twelve regions which highlights the need to develop substance use prevention and harm reduction services in a timely manner to protect these populations from adverse health outcomes including HIV. Our study serves as a foundation for understanding the nature of the drug use epidemic throughout a wide area of the nation. Data can inform geographic targeting of HIV prevention and care interventions and provide a sampling frame with points of access to the population's future research.

REGION	PWUD (Males)	PWUD (Females)	PWID (Males)	PWID (Females)
Tanga	5000 (3000-7000)	190 (120-400)	475 (300-600)	65 (40-100)
Mwanza	2800 (1500-4000)	500 (300-800)	250 (180-400)	50 (30-80)
Arusha	2500 (1000-5000)	200 (70-300)	175 (80-300)	55 (30-110)
Pwani	1475 (1000-2700)	64 (43-117)	150 (50-250)	14 (5-23)
Morogoro	1250 (750-1800)	250 (150-360)	260 (180-500)	37 (26-71)
Dodoma	913 (460-1600)	183 (92-320)	100 (50-130)	33 (17-43)
Mbeya	775 (500-1200)	45 (30-60)	55 (40-70)	9 (5-15)
Kilimanjaro	450 (200-650)	113 (50-163)	80 (55-125)	27 (18-42)
Shinyanga	308 (140-410)	11 (6-30)	25 (12-35)	-
Kigoma	100 (50-150)	-	-	-
Geita	95 (50-120)	13 (5-20)	3 (0-10)	-
Mtwara	65 (35-150)	0 (0-1)	7 (2-10)	0 (0-0)

[Estimated number of PWUD and PWID, by region]

MOPEC496

Using GPS data to uncover a "hidden" HIV epidemic

B. Coburn, J. Okano, S. Blower
UCLA, Semel Institute for Neuroscience and Human Behavior, Los Angeles, United States
Presenting author email: jokano@ucla.edu

Background: Treatment-as-prevention (TasP) is being considered as a global policy to control the HIV pandemic. To implement the rollout of TasP in an efficient manner, it is essential to estimate the number of HIV-infected individuals and where they live. Here we show how to solve this problem by using geospatial statistical techniques and global positioning (GPS) data for Lesotho, which has one of the most severe HIV epidemics worldwide (prevalence 24%).
Methods: We used HIV prevalence data collected in the 2009-10 Lesotho Demographic and Health Survey (GPS data based on geographic cluster sampling) and geographic population data from WorldPop (raster image data based on settlement mapping and satellite imagery data) to estimate the number of HIV-infected individuals and where they live throughout Lesotho. We use geostatistical methods (e.g., adaptive bandwidth kernel density estimation and ordinary kriging) to map prevalence and the density of infection throughout the country.

Results: The predictive map shows that prevalence is high (on average >20%) throughout Lesotho, but that prevalence varies substantially with geography (ranging from 5% to 45%). We found prevalence was higher for women than in men almost everywhere. We found substantial geographic variability in prevalence for both genders. We mapped the density of infection at a resolution of 100 m. We found that the geographical distribution of HIV-infected individuals and the density of infection; density ranges from 600 HIV-infected individuals per km² to less than 5 HIV-infected individuals per km². We used this map to determine the specific location of approximately 188,000 HIV-infected individuals aged 15 to 49 years old that live throughout Lesotho.
Conclusions: Our geospatial approach is an effective tool that could be used to find HIV-infected individuals in high-prevalence epidemics, establish where they live, and estimate the burden of disease. To maximize efficiency and cost-effectiveness, we recommend that geospatial approaches should be used in decisions about how to roll out TasP and other public-health interventions in sub-Saharan Africa.

MOPEC497

Unblocking the hurdles to key populations size estimations and effective service delivery among such groups: a study in response to effective planning for key populations in East Central Uganda

D. Businge[1,2], S. Kironde[3], A. Mugume[4], M. Osborne-Smith[5]
[1]JSI Research & Training Institute/STAR-EC, Strategic Information, Jinja, Uganda, [2]Strengthening TB and HIV Responses in East Central Uganda, Strategic Information, Jinja, Uganda, [3]JSI Research & Training Institute, AIDS Free, Washington DC, United States, [4]JSI Research & Training Institute Inc./STAR-EC, Jinja, Uganda, [5]JSI Research & Training Institute Inc., International Division, Boston, United States
Presenting author email: dbusinge@starecuganda.org

Background: STAR-EC is a USAID supported program implemented by JSI and covering three million people in East-Central Ugandan region. About 20% of fisher-folk who are part of Key Populations (KPs) in the region are HIV positive -a far higher prevalence compared to 5.8% (regional average). KPs are therefore increasingly being targeted under the national HIV response. However, there is absence of national census data and limited strategic-information on key population size, locations and characteristics. In 2012, a study was conducted to fulfil the aforementioned and enhance realistic targeting, planning and response to needs of such groups that are the highest nexus of new HIV infections.
Methods: Quantitative methods were used through a descriptive-cross-sectional study. Methods and procedures varied according to the uniqueness of each target-population. They included: physical counts, register review, snow balling and individual survey enumeration matrices while geographical-coordinate systems were used to generate maps illustrating hotspots. Additionally, qualitative methods such as key-informant interviews, focus group discussions and observations were used in triangulation and enhancing validity of quantitative results. After estimating target groups, community service agents, peers and health-workers were used to implement tailored interventions that addressed their unique-needs.
Results: A total of 82,339 KPs (78.2%males, 21.8%females; and 10.4% HIV+) were estimated from predominately identified KP groups representing 3% of regional population. Among these were: 1,497 sex workers majority aged 15-40 years operating in urban areas; 63,640 highly mobile fishing community population with spouses at different landing sites *(489 lodge based);*2,000 uniformed service personnel characterized with transactional nearby community sexual-contacts; different nationalities of truckers and their assistants (321 per night) formed the key customers of sex-workers at hotspots, 2,201 plantation-workers (mainly migrants) while 12,680'*bodaboda'*motorcyclists mainly aged 15-35 years were identified among emerging groups.Within one year of implementation, 70,473 (86%) KPs were reached with different HIV prevention and care services.
Conclusions: Improved and successfully targeted interventions are achievable once population estimation and characteristics of such complex groups (KPs) is established. There's a huge youthful-population of '*bodaboda' motorcyclists* whose characteristics typify them as emerging-KPs and should be increasingly targeted with interventions. Some KP groups characterized with spatial-population-distribution can be estimated and at lower costs.

MOPEC498

Estimating the size of the MSM population using multiple methods and data sources in Vancouver, British Columbia

N. Lachowsky[1,2], A. Rich[1], Z. Cui[1], N. Oliveira[1], G. Colley[1], P. Sereda[1], J. Wong[3], S. Wong[3], A. Lal[1], J. Jollimore[4], E. Roth[5,6], R. Hogg[1,7], D. Moore[1,2,3]
[1]British Columbia Centre for Excellence in HIV/AIDS Research, Vancouver, Canada, [2]Faculty of Medicine, University of British Columbia, Vancovuer, Canada, [3]British Columbia Centre for Disease Control, Vancouver, Canada, [4]Health Initiative for Men, Vancouver, Canada, [5]Department of Anthropology, Faculty of Social Sciences, University of Victoria, Victoria, Canada, [6]Centre for Addictions Research BC, Victoria, Canada, [7]Faculty of Health Sciences, Simon Fraser University, Burnaby, Canada
Presenting author email: dmoore@cfenet.ubc.ca

Background: Lack of a reliable population size estimate of men who have sex with men (MSM) impedes research and epidemiologic depictions of the HIV epidemic.
Methods: We estimated the Metro Vancouver MSM population size drawing on four data sources: Momentum Health Study cross-sectional questionnaire of MSM aged >15 years recruited from February 2012 - February 2014 using respondent-driven sampling, British Columbia Centre for Disease Control's HIV testing data from February 2012 - February 2014 for three MSM-specific/popular sexual health clinics, the 2011-2012 Canadian Community Health Survey (CCHS) administered by Statistics Canada, and Facebook (social networking site). Estimates were calculated using the indirect method ($N=n/p$), where N is the population estimate, n is the number of MSM in the group (e.g., number of MSM-identified tests at a particular sexual health clinic, number of Facebook profiles indicating "men interested in men") and p is the proportion of the Momentum Health Study participants self-reporting such membership (e.g., having tested at that clinic in the past 2 years, having a current Facebook profile). Estimates using HIV testing site data were adjusted by average number of tests in the past two years reported by Momentum respondents. *'Wisdom of The Crowds'* (WOTC) method was used to produce an additional point estimate based on Momentum participants' estimates of the local MSM population.
Results:

Data Source & Method	Estimate	Notes
WOTC	45,800	"To the best of your knowledge, how many men who have sex with men, whether they identify as gay or not, do you think live in the Greater Vancouver region?"
Facebook	23,700	Data from Facebook required user profiles to include personal gender identity and preferred gender of partners
Sexual Health Clinic HIV Testing Data, Average, adjusted	44,300	Adjusted for the average number of tests Momentum participants reported on average in the past 2 years
Canadian Community Health Survey (CCHS) 2011-2012	22,100	Required disclosure of sexuality on government-sponsored, interviewer-administered questionnaire

[Table 1. Population estimates by data source]

Table 1 presents the range of population estimates. CCHS and Facebook data sources resulted in the lowest population estimates (22,100 and 23,700 respectively), but required more public disclosure of one's sexuality. Similar estimates, but nearly twice the size, were produced using HIV testing data and the WOTC method (44,300 and 45,800 respectively). The 2011 Vancouver census male population aged 15+ was 948,010, resulting in MSM prevalence estimates ranging from 2.3-4.8%. This estimated range is similar to what the US-CDC reports for the US.
Conclusions: Using multiple data sources, our estimates of the Metro Vancouver MSM population (22,120-45,800 or 2.3-4.8% of the metropolitan male population) are similar to estimates in other jurisdictions. These findings will help support better epidemiologic understanding of the HIV epidemic among MSM as well as policy, prevention, and care program decision-making.

Methodological challenges to scale up and optimization of services

MOPED681

Survey of healthcare professionals on the role of pharmacists in an outpatient HIV clinic setting

A. Wong[1], P. Giguère[2], L. Robinson[3], D. Martel[4], J. Toy[5], L. Sulz[6], N. Sheehan[7], B. Lemire[7], M. Foisy[8]
[1]McGill University Health Centre, Montreal, Canada, [2]The Ottawa Hospital, Ottawa, Canada, [3]Windsor Regional Hospital, Windsor, Canada, [4]Centre Hospitalier de l'Université de Montréal, Montreal, Canada, [5]St. Paul's Hospital, Vancouver, Canada, [6]Regina General Hospital Regina Qu'Appelle Health Region, Regina, Canada, [7]McGill University Health Centre, Pharmacy, Montreal, Canada, [8]Northern Alberta HIV Program, Alberta Health Services, Edmonton, Canada
Presenting author email: alisonyijinwong@gmail.com

Background: Pharmacists play a variety of roles in the interdisciplinary care of HIV-infected patients. The objective of this study was to describe how HIV healthcare professionals perceive the relative importance of pharmacist activities and compare pharmacists' perception to the other disciplines.
Methods: A descriptive cross-sectional survey was developed and sent to Canadian HIV practitioners involved in interdisciplinary teams, including pharmacists, physicians, nurses, etc. Data was collected anonymously in Fluid Survey™, a secure online survey tool, using a snowball sampling technique.
Results: Of the estimated 335 emails requesting participation, 95 participants completed the survey (response rate of 28%). Of the 53 criteria, 19 (36%) were characterized as "very important" by more than 50% of respondents. There was a high level of agreement between pharmacists, physicians and nurses on the top 5 most important pharmacist activities requiring patient referral: evaluation of patients on complex treatments, counselling for initiation in ARV therapy, assessment of drug interactions, counselling for change in ARV therapy and patient assessment for recommendations to change ARV therapy; the latter was considered less important by physicians (ranked 8th), whereas assistance in securing drug coverage was rated higher (ranked 3rd). When examining important patient characteristics requiring pharmacy referral, there was a high level of agreement between pharmacists and nurses who ranked compromised organ function, peri-organ transplant, malignancies requiring therapy and pregnancy as highest priority; pharmacists also identified paediatrics (ranked 1st) whereas nurses added the presence of multiple co-morbidities (ranked 4th). Physicians rated paediatrics, pregnancy, no legal status in Canada, refugee status and hospitalization as the 5 most important criteria. Despite the fact that 53% responded that a screening tool would not help identify at risk patients, 75% of respondents agreed that a short and simple screening tool could be easily implemented into clinical practice.
Conclusions: A large variety of pharmacist activities were considered "very important" by the majority of participants. The different perceptions of the role of a pharmacist in the care of HIV patients warrants the development of a short, simple screening or referral tool to identify patients most likely to benefit from a pharmacist consult.

MOPED682

Perspectives of HIV-infected adolescents on disclosure of HIV status in Western Kenya

C. McAteer[1,2], L. Fischer[1,2], W. Nyandiko[2,3], M. Scanlon[1,2], I. Marete[2,3], R. Vreeman[1,2,3]
[1]Indiana University School of Medicine, Pediatrics, Indianapolis, United States, [2]Academic Model Providing Access to Healthcare (AMPATH), Eldoret, Kenya, [3]Moi University, College of Health Sciences, School of Medicine, Department of Child Health and Paediatrics, Eldoret, Kenya
Presenting author email: cmcateer@iu.edu

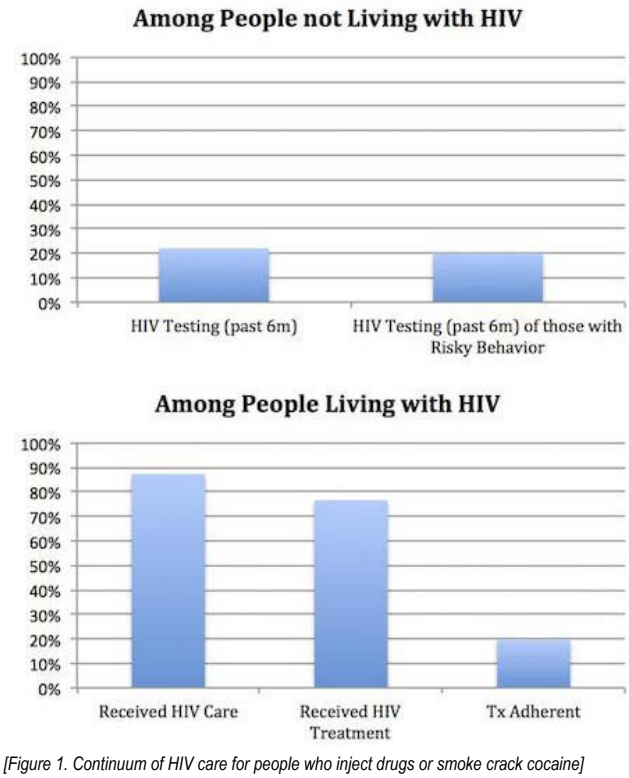
Background: Best practices for HIV disclosure to infected adolescents are not defined, and there are few data on disclosure practices from the viewpoint of HIV-infected adolescents. We sought to better understand HIV-infected adolescents' perspectives on disclosure in a large HIV care system in Kenya.
Methods: We conducted a qualitative study using focus group discussions (FGD) with HIV-infected adolescents who knew their HIV status and were receiving HIV care at 3 AMPATH clinics in western Kenya. A trained facilitator led the FGD in Kiswahili using a semi-structured interview guide that was based in grounded theory. FGD recordings were translated into English, transcribed, and analyzed using constant comparison, progressive coding, and triangulation to arrive at a contextualized understanding of HIV disclosure from the perspective of infected adolescents.
Results: Twenty-three HIV-infected adolescents participated in 3 FGD. Adolescents' current average age was 13.5 years, and average self-reported age of disclosure was 10.9 years. Most denied knowing they were HIV-infected before explicitly being told. Per adolescents, clinicians most often conducted disclosure, followed by close relatives (e.g., mother, aunt). Adolescents suggested that disclosure should occur by someone close to the child and should be a process over time, rather than a single event. Adolescents suggested varying ages for disclosure, ranging from 6-18 years, but most agreed that physical and cognitive maturity should be considered prior to disclosure. Services provided by healthcare workers and clinics were described as helpful in the disclosure process, specifically the availability of post-disclosure peer support groups and educational videos. The self-perceived impact of disclosure was mixed, but largely positive; most adolescents saw knowing their status and managing their health (e.g. medication adherence and avoiding HIV transmission) as positive advances, while others reported disclosure did not affect them. Few negative emotional reactions (e.g. "shock" and "confusion") from disclosure were described, although adolescents noted their caregivers expected more negative reactions.
Conclusions: Adolescents in western Kenya provided valuable insights (e.g. considering maturity level before disclosure and disclosing gradually over time) into preferred practices of disclosure timing and methods. Clinicians should explore how children's beliefs, preferences, and needs can be incorporated into disclosure.

MOPED683

Criminal justice involvement and the continuum of HIV care among people who inject drugs or smoke crack cocaine in Oakland, CA, USA

B.H. Lambdin[1,2,3], J. Lorvick[4], M. Comfort[4], A. Lopez[4], T. Jenkins[4], A.H. Kral[4]
[1]Pangaea Global AIDS, Oakland, United States, [2]University of California, Epidemiology and Biostatistics, San Francisco, United States, [3]University of Washington, Global Health, Seattle, United States, [4]Research Triangle Institute, San Francisco, United States
Presenting author email: blambdin@pgaf.org

Background: HIV disproportionately affects people who inject drugs (PWID) or smoke crack cocaine (PWSC). Concurrently, PWID and PWSC are more likely than people who do not use illicit drugs to be involved in the criminal justice system, complicating access to coordinated HIV prevention, care and treatment services. We conducted a community-based study of PWID and PWSC to characterize and assess predictors of access to the continuum of HIV services.
Methods: This cross-sectional survey utilized targeted sampling methods to recruit PWID and PWSC in Oakland, California between 2011 and 2013 (N=2,094). Participants were surveyed using a computer-assisted personal interview and received rapid HIV antibody testing. Multivariable logistic regression models were built to assess for associations between predictors and access to the continuum of HIV care.
Results: In the past 6 months, 24% of respondents had been incarcerated and 46% had been under community supervision. Eighty-five percent had ever and 22% had in the past 6 months tested for HIV. HIV antibody prevalence was 2.6% (95% confidence interval [95%CI]: 1.9-3.4%). Men who have sex with men (adjusted Odds Ratio [aOR]=13.41; 95%CI: 5.76-31.18), transgender people (aOR=27.37; 95%CI: 4.59-163.09) and having been in prison (aOR=1.99; 95%CI: 1.03-3.87) was associated with being HIV-positive. Figure 1 illustrates access to the continuum of HIV care, disaggregated by HIV status.



[Figure 1. Continuum of HIV care for people who inject drugs or smoke crack cocaine]

Participating in risky sexual or injection practices in the past 6 months did not increase the likelihood of having been HIV tested (p=0.183). People with a history of incarceration (aOR=1.54; 95%CI: 1.07-2.23), community supervision (aOR=1.50; 95%CI: 1.06-2.13) and drug treatment (aOR=1.60; 95%CI: 1.13-2.27) in the past 6 months were associated with an increased likelihood of HIV testing. Though high levels of linkage to HIV care and treatment were reported, only 20% remained HIV treatment adherent. Reasons for non-adherence included drug use (32%), adverse side effects (28%), and entry/release from incarceration (13%).

Conclusions: These findings highlight unrealized public health opportunities among this high-risk population. Interventions placed in correctional or community supervision settings, which increase routine HIV testing and ensure proper linkage and adherence support among PWID/PWSC, are critical to maximize the prevention and treatment benefits of antiretroviral therapy and end the AIDS epidemic.

MOPED684

Lower ART retention by 2010 guideline revision in resource-limited settings, Zambia

N. Kayama[1], K. Komada[2,3], C. Dube[1], A. Mwango[4]
[1]Mumbwa District Community Medical Office, Mumbwa, Zambia, [2]Japan International Cooperation Agency, Project for Scaling up of Quality HIV/AIDS Care Service Management (SHIMA), Lusaka, Zambia, [3]National Center for Global Health and Medicine, Bureau of International Medical Cooperation, Tokyo, Japan, [4]Ministry of Health, Clinical Care and Diagnostic Services, Lusaka, Zambia
Presenting author email: shimaproject@gmail.com

Background: The Zambian government has been scaling up Antiretroviral therapy (ART) to selected Rural Health Centres (RHCs) since 2007. The guidelines for ART in Zambia were revised in 2010 to follow the recommendation from WHO and revised again in 2014 to follow the new WHO guidelines. However, the impact of the revision in 2010 in RHCs was not evaluated enough.

Methods: The clinical files of all the adult patients (>14 years) who newly initiated ART from 2008 to 2012 at Lungobe RHC, Mumbwa district were reviewed. The number of new ART patients and their characteristics were compared by the year. The One year retention rate on ART was analysed by the Kaplan-Meier method and compared among the patients who initiated ART before the guideline revision (2008 and 2009), in the year of the revision (2010), and after the revision (2011 and 2012). Cox regression analysis was used to evaluate independent factors associated with retention.

Results: Total 412 patients were enrolled in the study. There was no remarkable change in human resource in Lungobe RHC from 2008 to 2012. The number of patients who initiated ART was rapidly increased from 76 in 2009 to 106 in 2010, while it was decreased to 69 in 2011. The main ART regimen in 2008 was d4T based (81.3%), and shifted to AZT based (64.5%) in 2009 and finally to TDF based (70.8%) in 2010. One year retention rate was 76.2% for the clients who initiated in 2010, while those were from 84.1 to 88.0% in the other years.

Year		2008	2009	2010	2011	2012
ART initiation	n	75	76	106	69	86
Age	median [IQR]	37 [30-45]	37 [32.5-45]	36 [32-45]	37 [34-45]	38 [32-46]
Sex	Male (%)	34 (45.3)	35 (46.1)	43 (40.6)	27 (39.1)	34 (40.0)
WHO stage	III or IV (%)	36 (48.0)	54 (72.0)	64 (62.1)	50 (72.5)	47 (59.5)
CD4 count (Cell/mm3)	mean [95%CI]	180 [155-206]	186 [164-209]	203 [181-225]	196 [170-224]	187 [158-216]
	d4t base (%)	61 (81.3)	18 (23.7)	4 (3.8)	4 (5.8)	6 (7.2)
ART regimen	AZT base (%)	10 (13.3)	49 (64.5)	27 (25.5)	26 (37.7)	20 (24.1)
	TDF base (%)	4 (5.3)	9 (11.8)	75 (70.8)	39 (56.5)	57 (68.7)
1 year retention rate	% [95%CI]	86.7% [78.7-94.5]	88.0% [80.5-95.5]	76.2% [67.8-84.7]	84.1% [75.2-92.9]	88.0% [80.8-95.1]

[Characteristics of new ART client (2008-2012)]

Compared to before the revision, initiating ART in 2010 were less likely to retain (Hazard ratio: 2.53, 95%CI: 1.25-5.09), while initiating after the revision didn't affect significantly. (Hazard ratio: 1.15, 95%CI: 0.54-2.46)

Conclusions: The guideline revision may have affected temporally the quality of ART services in rural area in Zambia because of rapid increase in patients' number and rapid shift of ART regimen. Considering the capacity of RHC, new guidelines should be introduced carefully to keep the quality of services. Further investigation is required in other facilities and also focusing on the guideline revision in 2014.

MOPED685

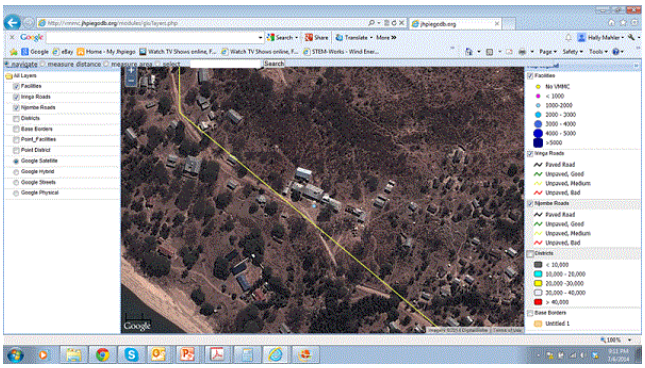
Use of novel geographic information systems (GIS) improves planning, delivery, and tracking of voluntary medical male circumcision (VMMC) scale up in Tanzania

H.R. Mahler[1], Y. Kulindwa[1], A. Liu[2], S. Searle[2], A. Hellar[1], M. Plotkin[2], J. Lija[3], E. Mlanga[4], E. Njeuhmeli[5], K. Curran[2,6]
[1]Jhpiego - an affiliate of Johns Hopkins University, Dar es Salaam, Tanzania, United Republic of, [2]Jhpiego- an affiliate of Johns Hopkins University, Baltimore, United States, [3]Ministry of Health and Social Welfare, National AIDS Control Programme, Dar es Salaam, Tanzania, United Republic of, [4]USAID Tanzania, Dar es Salaam, Tanzania, United Republic of, [5]USAID, Washington, DC, United States, [6]Johns Hopkins University, Bloomberg School of Public Health, Baltimore, United States
Presenting author email: hally.mahler@jhpiego.org

Background: Supporting the Ministry of Health and Social Welfare, Jhpiego (funded by USAID through PEPFAR) has worked since 2009 in three regions of Tanzania with a goal of providing VMMC to 80% of uncircumcised males aged 10-34, per national and regional targets. These regions have 600+ health facilities/villages. By 2012, traditional methods of selecting, preparing and tracking outreach service delivery sites became inefficient. Program managers invested in GIS technology to create continuously updated online maps to inform better decision-making.

Methods: Routine VMMC de-identified client data is collected as part of the clinical services and entered into a database. Geocoded data on general facility and community information, access to electricity and water, population catchment size, road access, facility size, affiliation, and mobile phone network availability were collected at every facility and entered into a database, along with census data. This data was overlaid into Google Maps through OpenLayers software, giving program managers a web-based view of various parameters associated with VMMC service delivery for strategic campaign site selection and progress tracking.

Results: Campaign site selection was significantly more effective with the assistance of GIS technology. For example, during a six-week VMMC campaign in 2012 the program served 25,816 males in rural communities, compared with 14,476 over the same timeframe in the previous year. Program managers now conduct site selection activities without physically visiting sites. Features such as the satellite layers on the maps allow program managers to view sites for demand creation activities. Using GIS's decision support capabilities, program managers also identify potential sites mobile VMMC services, plan campaign logistics, and analyze circumcisions performed by age within specific communities.



[Google Maps Satellite View of Health Facility]

Conclusions: GIS enabled the Tanzania VMMC program to effectively track scale up and target planning and resources. As of October 2014 more than 400,000 VMMCs have been performed in these three regions, two of which achieved more than the 80% target of males aged 10-34 with the assistance of GIS. However coverage is not equal in all communities. The GIS system continues to allow the team to target services to communities that are not yet saturated for efficient use of program resources.

MOPED686

Analysis of the change in facility-level ART unit costs after implementation of the new WHO treatment guidelines in Malawi

K. Callahan[1], A. Gunda[2], S. Phanitsiri[1], M. Kaur[3], L. Mgomezulu[2], E. Tagar[1], F. Chimbwandira[4], A. Jahn[5]
[1]Clinton Health Access Initiative, Boston, United States, [2]Clinton Health Access Initiative, Lilongwe, Malawi, [3]Clinton Health Access Initiative, Delhi, India, [4]Malawi Ministry of Health, Lilongwe, Malawi, [5]International Training and Education Center for Health (I-TECH), Lilongwe, Malawi
Presenting author email: kcallahan@clintonhealthaccess.org

Background: The 2013 WHO HIV Treatment Guidelines expanded ART eligibility criteria and recommended uptake of improved drugs, labs and service delivery protocols. Malawi implemented the new guidelines in 2014; however, it has led many to question the cost implications of such ambitious scale up. The 2010 "Multi-Country Analysis of Treatment Costs for HIV/AIDS (MATCH)" study established that average facility-level treatment costs were $136 per patient per year (PPPY) in Malawi. Following on the MATCH analysis, this study costs ART service delivery at five of the MATCH facilities in Malawi, using the same methodology, to observe how costs have changed over time.
Methods: In 2010, MATCH collected comprehensive data on one year of ART costs in 30 facilities across Malawi, selected using stratified random sampling. In 2014, the same data points were examined at a diverse sample of five of the original facilities. The study evaluates costs including drugs, laboratory services, direct and indirect personnel, equipment and facility running costs.
Results: Between 2010 and 2014, the five sampled facilities experienced an average of 163% growth in HIV patient volumes. ARV costs increased by 60%, as a result of the switch from d4T to TDF-based regimens; however, this was largely offset by reductions in service delivery costs. These include fixed costs that were spread across increased patient volumes, and lower personnel costs as a result of multi-month ARV prescriptions and task shifting. Lab costs remained low due to limited access to viral load and other tests nationwide. Overall, average cost increased slightly from $134 PPPY in 2010 to $146 PPPY in 2014.
Conclusions: Initial results suggest that, to date, ART scale up may lead to even lower service delivery costs than previously observed, as fixed costs are spread over larger patient numbers and trends such as task shifting reduce HRH costs. In Malawi, these cost reductions were offset by increased ARV costs, but in countries that had previously switched to TDF-based regimens, total ART costs on a per-patient basis may be going down. This study will be repeated in Zambia in 2015 to provide an additional data point.

Impact evaluation of different models of service delivery

MOPED687

Text message reminder-recall to increase HPV immunization uptake in young HIV-1-infected patients

S. Keeshin[1], J. Feinberg[2]
[1]University of Utah, Pediatrics, Salt Lake City, United States, [2]University of Cincinnati, Internal Medicine, Cincinnati, United States
Presenting author email: susana.keeshin@hsc.utah.edu

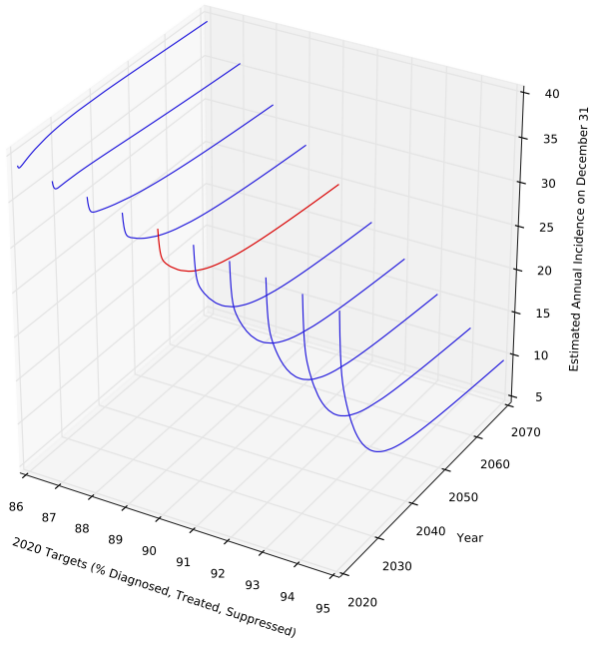
Background: This quality improvement pilot project was conducted to evaluate the impact of text message immunization reminder-recall in young HIV-1 positive patients (pts) in a large urban academic HIV clinic.
Methods: All HIV pts age 16-26 were identified who had one visit within the last calendar year. Of the 11 physicians in our clinic, one physician used text reminders exclusively and the other 10 physician patient panels served as the control. Reminders were sent monthly to pts who had not completed a 3-dose HPV vaccine series. We compared immunization uptake for pts who received reminders vs. those who did not. We used multivariable logistic regression to assess the impact of age, gender, race/ethnicity, and insurance status.
Results: A total of 255 HIV pts age16-26 were seen in our clinic from July 1 2013-June 30, 2014. Of the 28 pts who received text reminder-recall, compared to control, they were more likely to be black and uninsured compared to the 212 pts who received standard of care without any reminder-recall; 15 pts who died or moved were not included in the final analysis. At 6 month, significantly more pts in the intervention group received ≥ 1 HPV vaccination, 60.9% vs. 19.4% (41.5 percentage point difference, p < . 001), and all 3 HPV (13% vs. 4.3%; 8.7 percentage-point difference, p< .107). At 12 months those with ≥ 1 HPV vaccination was 89.3% vs. 32.1%, (57.2 percentage-point difference,
p< . 001), and all 3 HPV was 32.1% vs. 9.4%, (22.7 percentage-point difference, p< . 001). After controlling for age, gender, race/ethnicity, and insurance status text message reminders were still significantly associated with improved HPV vaccination uptake.
Conclusions: Text message reminder-recall improved HPV immunization uptake in a young HIV-1 infected, low-income urban population. As communication by texting is characteristic of teens and young adults in the general population, text and email reminder-recalls should be considered a viable option to improve vaccination rates among young HIV pts. As secure platforms for texting protected health information are developed, more clinics and caregivers that treat adolescents/young adults will adopt texting to communicate with patients.

MOPED688

Health system modelling to evaluate operational strategies for the implementation of UNAIDS 90-90-90 targets in Vancouver, Canada

K. Vasarhelyi[1,2], L. Ahrenberg[2], S. Kok[2], R. Gustafson[3], R. Barrios[3,4], A. Nadaf[2,5], A. van der Waall[2], B. Ramadanovic[2], B.G. Williams[6], U. Isip[2,5], A.R. Rutherford[2,5]
[1]Simon Fraser University, Faculty of Health Sciences, Burnaby, Canada, [2]Simon Fraser University, IRMACS, Burnaby, Canada, [3]Vancouver Coastal Health, Vancouver, Canada, [4]British Columbia Centre for Excellence in HIV/AIDS, Vancouver, Canada, [5]Simon Fraser University, Department of Mathematics, Burnaby, Canada, [6]SACEMA, Stellenbosch, South Africa
Presenting author email: kvasarhe@sfu.ca

Background: UNAIDS predicts that reaching 90-90-90 targets by 2020 will reduce the HIV epidemic to low-level endemic disease by 2030. We explored potential outcomes of reaching 90-90-90 and further targets in Vancouver, Canada, where Treatment as Prevention—in operation since 2000—already achieved high service delivery levels (75% diagnosed, 83% treated, 77% suppressed) and substantially reduced the epidemic.
Methods: We used a validated system dynamics model of Vancouver's HIV care continuum (doi:10.1007/s10729-014-9312-0) to simulate HIV service delivery expansion. To reach targets, we increased diagnoses by scaling testing rates, and antiretroviral therapy coverage by scaling probabilities of treatment initiation and loss to follow-up. The proportion virally suppressed was fixed at the target. We determined 2030 HIV incidence for symmetrical 2020 targets—including 90-90-90—up to an achievable maximum, for men who have sex with men (MSM), a socially linked group of injection drug users and street-based female sex workers (IDU-FSW), and the general population, which, respectively, had 15%, 18% and 0.1%, prevalence of HIV in 2013.
Results: The figure shows expected 2030 incidence outcomes of various 2020 targets for IDU-FSW. Compared to 2010 levels, achieving 90-90-90 and 95-95-95 targets, would respectively reduce new infections per year in 2030 by: 38% and 69% (to 74 and 37 cases) for MSM; 36% and 68% (to 28 and 14 cases) for IDU-FSW; 53% and 75% (to 6 and 3 cases) for the general population. Delays in linkage to care and viral suppression limited achievable treatment coverage to 95% for MSM and IDU-FSW and 97% for the general population. With maximal service delivery expansion, 9, 3, and 1 new infections per year are predicted for the three populations.
Conclusions: UNAIDS targets provide a useful narrative for accelerating progress toward ending AIDS. Reaching and exceeding 90-90-90 targets could substantially reduce the HIV epidemic, even in the resource-rich Vancouver setting. Our estimated 90-90-90 impact is likely to be conservative due to early TasP implementation in Vancouver. Our findings highlight the disproportionate effort required in small epidemics to deliver services to the most hard-to-reach groups and individuals, which is a challenge that may be expected during the final stages of ending AIDS.



[2030 outcomes of 2020 targets (90-90-90 in red)]

MOPED689

Healthcare provision for truck drivers in sub-Saharan Africa: a systematic review of interventions, methods of evaluation and impact

S.T. Lalla-Edward[1], S. Fobosi[1], J. Stadler[1], F. Venter[1], G.B. Gomez[2,3]
[1]Wits Reproductive Health and HIV Institute, Johannesburg, South Africa, [2]Amsterdam Institute for Global Health and Development, University of Amsterdam, Amsterdam, Netherlands, [3]London School of Hygiene and Tropical Medicine, Department of Global Health, London, United Kingdom
Presenting author email: slalla-edward@wrhi.ac.za

Background: Mobile populations can be at higher risk of acquisition and transmission of HIV and governments have prioritised these populations in their National Strategic Programmes. In particular, truck drivers, due to the nature of their occupation, can face important challenges accessing healthcare. Currently, the implementation of effective health interventions for truck drivers is hindered by the lack of knowledge of what is currently available and the impact of services on health outcomes. The aim of this review is:
(1) to describe health interventions implemented in sub-Saharan Africa and the methods used to evaluate them;
(2) to assess the impact these interventions have had on truck drivers' health outcomes.
Methods: A broad strategy using both MeSH headings and free text, with no language limitations, was used to search PubMed/Medline, ISI Web of Knowledge, and online search engines. We included all publications (peer-reviewed or reports) describing a health intervention in sub-Saharan Africa and its evaluation where the main clients were truck drivers. Experts and organisations working with truck drivers were consulted for unpublished reports. We extracted data related to services provided, location, provider, evaluation method, and outcomes measured.
Results: After removing duplicates, we screened 6,479 records. Of the 229 articles eligible, 21 documents were included. These described 16 interventions across 17 countries and mainly focused on HIV prevention and sexual health services. Evaluation methods varied from pre- and post-intervention surveys to the analysis of routinely collected data. Outcomes reported included individual-level (e.g. HIV knowledge, sexual behaviour) and programme-level (e.g. attendance, client satisfaction) outcomes. While changes in knowledge, attitudes, and behaviours have been attributed to the interventions; impact on health outcomes and its attribution to the interventions remains a challenge.
Conclusions: Transport companies have recognised that HIV/AIDS can drain productivity levels, due to absenteeism and training of replacement workers. In recent years, the number of initiatives providing services tailored to truck driver's needs across sub-Saharan Africa has increased. It is important for managers and funders to understand the impact on health outcomes of these initiatives. This review provides a starting point on how to build on past evaluations to answer this key question.

MOPED690

The cost-effectiveness of the mothers2mothers Mentor Mother Model as a psychosocial well-being intervention

K. Schmitz[1], E. Scheepers[2], E. Okonji[2], S. Sandfolo[2], V. Kawooya[3]
[1]mothers2mothers, Department of Programmes and Technical Support, Cape Town, South Africa, [2]mothers2mothers, Research and Strategic Information, Cape Town, South Africa, [3]mothers2mothers Uganda, Jinja, Uganda

Background: mothers2mothers is a peer education and psychosocial support programme that enhances the effectiveness of PMTCT services. Aligned with a public health perspective and against the background of the positive influence of wellbeing on health and mortality, m2m aims to impact on the health of its clients by addressing the challenges facing HIV-positive pregnant women and mothers, thus improving their psychosocial wellbeing. m2m's impact on psychosocial wellbeing was used in a cost-effectiveness analysis of the m2m Mentor Mother Model implemented under the STAR-EC Programme in Uganda compared with a PMTCT intervention without psychosocial support.
Methods: A quasi-experimental matched area comparison design was used. Seven hundred and ninety six (796) pregnant women and new mothers accessing PMTCT between June 2012 and March 2014 in 31 intervention facilities (where m2m Mentor Mothers provided peer education and psychosocial support) and 31 matched control facilities (where no peer education and psychosocial support were provided) participated in facility based Psychosocial Wellbeing surveys. A composite measure of psychosocial wellbeing was constructed using principle component analysis. Incremental effectiveness was calculated as the difference in percentage points psychosocial wellbeing between intervention and control groups multiplied by the total women needing PMTCT in 2014 in Uganda as estimated by Uganda's Ministry of Health, using the AIM model in SPECTRUM. Incremental cost was the cost of scaling up the m2m intervention to public health facilities in Uganda, following an ingredients approach from a provider perspective. Economic costs were captured, including donated goods and opportunity cost. A discount rate of 3% was used.
Results:

	Control	Intervention	Incremental effect
Have poor psychosocial well being	63.5%	55.3%	
Have good psychosocial well being	36.5%	44.7%	8.2 p.p. (p=0.010)
Total women needing PMTCT in Uganda (2014) - Calculated in AIM (SPECTRUM)			90,750
% Women with better psychosocial wellbeing due to m2m			8.2%
Number of women with better psychosocial wellbeing due to m2m			7,442
Incremental cost (USD) - for scaling up p m2m nationwide			4 478,930
Incremental effectiveness (women with better psychosocial wellbeing)			7,442
Incremental cost effectiveness ratio (ICER)			601.9
Decision rule for ICER	<GDP per capita is considered very cost-effective	1-3 × GDP per capita is considered cost-effective	>3 × GDP per capita is considered not cost effective

[Cost effectiveness analysis]

The incremental cost per woman with psychosocial wellbeing was USD 601.90. Based on the threshold of GDP/GNI per capita in Uganda (USD 572, 2013), the m2m intervention was assessed cost effective as a psychosocial wellbeing intervention. The intervention was also cost-effective as measured against the sub Saharan Africa threshold (USD 1,701, 2013).
Conclusions: Psychosocial support is sometimes overlooked in the care and treatment of PMTCT clients. Yet, literature suggests that subjectively experienced wellbeing impacts on healthy choices and improves health and longevity. m2m's model of care is an important, cost-effective component of service delivery in the area of public health.

MOPED691

Investigating the influence of peer mentor mother approach on the psychosocial well-being of HIV-positive pregnant women and new mothers accessing prevention of mother to child transmission of HIV services

E.F. Okonji[1], E. Scheepers[2], K. Schmitz[1], V. Kawooya[3]
[1]mothers2mothers, Evaluations and Operations Research, Cape Town, South Africa, [2]mothers2mothers, Research and Strategic Information, Cape Town, South Africa, [3]mothers2mothers, Jinja, Uganda

Background: mothers2mothers (m2m) employs and trains mothers living with HIV ("Mentor Mothers") to provide peer education and psychosocial support to pregnant women and new mothers as well as tracking and retaining them in PMTCT care. Through the education and psychosocial support that Mentor Mothers provide women, they develop the beliefs, attitudes and skills necessary to overcome negative social norms that impact on them, their families and communities.
Self-efficacy is at the centre of m2m's theory of change which states that through improved self-efficacy, and seeing a mentor mother women are better able to overcome some of the barriers to healthy behaviour and PMTCT service uptake. m2m empowers women through improving their self efficacy. In 2014 an external evaluation was conducted on the m2m Mentor Mother Model implemented under the STAR-EC Programme in Uganda in which one of the objectives was to investigate whether maternal psychosocial well-being and empowerment outcomes were associated with exposure to Mentor Mothers.
Methods: A quasi-experimental matched area comparison design was used. Seven hundred and ninety six (796) pregnant women and new mothers accessing PMTCT between June 2012 and March 2014 in 31 intervention facilities (where m2m Mentor Mothers provided peer education and psychosocial support) and 31 matched control facilities (where no peer education and psychosocial support were provided) participated in facility based Psychosocial Wellbeing surveys. A standardised questionnaire that was informed by the m2m Theory of Change was administered. Bivariate and multivariate inferential statistical analysis was done using STATA 12. Propensity Score Matching was used to investigate the net effect attributable to the m2m standard-of-care.
Results: Clients exposed to m2m support demonstrated better psychosocial wellbeing and empowerment outcomes compared to non m2m exposed clients. i.e. coping self-efficacy (86,6% vs 64.5%; p-value 0.001), and better coping behaviour (69.4% vs 56.9%; p-value 0.001).
No significant difference were observed between clients who demonstrated HIV treatment adherence self-efficacy (HIV-ASES) in both study arms (97.7% vs 97.4%; p-value 0.395).
Conclusions: Exposure of pregnant women and new mothers living with HIV to m2m's psychosocial support positively impacts on their psychosocial wellbeing and empowerment compared to women not exposed to the mentor mother support services.

Psychosocial wellbeing outcome indicators	Average effects among matched exposed subjects in m2m sites	Average effects among matched unexposed subjects in control sites	Net effect (Percentage points)	P-Value
Experience of social support	80.10%	71.70%	8.4	0.003
Demonstrates HIV Disclosure and Safer Sex Self-Efficacy	71.70%	50.70%	21	0.001
Did not experience Depression	83.30%	78.10%	5.2	0.028
Experience of Good relationship with health worker	95.20%	86.00%	9.2	0.001
Experience of Good relationship with partner	72.20%	58.30%	13.9	0.001
Demonstrates coping with stigma	40.20%	31.20%	9	0.006
Demonstrates no experience of internalized stigma	99.50%	97.90%	1.6	0.025
Accurate HIV Knowledge	87.10%	81.80%	5.3	0.015
Positive Gender attitudes	44.70%	36.50%	8.2	0.01

[Comparing psychosocial well-being outcomes]

MOPED692

Impact of harm reduction interventions under the community action on harm reduction "Hridaya" programme on safe injecting and sexual behaviours among people who inject drugs in India

V. Arumugam, J. Robertson, K. Biswas, C. Sharma, F. Joseph, S. Mehta
India HIV/AIDS Alliance, New Delhi, India
Presenting author email: aviswanathan@allianceindia.org

Background: Injecting drug use has emerged as an important route for HIV transmission in India. The government currently estimates that there are approximately 200,000 people who inject drugs(PWID) in India (NACO, 2011). Surveillance shows HIV prevalence among PWID at 7.14% (NACO, 2011). India HIV/AIDS Alliance implements the Hridaya programme in the Indian states of Bihar, Haryana, Uttarakhand, Jammu and Manipur as part of the five-country, Dutch government-funded Community Action on Harm Reduction initiative (CAHR). The programme strengthens harm reduction services for PWID and their close contacts within government-supported Targeted Interventions for HIV prevention.
Methods: A cross-sectional survey at the end of phase one of the programme (2012-14) was conducted as part of an impact assessment using the same methodology used for the baseline in 2012. A total of 600 semi-structured interviews and 50 case studies with PWID were conducted, along with twelve key informant interviews. PWID were selected for semi-structured interviews through systematic random sampling using client information from partner NGOs at selected sites.
Results: The majority of respondents were young (mean age:31.7 years), had no education/primary education(51.4%), worked as unskilled workers (38.5%), were married (49.7%) and had a permanent partner and lived at home(94.3%). The mean duration of injection drug use was about seven years. The most common frequency of injections was daily(38.7%), and the most common frequency of injection on the injection day was one to three times (93.5%). Significant reduction in injecting with used equipment was observed (22% at baseline to 5% at endline, p< 0.001) as was an increase in condom use with commercial sex partners (52% at baseline to 90% at endline,p< 0.001). A large majority of respondents (91%, versus 74% at baseline)had not sold or lent their injecting equipment in the previous 30 days (p< 0.001).
Conclusions: Reductions in reuse and lending or sale of injecting equipment show a positive change in injecting behaviour. Hridaya programme components have contributed to safer injecting and sexual behaviours among PWID. Similar strategies can be scaled up in other states of India to strengthen harm reduction efforts for this vulnerable population.

MOPED693

Clinical outcomes of HIV care delivery models in the US: a systematic review

A. Kimmel[1], E. Martin[2], H. Galadima[1], A. Tehrani[1], J. Cyrus[1], M. Henderson[1], K. Freedberg[3,4], A. Krist[5]
[1]Virginia Commonwealth University, Richmond, United States, [2]University at Albany, SUNY, Albany, United States, [3]Massachusetts General Hospital, Boston, United States, [4]Harvard Medical School, Boston, United States, [5]Virginia Commonwealth University, Fairfax, United States

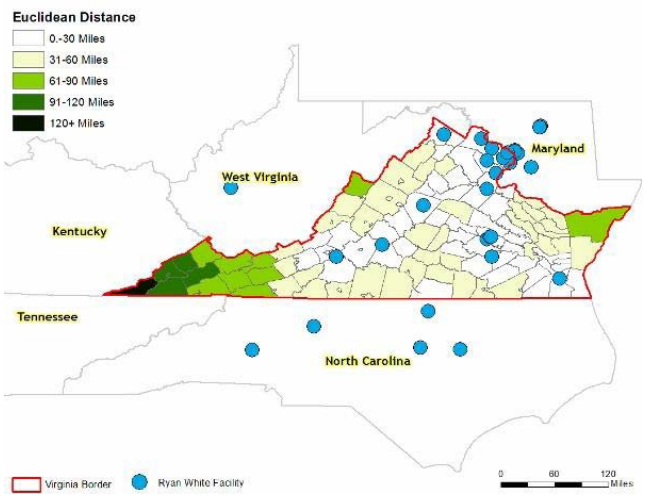
Background: The US faces national challenges in HIV care delivery. These include decreasing HIV specialists, shortages of primary care physicians, an aging HIV-infected population, and policies across health care shifting chronic disease care from specialty to primary care providers. Alternative HIV care delivery models may address these needs. We systematically reviewed evidence on patient-level health outcomes of different HIV care delivery models in the US.
Methods: We identified randomized trials and observational studies in PubMed and ISI Web of Knowledge, March 1987-June 2014. Eligible studies examined a model, process, or system for providing outpatient HIV care delivery in the US and reported patient-level clinical outcomes. Two reviewers independently screened studies and extracted data using predefined criteria. We categorized care delivery models as:
task shifting (redistributing HIV care to non-physicians),
shared (co-managed HIV care by generalists and HIV expert physicians),
specialist (HIV care by HIV expert physicians only), and
integrated (comprehensive team management of HIV and primary care).
We evaluated mortality, items on the HIV care continuum (retention, ART initiation, HIV RNA suppression), aging-related outcomes (cardiovascular disease, hypertension, or diabetes screening or treatment), and other primary care outcomes (mental health, substance abuse, or hepatitis C screening). Descriptive synthesis summarized the evidence; we did not conduct a formal meta-analysis due to heterogeneity in reporting.
Results: We identified 3109 studies, with 13 meeting eligibility criteria. Eight of 13 (61%) reported outcomes related to specialist care, 3/13 (23%) integrated care, 1/13 (8%) task shifting, and 1/13 (8%) shared and specialist care. Across all studies, the majority reported mortality and antiretroviral use, with specialist care at the provider or clinic level generally associated with improved HIV-related outcomes. We found limited outcomes for retention in care, HIV RNA suppression, and mental health, substance abuse, and hepatitis C screening. We identified no aging-related outcomes. Studies were mainly from the early combination antiretroviral therapy era and urban areas in the Northeast and Northwest.
Conclusions: Evidence on the impact of alternative HIV care delivery models on clinical outcomes is extremely limited. Better understanding of these outcomes, especially in different patient populations and geographic locations, is urgently needed.

MOPED694

Geographic variation in access to HIV care for low-income adults: the case of Virginia

A. Kimmel, H. Galadima, D. Wheeler
Virginia Commonwealth University, Richmond, United States

Background: In the US, federally funded Ryan White Part C (RW) providers offer comprehensive primary and specialty HIV care to low-income, HIV-infected adults. Continued RW funding is uncertain given limited expansion of Medicaid public insurance coverage under the Affordable Care Act. We examined geographic variation in access to Part C providers, using the state of Virginia as a case study.
Methods: We used publicly available data to visualize HIV prevalence and RW provider locations in Virginia. Data included:
1) county-level adult and adolescent HIV cases per 100,000 population (2010, Centers for Disease Control and Prevention via AIDSvu.org);
2) location of Ryan White providers (Health Resources and Services Administration), and
3) provider funding type to identify RW grantees (Tracking Accountability in Government Grants System).
Physical addresses of provider facilities were geocoded to create spatial coordinates. Data also included services offered (HIV testing, HIV treatment and care, mental health and substance abuse treatment, ancillary services) and facility type (academic medical center, non-academic hospital/health system, community health center, community-based HIV-specific provider, other community-based provider). Thematic maps created using ArcGIS v10 were used to visually assess access to HIV care.
Results: We identified 11 RW providers in 18 locations across 15 counties and county-equivalent, independent cities in Virginia (of 133 statewide). RW providers are clustered near urban areas in central (Richmond metropolitan area) and northern (Washington, DC, metropolitan area) Virginia, where HIV rates exceed 175 cases per 100,000 population. Median distance between each county centroid and the nearest RW clinic (within or outside of Virginia) is 28.8 miles (range 0.7-124.5 miles) (**Figure**), with limited RW providers in less densely populated but high-burden areas like rural western Virginia. Findings were similar when considering number of HIV cases vs rates. Providers represent mainly academic medical centers and non-academic hospitals/health systems; services offered across providers vary.



[Figure]

Conclusions: As the HIV epidemic includes more semi-urban and rural areas, access to comprehensive HIV care is a priority. Implementation of alternative care delivery models that can address this evolving demand is critical. Next steps include developing a single metric to evaluate county-level RW accessibility based on clinic distance, HIV rate, poverty, and uninsurance.

MOPED695

Patient satisfaction with methadone maintenance treatment in Vietnam: a comparison of standalone- and integrative- service delivery models

H.T.T. Phan[1], B.X. Tran[2], V.M. Nong[3], C. Latkin[2]
[1]Ministry of Health, Authority of HIV/AIDS Control, Hanoi, Vietnam, [2]Johns Hopkins Bloomberg School of Public Health, Department of Health, Behavior and Society, Baltimore, United States, [3]Hanoi Medical University, Institute for Preventive Medicine and Public Health, Hanoi, Vietnam
Presenting author email: bach@jhu.edu

Background: Methadone Maintenance Treatment (MMT) services have been rapidly scaled up in Vietnam, with the goal of covering 80,000 drug users by 2015. Identifying highly effective delivery models is necessary, however, little is known about experience and preference of clients at different clinics. We assessed satisfaction of drug users taking MMT at standalone- versus integrative- clinics in two provinces of Vietnam.
Methods: A cross-sectional survey was conducted among 1016 patients enrolling 5 MMT sites in Hanoi and Nam Dinh in 2013. Patients' satisfaction was measured using a 10-item interview scale. Construct validity of the measure was assessed using exploratory factor analysis. Censored linear regression was used to determine factors associated with satisfaction of patients.
Results: The mean score of satisfaction was high in all three domains of the measure, it was the highest in "Health workers' competency" (9.2/10; 95% CI=9.12-9.27); and the lowest in "Quality, counseling and guidelines" (9.12/10; 95%CI=9.04-9.19), and "Services availability" (9.12/10; 95% CI=9.03; 9.20). There was 36.5% and 34.9% reported completely satisfied with overall service quality and treatment outcomes, respectively. In multivariate analysis, patients taking MMT integrated with general health care services had significantly higher satisfaction than patients of MMT stand-alone model. Other factors related to higher satisfaction included younger age, higher education, and not have health problems in self-care and pain/depression.
Conclusions: Integrating MMT with general health care services is preferred and may improve the efficiency and quality of MMT in large drug using populations.

MOPED696

Using unique identifiers with key population HIV prevention programmes to measure coverage, prevalence and incidence: TB/HIV Care Association's sex worker HIV prevention model and data from Durban, South Africa

A. Lambert[1], R. Ogle[2], H. Mhlophe[2], P. Modikoe[1], H. Hausler[3]
[1]TB/HIV Care Association, Key Populations, Cape Town, South Africa, [2]TB/HIV Care Association, Key Populations, Durban, South Africa, [3]TB/HIV Care Association, CEO, Cape Town, South Africa
Presenting author email: andy@tbhivcare.org

Background: HIV prevention programming often only reports numbers reached with HIV testing and counselling (HTC) as their primary indicator for reduction in HIV infections. However, in the absence of a standard programmatic or national service user unique identifier system, HIV prevention programmes tend to over-report HIV testing, are unable to determine proportion of a population reached against size estimates, and are unable to determine accurate prevalence and incidence figures to monitor outcomes and impact of HIV prevention programmes.
Methods: In October 2011, TB/HIV Care Associaton (THCA) was awarded a five year CDC/PEPFAR grant to develop a sex worker (SW) peer-linked mobile HIV prevention programme in five urban areas of South Africa. THCA provides a variety of HIV/AIDS/STI/TB (HAST) services using a simple anonymous unique identifier based on initials and date of birth. This identifier allows THCA to identify unique numbers of SWs reached, to identify more realistic HIV prevalence figures, and to capture incidence data from a longitudinal group of HIV negative SWs.
Results: From July 2012 to July 2014, THCA provided 3,276 health screens to 2,861 unique SWs, and 3,062 HIV screens (known and unknown status) to 2,756 unique SWs (778 known HIV positive and 1,978 unknown) in Durban, South Africa. The unique number of HIV+ SWs was 1,493 for an HIV prevalence of 54% (1,493/2,756). Ten seroconversions were documented within a cohort of 122 SWs who initially tested HIV negative and later seroconverted for an overall incidence of 8%. Year one identified 39 HIV negative SW with 4 serconverstion (10.25% incidence) and in year two 83 and 6 respectively (7.2% incidence). Additionally, using the South African National AIDS Council's (SANAC) SW size estimation of 5,670 SW in THCA's catchment area in the Durban area, THCA documented having had reached 50% of SWs (2,861/5,670) in two years.
Conclusions: Rigorous data collection using unique idenfiers will help target key affected populations with effective programmes, and assist the government to allocate resources where they are needed most. Ultimately consistent and effective use of programmatic data will help drive the number of infections among KPs and the general population down.

MOPED697

Long-term ART outcome and operational challenges in rural health centres supported by mobile team: a prospective cohort study in a rural district, Zambia

N. Kayama[1], K. Komada[2,3], C. Dube[1], A. Mwango[4]
[1]Mumbwa District Community Medical Office, Mumbwa, Zambia, [2]Japan International Cooperation Agency, Project for Scaling up of Quality HIV/AIDS Care Service Management (SHIMA), Lusaka, Zambia, [3]National Center for Global Health and Medicine, Bureau of International Medical Cooperation, Tokyo, Japan, [4]Ministry of Health, Clinical Care and Diagnostic Services, Lusaka, Zambia
Presenting author email: k-komada@it.ncgm.go.jp

Background: Universal coverage of antiretroviral therapy (ART) still remains ongoing challenge especially in resource-limited settings. The Zambian government commenced to provide ART services at District Hospital in 2005, and scaled them up to selected Rural Health Centres (RHCs) in 2009 through the regular outreach services, named "National Mobile ART Services". The outreach team comprising medical professionals from district hospital visits those RHCs every two weeks and assists with ART services. We have conducted a prospective cohort study to evaluate long term outcomes and operational challenges in ART services at RHCs in comparison to those at District Hospital in Mumbwa district, Zambia.
Methods: Adult patients (>14 years) who newly initiated ART at Mumbwa District Hospital and 8 RHCs in Mumbwa district between September 2010 and December 2010 were enrolled in our study and followed for more than 42 months (until July 2014). The retention and survival rates were analysed by the Kaplan-Meier method and compared between patients treated in District Hospital and RHCs. Cox regression analysis was used to evaluate independent factors associated with retention and survival.
Results: Total 358 cases were enrolled in the cohort. The analysis was done for 276 cases treated with TDF/FTC/NEV or TDF/FTC/EFV. The retention rate at 1260 days was 72.4% (95%CI:63.8-79.4) in RHCs and 74.0% (95%CI:65.2-80.9) in District Hospital. There was no significant difference in the retention rate through observation period (P=0.69 by the log-rank test). Being treated in RHCs did not affect the retention significantly (Hazard ratio:1.24, 95% CI:0.67-2.30). 22.5% of the patients initiated TDF based regimen without monitoring their renal

function, and the patients in RHCs were less likely to be tested for Creatinine (p=0.04). The patients with renal dysfunction (Creatinine clearance < 30) were less likely to survive (HR:11.98, 95%CI:1.74-82.50) as well as low CD4 count (< 160) (HR:9.88, 95%CI:1.21-80.66).
Conclusions: The ART retention rates through more than 42 months observation were not different between RHCs and District hospital. However, some patients initiated TDF without monitoring their renal function especially in RHCs. Mobile HIV services may be an effective strategy to expand service coverage area but require more attention on how to support laboratory services in RHCs.

MOPED698

Scaling up access to second line antiretroviral therapy in rural Zimbabwe: impact of routine viral load, model of care and re-suppression after switch

Y. Htung Naing[1], H. Bygrave[2], C. Metcalf[2], D. Munyaradzi[1], S. Simons[1], T. Bonyo[1], G. Chenjirai[1], J. Steinberg[1]
[1]Medecins Sans Frontieres, Harare, Zimbabwe, [2]Medecins Sans Frontieres, Southern Africa Medical Unit, Cape Town, South Africa
Presenting author email: helen.bygrave@joburg.msf.org

Background: In many resource-limited settings, access to second-line antiretroviral therapy (ART) is centralised and prescribed only by doctors. After implementing routine viral load (VL) monitoring in two rural districts in Zimbabwe in 2012, switching of patients to second-line ART and their follow-up was decentralised to all primary care clinics, and carried-out by a multidisciplinary team.
Methods: Information was extracted from patient and laboratory records and analysed to assess virological response to second-line ART. The analysis used data from 358 patients with confirmed virological failure, who switched to second-line ART between June 2008 and November 2014. Binary logistic regression was used to identify factors associated with a poor virological response.
Results: Second-line ART initiations increased from 13 in 2011 to 243 in 2014. Of the patients in the analysis 58.0% were female; with a median age of 33 years; a median time on first-line ART of 3.7 years; and a median follow-up after switching of 42.7 weeks. The median pre-switch VL was 30,940 copies/ml (IQR: 12,285 - 88,000), with 22.6% having a VL of >100,000 copies/ml. Of 196 patients retested 3 to 6 months after switching to second-line ART, 72.5% re-suppressed to < 1,000 copies/ml, and an additional 11.7% had a ≥1.0 log drop in VL. At the most recent test, 72.9% had a VL < 1,000 copies/ml. Of those who initially re-suppressed and had a subsequent VL test, 17.7% had viral rebound. Patients were significantly less likely to re-suppress if they were < 15 years old (adjusted risk ratio [aRR]: 2.56; 95% CI: 2.00 - 3.28); female (aRR: 1.57; 95% CI: 1.23 - 2.01); had an initial VL ≥50,000 copies/ml versus < 10,000 copies/ml (aRR: 1.67; 95% CI 1.10 - 2.54); or switched < 3 years versus
3 - 5 years after starting ART (aRR: 1.63; 95% CI: 1.25 - 2.13).
Conclusions: Although the majority of patients responded to second-line ART, a sizeable minority had an inadequate response. This illustrates the importance of ongoing VL monitoring and adherence counselling for patients on second-line ART. Children and adolescents are at particular risk of ongoing adherence challenges, resulting in a poor response to second-line ART.

Scale up of point-of-care technologies

MOPED700

Effects of clinical flow and patient initiation mentorship on point-of-care CD4 testing

S. Procter[1], T. Magombo[1], R. Mwenda[2], J. Kandulu[2]
[1]Clinton Health Access Initiative (CHAI), Lilongwe, Malawi, [2]Malawi Ministry of Health, Diagnostics Division, Health Technical Support Services, Lilongwe, Malawi
Presenting author email: sprocter@clintonhealthaccess.org

Background: Malawi has scaled-up Point-of-Care (POC) CD4 testing to 122 publicly operated health facilities covering 34% of the pre-ART cohort. Using a training-of-trainers approach over 500 health workers were trained in 2013. However, the patient flow and support systems to maintain a decentralized laboratory network are only now being developed through guidance on health facility level best-practices and regular mentorship visits.
Methods: Biannual mentorship visits reached over 97% of facilities offering on-site POC CD4 in 2014. Trained laboratory technicians from the district health office traveled to health facilities for a day-long site visit, which included observation of sample collection and processing, a careful examination of documentation for patient initiation on ART, and corrective actions, as needed. The mentors used a five-page assessment tool to capture key data, including testing volumes, clinical integration, technical use of POC CD4 devices, and patient care. Data from the two rounds of POC CD4 mentorship were analyzed in Excel.
Results: Overall, 97% of patients with CD4 < 350 received a test result and were initiated on treatment. After the first round of mentorship there was a 19% reduction in the average days elapsed between CD4 result and ART initiation, demonstrating improved turn-around-time (TAT). The TAT dropped from 7.98 days to 6.46 days. For patients with CD4 > 350 only 79% of POC CD4 results were accurately documented in patient records, with the same proportion scheduled for a subsequent visit. However, this result may be indicative of POC CD4 sites acting as hubs for patients at nearby health facilities, who seek testing services, but then return to their nearest facility to receive HIV care and treatment.
Conclusions: POC CD4 testing offers significant benefits to patients through increased access to CD4 testing, however maximum benefits cannot be realized without careful consideration for patient flow at the health facility level and regular mentorship to ensure that all POC CD4 results are well documented, clinically relevant, and used to improve patient care. Any implementation of POC CD4 should make provisions for these factors, especially to achieve the 90-90-90 targets laid out in the Diagnostics Access Initiative (DAI).

MOPED701

Effect of PIMA point of care instruments for CD4 counting on time to ART initiation in rural Botswana

M. Moyo[1], L. Mupfumi[2], T. Matsuokwane[1], T. Mogashoa[1], M. Mine[1], K. Mugisha[3], L. Tsalaile[3], T. Gaolathe[1]
[1]Botswana Harvard AIDS Institute Partnership, Master Trainer Program, Gaborone, Botswana, [2]Botswana Harvard AIDS Institute Partnership, Clinical Trials Unit, Gaborone, Botswana, [3]ACHAP, Tutume Treatment Optimization Pilot, Gaborone, Botswana
Presenting author email: mulamulimoyo@yahoo.com

Background: Point of care (POC) CD4 platforms have the potential to reduce delays in linkage to care and antiretroviral therapy (ART) initiation. We implemented the PIMA POC technology in Tutume, north of Botswana and determined the impact on time to ART initiation.
Methods: PIMA testing was introduced at 6 rural clinics in Tutume in August 2013 as part of a treatment optimization strategy to improve care for HIV-infected patients. Electronic data records of patients initiating ART at the clinics were reviewed to determine the impact of POC testing on time to ART initiation. Data on time to ART initiation were collected and compared between the periods prior to and following PIMA implementation.
Results: A total of 400 records were reviewed for patients initiating ART between Jan 2013 and Feb 2014. The proportion of patients initiating ART was higher in the post-PIMA period (57% vs. 43%; p=0.01). The median time from CD4 testing to ART initiation decreased from 24 days (IQR 12-41) to 20 days (IQR 10-35; p=0.07) in the pre- and post- PIMA periods respectively. The time to ART initiation was significantly reduced in newly diagnosed patients; 16 days (IQR 9-27) post-PIMA compared to 26 days (IQR 14-53; p=0.01) pre-PIMA. This was as a result of a significantly reduced time from HIV diagnosis to CD4 testing form 5 days (IQR 1-16) to 0 days (IQR, 0-5; p< 0.001).
Conclusions: Point of care CD4 testing significantly reduces the time to ART initiation for newly diagnosed patients. It therefore has the potential to improve retention of patients in ART programs.

Scale up of viral load monitoring

MOPED702

Is CD4 monitoring needed where there is routine viral load? A cohort analysis from Kibera, Kenya

W. Kizito[1], B.B. Ngoy[1], H. Ritter[1], W. Etienne[2], K. Kranzer[3], H. Bygrave[4]
[1]Medecins Sans Frontieres, MSF Nairobi Kenya, Nairobi, Kenya, [2]Medecins Sans Frontieres, Brussels, Belgium, [3]London School of Hygiene and Tropical Medicine, London, United Kingdom, [4]Medecins Sans Frontieres, Southern Africa Medical Unit, Cape Town, South Africa
Presenting author email: helen.bygrave@joburg.msf.org

Background: In 2013, WHO recommended viral load (VL) monitoring as the strategy of choice for patients on ART, and it has been suggested that CD4 monitoring may be stopped. There is, however, little data on the safety of this approach from resource-poor settings. In a retrospective cohort study we aimed to determine the safety of VL monitoring alone in an MSF ART programme in Kibera, Kenya.
Methods: Data was extracted from an electronic patient database. Adult patients >15 years initiated on ART between January 2011 and December 2012, with paired VL and CD4 data (interval +/-90 days) at months 12 and 24 were included in the analysis. Routine VL was performed yearly and CD4 6-monthly. VL was tested on plasma samples using the Roche platform.
Results: 794 (63%) and 194 (60%) of those remaining in care at months 12 and 24 received a paired CD4 and VL test; 70% were female. At baseline, median age was 32 years (IQR 27-40) and CD4 258 cells/mm^3 (IQR 138-337). 265 (33%) had baseline CD4 < 200 cells/mm^3. Of

those with sequential VL < 1000 copies/mL, 601 (85%) and 169 (90%) maintained CD4 >200 cells/mm^3 at months 12 and 24, respectively. Of those with baseline CD4 >200 cells/mm^3 who remained suppressed < 1000 copies/mL, nine (2%) dropped below 200 cells/mm^3 at month 12 (zero at month 24). Of these nine patients, three were retested at month 24 with a viral load < 1000 copies/mL and two returned to >200 cells/mm^3. Of the 133 (50%) whose CD4 increased to >200 cells/mm^3 at month 12, and remained virologically suppressed, 27/31 tested (87%) remained >200 cells/mm^3 at month 24.

Conclusions: When virologically suppressed at < 1000 copies/mL, most patients maintained CD4 >200 cells/mm^3. As more patients are enrolled at higher CD4 counts this proportion is likely to increase. Of those with baseline CD4 >200 cells/mm^3, only a very small proportion had a subsequent low CD4 count, in line with previous findings. Our results suggest it could be safe to stop routine CD4 in such settings where there is access to routine VL.

MOPED703

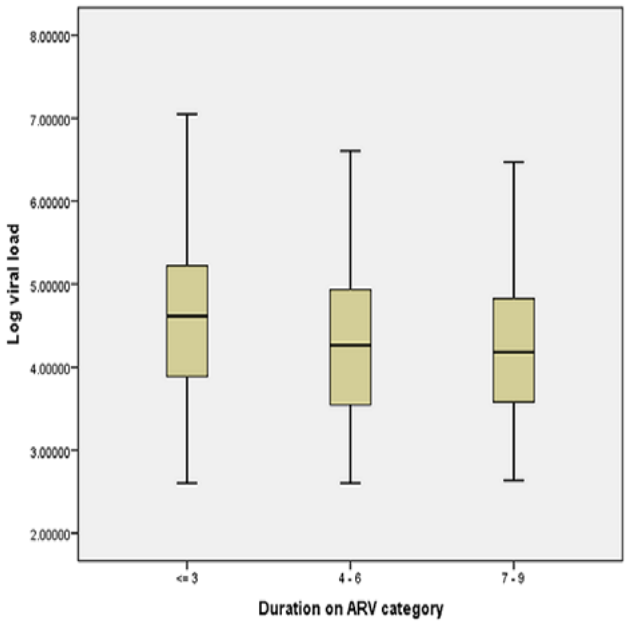
Introduction of viral load in routine settings in Kenya: implications for programs

J. Sunguti Luke[1], A. Gohole[1,2], M. Kitheka[1,2], M. Mudany[1,2], P. Munyao[1,2], P. Gathii[1], S. Bii[3], L. Karimi[4]
[1]APHIAplus Kamili, Embu, Kenya, [2]JHPIEGO, Nairobi, Kenya, [3]USAID, Nairobi, Kenya, [4]Ministry of Health, Meru County, Meru, Kenya
Presenting author email: mkitheka@aphiapluskamili.org

Background: Routine laboratory monitoring is part of the basic care package offered to people living with HIV. In line with WHO recommendations, Kenya has adopted the use of viral load tests to monitor patients on antiretroviral therapy (ART). This study describes viral suppression among patients on ART suspected to have had treatment failure in Eastern and Central Kenya, where the USAID-funded APHIA*PLUSK*AMILI project supports HIV services. Indications for viral load testing included clinical failure (new or recurrent WHO stage 3 or 4 disease) and immunological failure (CD4 fall by >30% from peak or failure of CD4 count to rise to > 100 cells/mm^3 after 12 months of ART).

Methods: A retrospective, cross sectional analysis of patient data collected between January 2013 and June 2014. The main outcome variable of interest was viral suppression, defined by the Kenyan Ministry of Health as VL < 1000 copies/ml. Blood samples were collected as DBS (90%) or frozen plasma (10%). These were analysed by the Standard Roche COBAS(®) Amplicor™ HIV-1 Monitor(®) Test and Abbott HIV-1 RealTime™ assay. Statistical analysis was conducted using the software SPSS v20 for Windows, with an alpha value of .05 used to indicate significance.

Results: Of the 27,418 patients on ART, 1,375 (aged between 2 and 80 years) were suspected to have treatment failure and were analysed for viral load. 597 (43%) patients had viral suppression. The median viral load was 3,317 (IQR 0-47,547). Patients aged below 40 years and those with ≤ 3 years on ARVs



[Duration on ARVs (yrs)]

were associated with a high viral load (p < .001 and p < .01 respectively). Sex of the patient and ARV combination were not associated with the viral load.

Conclusions: Viral suppression in patients suspected to have had treatment failure is significant. This study brings out the discrepancy between clinical, immunological and viral load monitoring. In line with WHO recommendations, viral load test is important in patients on ART as it identifies genuine treatment failure, minimizes unnecessary switching leading to reduced costs and high quality care.

MOPED704

Adaptive viral load monitoring for second-line ART in Côte d'Ivoire: cost-effectiveness and budget impact analysis

E.N. Ouattara[1,2], S.P. Eholié[1,3], M. Robine[4], R.L. MacLean[4], R. Moh[1,3], E. Losina[4,5], D. Gabillard[2], A.D. Paltiel[6], C. Danel[1,2], R.P. Walensky[4], X. Anglaret[1,2], K.A. Freedberg[4,7]
[1]Programme PAC-CI/ANRS Research Site, CHU de Treichville, Abidjan, Cote D'Ivoire, [2]Centre Inserm 897, University of Bordeaux, Bordeaux, France, [3]Treichville University Hospital, Department of Infectious and Tropical Diseases, Abidjan, Cote D'Ivoire, [4]Massachusetts General Hospital, Harvard Medical School, Divisions of General Internal Medicine and Infectious Disease and Medical Practice Evaluation Center, Boston, United States, [5]Brigham and Women's Hospital, Harvard Medical School, Department of Orthopedic Surgery, Boston, United States, [6]Yale School of Medicine, New Haven, United States, [7]Harvard TH Chan School of Public Health, Department of Health Policy and Management, Boston, United States
Presenting author email: nindougou@gmail.com

Background: Routine HIV viral load monitoring is recommended by the WHO to optimize outcomes of second-line antiretroviral therapy (ART) in sub-Saharan Africa. We evaluated the cost-effectiveness and budget impact of new viral load monitoring strategies in Côte d'Ivoire.

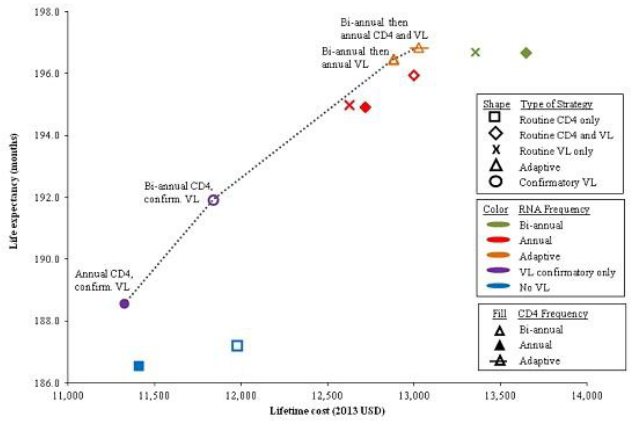
Methods: We used the Cost-Effectiveness of Preventing AIDS Complications (CEPAC) International Model to compare clinical outcomes, costs, incremental cost-effectiveness ratios (ICERs), and 5-year budget impact of 11 laboratory monitoring strategies in patients on or initiating ART from 2013-2018. We varied viral load testing availability and frequency and considered "adaptive" strategies, where testing frequency decreased from bi-annual to annual in patients virologically suppressed after one year. We assumed that a 6-month adherence intervention was performed before switching any regimen if laboratory tests suggested ART failure. Mean age of the cohort was 40 years, viral load cost was $33, and annual first- and second-line ART costs were $123 and $391, respectively. The current standard of care (SOC: bi-annual CD4 testing) served as the basis of comparison. We used the 2013 per-person GDP in Côte d'Ivoire ($1,530) to define "cost-effective." In sensitivity analyses, we evaluated parameter uncertainty.

Results: Projected discounted life expectancy for the SOC strategy was estimated at 187.2 months; mean time to observed first-line ART failure was 104.2 months (Table). Adding confirmatory viral load increased survival to 191.9 months, increased time to first-line failure to 124.8 months, and was cost-saving compared to SOC. Adaptive viral load monitoring alone increased survival to 196.5 months (ICER: $2,800/YLS) and increased the 5-year budget by $39 M (7.7%) compared to SOC. Adaptive monitoring with CD4 and viral load had an ICER of $4,600/YLS compared to viral load alone (Figure). In sensitivity analyses, the adaptive viral load strategy was budget neutral if viral load cost was reduced by 30% or if annual second-line ART cost was reduced by 10%.

Conclusions: Using viral load to confirm failure by CD4 criteria will be cost-saving in Côte d'Ivoire. Adaptive viral load monitoring, with or without CD4 testing, will be cost-effective by GDP criteria. With modest reductions in either viral load or second-line ART costs, routine adaptive viral load monitoring would improve outcomes without increasing costs.

	Cost-effectiveness			ART regimen		Budget impact over 5 years	
	Discounted life expectancy (months)	Discounted lifetime cost (USD)	ICER (USD/YLS)	Mean time to observed 1st-line failure	% Virologically suppressed at 5 years	Cost (million USD)	% Budget increase
Annual CD4 with confirmatory viral load	188.6	11 320	--	132.6	73.9	485	-4.0
Bi-annual CD4 with confirmatory viral load	191.9	11 840	1,800	124.8	75.5	502	-0.8
Bi-annual CD4 (Standard of care - SOC)	187.2	11 980	Dominated	104.2	72.6	506	Ref.
Adaptive: bi-annual then annual viral load	196.5	12 880	2,800	97.0	82.2	545	7.7
Bi-annual CD4 and annual viral load	196.0	13 000	Dominated	98.9	81.7	539	6.5
Adaptive: bi-annual then annual CD4 and viral load	196.8	13 030	4,600	97.2	82.4	551	9.0
Bi-annual viral load alone	196.7	13 350	Dominated	95.5	82.7	559	10.6
Bi-annual CD4 and viral load	196.7	13 650	Dominated	95.3	82.7	572	13.0

[Outcomes of selected monitoring strategies]



[Efficient frontier for all monitoring strategies]

MOPED705

Introduction of a routine viral load algorithm in rural Zimbabwe: programmatic strategies for implementation and impact on second line needs

Y. Htung Naing[1], H. Bygrave[2], S. Simons[1], D. Munyaradzi[1], C. Metcalf[2], T. Roberts[3]
[1]Medecins Sans Frontieres, Harare, Zimbabwe, [2]Medecins Sans Frontieres, Southern Africa Medical Unit, Cape Town, South Africa, [3]Medecins Sans Frontieres Access Campaign, Geneva, Switzerland

Background: In 2012, routine viral load (VL) monitoring was implemented among 14,000 patients on antiretroviral therapy (ART) in 26 clinics in Buhera district Zimbabwe, assisted by a mobile mentorship team. Dried blood spots were tested using the bioMérieux NucliSENS assay. Patients with a VL >1,000 copies/ml received enhanced adherence counselling (EAC), including completion of a high viral load form and VL repeated after three months. Those with a persistently high VL were switched to second-line ART. Implementation of the algorithm was assessed in 2014.
Methods: Data were extracted from patient folders, electronic medical records, counselling registers and a laboratory database, and combined to assess adherence to the VL algorithm between March 2013 and September 2014. Virological outcomes were further assessed by patient age and time on ART.
Results: 4661 patients were included in the analysis. Coverage of routine annual VL testing was 92.0%. Of those tested in the previous year, 13.9 % had a VL >1000 copies/ml. A VL >1000 copies/ml was more common in children < 15 years (32.3 %; 95% CI: 29-35%) than those aged ≥15 years (14.0 %; 95%CI: 13-15%), but showed little variation by time on ART (13.8% at 3 months, 14.9% at 12 months, 15.3% at 24 months, and 12.3% at 36 months on ART). Of those eligible, 57.4 % had documented evidence of EAC and 67.8% had a repeat VL test. Of those retested, 43.1% re-suppressed, and 36.9 % (1.1 % of all those tested) were switched to second-line ART.
Conclusions: Routine VL testing is feasible in resource-limited settings. Monitoring and evaluation of adherence to the VL algorithm is essential in order to ensure appropriate response to high VL results. Essential components of implementation include patient education, clinician training on the VL algorithm, task-shifting of sample preparation, provision of EAC, and decentralisation of access to second-line ART.

National and international financing initiatives

MOPED706

HIV prevention research & development funding trends 2000-2014: investment priorities to fund innovation in an evolving global health and development landscape

E. Donaldson[1], K. Fisher[1], T. Harmon[2], P. Harrison[1], J.A. Izazola-Licea[3], D. Mattur[3], A. Naeveke[2], M. Warren[1]
[1]AVAC, New York, United States, [2]International AIDS Vaccine Initiative, New York, United States, [3]UNAIDS, Joint United Nations Programme on HIV/AIDS, Geneva, Switzerland
Presenting author email: edonaldson@avac.org

Background: Since 2004, the HIV Vaccines and Microbicides Resource Tracking Working Group has employed a comprehensive methodology to track trends in research and development (R&D) investments and expenditures for biomedical HIV prevention, including HIV vaccines, microbicides, PrEP, treatment as prevention and medical male circumcision.
Methods: Data were collected on annual disbursements by public, private and philanthropic funders for product development, clinical trials and trial preparation, community education and policy advocacy efforts to estimate annual investment and expenditure in HIV prevention R&D. Investment trends were assessed and compared by year, prevention type, research phase, funder category and geographic location.
Results: The Working Group collated and analyzed 2014 data for all areas of HIV prevention R&D. In contrast to the broader context of slight year-to-year increases in funding for international development and health research, funding for HIV prevention R&D overall continued to decline, although this trend did not consistently apply to all funders, sectors or technologies. US investment in HIV R&D continued a flat trend, but European public sector funding increased slightly under the European Union's recently launched Horizon 2020 initiative. Public sector research agencies increased support for HIV prevention R&D, with larger investments by several middle-income countries suggesting a potentially critical shift. Philanthropic support for HIV prevention R&D continued a decline that began several years ago. Commercial-sector funding saw a nominal increase.
Conclusions: Monitoring HIV prevention R&D investment trends permits identification of investment needs, prioritization of research areas and assessment of the impact of public policies that increase or decrease investment. Investment data also supports the fact base for advocacy around spending levels, resource allocations and messages around the value of sustained investments in the research required to build on the success of recent trials, bring novel HIV prevention candidates into the pipeline and support follow-on clinical trials to assure the safety, immunogenicity, efficacy and acceptability of new HIV prevention products. As United Nations negotiations toward updated global development goals proceed, articulating the value of HIV prevention research investments in the wider context of public, private and philanthropic funding priorities will be increasingly important to ensure continued support for the development of new prevention technologies.

Transitional financing

MOPED707

Planning for the transitioning of PEPFAR investments to Government in Nigeria: Kwara State experience

E. Atuma[1], A. Ayinla[2], S. Akande[1], S. Faramoju[3], J. Ezekiel[4], M. Salami[1]
[1]Management Sciences for Health, HSS, Abuja, Nigeria, [2]Kwara State Ministry of Health, Ilorin, Nigeria, [3]Management Sciences for Health, Abuja, Nigeria, [4]USAID Nigeria, HIV and AIDS Treatment and Care, Abuja, Nigeria
Presenting author email: atumaemma@yahoo.com

Background: A range of clinical, systems strengthening and community services are supported by PEPFAR to ensure quality care and support for persons living with HIV (PLHIV). In its program review for Nigeria early 2014, PEPFAR indicated that it will transition clinical chemistry, hematology laboratory tests and maintain a cap on ART enrollments in states with lower than national prevalence rates. One of these states is Kwara with a HIV prevalence rate of 1.4% as against the National prevalence of 3.4% (NARH2012). USAID Nigeria, through Management Sciences for Health (MSH), supported Kwara State to implement a model for incremental transitioning of PEPFAR investments to governments at sub-national level.
Methods: Using an ART treatment and care transition capacity assessment tool, MSH assessed Kwara state's readiness capacity across seven domains: leadership, policy, systems, quality of care, infrastructure and resources, fiscal management and partnership.
MSH with stakeholders developed a costed transition strategic plan that highlights the current

PEPFAR support with specific activities that will transition these support to the state institutions and communities in phases.
The plan included information on actual cost of services, forecasting of donor funding, and its projected decline as it impacts on life saved and gained. Based on this information, the ministry and stakeholders mapped alternative resources. These were presented to both the legislative and executive arms of government for their action and resource allocation.
Results: The state scored an aggregate of 37%, which is stage 2 (16-40%) on the tool representing basic capacity on the readiness assessment.
Kwara State government allocated special funds for 2015 fiscal year to the tune of $2.3m in its budget to support HIV services that were previously financed by PEPFAR.
Conclusions: HIV and AIDS services in the state can continue without disruption even after the transition of donor funding. However, ongoing dialogues between donors and host government are needed to sustain continuous HIV and AIDS service delivery within a context of mutual accountability and transparency.

Leveraging HIV funding to strengthen health systems beyond HIV programmes

MOPED708

Leveraging HIV funding to strengthen health systems beyond HIV programs: a case of infrastructural improvements in East Central Uganda

E. Kazibwe[1], S. Mashate[2], M. Kagugube[3], A. Mugume[4]
[1]JSI Research & Training Institute, Inc./STAR-EC Program, Finance & Administration, Kampala, Uganda, [2]STAR-EC, Technical Programs, Jinja Municipality, Uganda, [3]JSI Research & Training Institute, Inc./STAR-EC Program, Finance & Administration, Jinja Municipality, Uganda, [4]JSI Research & Training Institute, Inc., Jinja Municipality, Uganda
Presenting author email: ejkazibwe@live.com

Background: In Sub-Saharan Africa, health infrastructure poses a big challenge for health services delivery. As a result, community access to basic prevention, diagnosis and treatment of common illnesses such as malaria, TB, sexually transmitted infections is limited. Lack of infrastructure correlated with a shortage of health workers and the limited availability of basic medical equipment have resulted in patients trekking long distances to reach health facilities. Utilizing HIV&AIDS funding has become a critical avenue through which critically needed infrastructure can be provided as a contribution to health systems strengthening.
Methods: The Strengthening TB and HIV&AIDS Responses in East Central Uganda (STAR-EC) Programme with funding from USAID supported the installation of solar power generation sets including solar panels, batteries, and inverters at 18 health facility laboratories. Availability of power supply enabled these health facilities acquire laboratory equipment like point of care machines, microscopes, refrigerators for storage of blood among other health supplies. These have strengthened the onsite diagnostic capacity for TB, malaria, other opportunistic infections related to HIV&AIDS. To further enhance biosafety, the program also constructed placenta pits at 15 high volume sites for disposal of highly infectious bio-medical waste to protect the health workers, patients and surrounding communities from infectious pathogens.
Results:
· Sites with functional laboratories increased from 66 (75%) sites in 2010 to 85 (100%) sites in 2014 following the intervention
· For the period Oct 2010 to Sept 2014, 2,265,197 HIV antibody tests were performed, a further 17,256 DNA PCR tests were done with a confirmed positivity of 7.2%. This represented 1,205 exposed infants who were initiated on PMTCT/eMTCT
· Patient referral to tertiary sites for management of routine illnesses significantly reduced freeing health workers at referral hospitals to attend to more complicated illnesses
· Encouraged by the presence of this basic infrastructure other partners like the SCMS Project supported these sites with other equipment like hematology and clinical chemistry analyzers which improved the overall quality of health services provided.
Conclusions: In many resource constrained environments, utilizing HIV&AIDS funding has become a critical avenue through which communities can receive health resources hitherto thought impossible. The results above represent this fact succinctly.

Monitoring and evaluation of testing

MOPED709

Two-year performance of an early infant diagnosis program in rural north-central Nigeria

F. Yunusa[1], B. Harry-Erin[2], H. Swomen[1], C. Chime[3], H. Isah[4], F. Murtala-Ibrahim[2], P. Dakum[5,6], N.A. Sam-Agudu[5,6]
[1]Institute of Human Virology Nigeria, Community Department, Abuja, Nigeria, [2]Institute of Human Virology Nigeria, Strategic Information Department, Abuja, Nigeria, [3]Institute of Human Virology Nigeria, Molecular Laboratory Department, Abuja, Nigeria, [4]Friends in Global Health, Abuja, Nigeria, [5]Institute of Human Virology Nigeria, Clinical Department, Abuja, Nigeria, [6]University of Maryland Baltimore, Institute of Human Virology Epidemiology and Prevention, Baltimore, United States
Presenting author email: hswomen@ihvnigeria.org

Background: Prevention of mother-to-child transmission of HIV (PMTCT) in Nigeria has been challenging: only 3.9% of HIV-Exposed Infants (HEI) receive early infant diagnosis (EID), and >50,000 HEI acquire HIV annually, at an MTCT rate of ~30%. PMTCT scale-up is focusing on Primary Healthcare Centers (PHCs) in rural areas, where access, uptake and retention are especially low. This study was conducted to evaluate EID performance at PHCs in rural North-Central (NC) Nigeria.
Methods: This retrospective study examined a database of HEI receiving virologic HIV testing in a 2yr period (Oct. 2011 to Sept. 2013) at rural PHCs. These PHCs, located in 4 of the 7 NC states, had undergone integration of PMTCT services with antenatal care. HEI data (including testing age and results) from PHCs in Benue, Federal Capital Territory, Nasarawa, and Niger states were analyzed. "Population" EID coverage was calculated as no. HEI tested by age 2 months/all HEI (the true definition of EID coverage per the WHO). "Program" EID coverage was defined as no. HEI tested by age 2 months/all HEI who received testing. Chi square test was used to compare proportions.
Results: Data from 723 infants out of 2,543 expected HEI births at 127 PHCs were reviewed. Overall MTCT rate was 3.8%. MTCT rate in Yr 2 (3.0%) was lower than in Yr 1 (7.4%), p=0.02. Overall, "population" EID coverage was 19%; Yr 2 coverage (23.9%) was higher than Yr 1 (9.4%), p< 0.0001. Further results are displayed in Table 1.

Two-Year EID Program Performance at PHCs in 4 North-Central Nigerian States

HEI Characteristic	N evaluated	N (%)
Gender, Female	757	375 (49.5%)
Mother received PMTCT services	661	609 (92.1%)
No. HEI breastfeeding	691	647 (93.6%)
"Program" EID coverage: denominator = all HIV-exposed infants who received virologic testing		
Age at sample collection	723	Less than or equal to 2 months: 472 (65.3%) Greater than 2 months: 251 (34.7%) Median age of infants presenting at greater than 2 months: 5.5 months (3.0 to 8.0)
No. HEI HIV-positive	756	29 (3.8%)
"Population" EID coverage: denominator = all HIV-exposed infants expected		
Age at sample collection	2,543	Less than or equal to 2 months 472 (19.0 %)

[EID Program Performance at PHCs in NC Nigeria]

Conclusions: MTCT rates in our rural EID program were lower than national, with a significant reduction from Yr1 to Yr2. Population EID coverage (19%) was higher than national, with a marked improvement between Yr1 and 2, however, this was far below the 80% national target. There was a large drop-off between numbers of expected and tested HEI; likely due to death, loss to follow-up or transfers of care. Program EID covergae (65.3%) was closer to national target, suggesting more focus on reducing early HEI dropout in PMTCT. Client education, community tracking and inter-facility linkage should be strengthened to improve retention and timely HEI testing.

MOPED710

The cost of providing rapid HIV testing for screening men who have sex with men in new community sites compares favorably with established clinics in Sydney, Australia

D.P. Conway[1,2], P. Keen[1], M.S. Jamil[1], D.P. Wilson[1], A.E. Grulich[1], M. Holt[3], A. McNulty[4,5], J. Lockwood[4], D.L. Couldwell[6,7], A. Townsend[6], K. Price[8], J. Gray[8], R. Finlayson[1,9], C. Pell[1,9], P. Cunningham[10,11], R. Guy[1], NSW Rapid HIV Testing Evaluation Framework
[1]The Kirby Institute, University of New South Wales, Sydney, Australia, [2]Short Street Centre, St George Hospital, Kogarah, Australia, [3]Centre for Social Research in Health, University of New South Wales, Sydney, Australia, [4]Sydney Sexual Health Centre, Sydney Hospital, Sydney, Australia, [5]School of Public Health & Community Medicine, University of New South Wales, Sydney, Australia, [6]Western Sydney Sexual Health Centre, Western Sydney Local Health District, Sydney, Australia, [7]The Marie Bashir Institute for Infectious Diseases and Biosecurity, University of Sydney, Sydney, Australia, [8]AIDS Council of NSW, Sydney, Australia, [9]Taylor Square Private Clinic, Sydney, Australia, [10]St Vincent's Centre for Applied Medical Research, University of New South Wales, Sydney, Australia, [11]NSW State Reference Laboratory for HIV, St Vincent's Hospital, Sydney, Australia
Presenting author email: dconway@kirby.unsw.edu.au

Background: Rapid HIV testing (RHT) is well established in many countries, but is relatively new in Australia. We compared the cost of providing RHT with the Trinity Uni-Gold assay for screening men who have sex with men (MSM) in new community-based sites versus existing clinical sites in Sydney.
Methods: During the study period (October 2011-June 2014), RHT was delivered at five sites: two new community sites (fixed and temporary), two established public sexual health clinics (SHCs) and a gay-friendly general practice clinic (GPC). SHCs delivered RHT in both express and general clinical sessions (shorter screening consults with enrolled nurses and longer consults with nurses and doctors for symptomatic patients, respectively). RHT was delivered by peer workers and nurses at community sites and by doctors and nurses at the GPC. We calculated RHT cost per patient tested and cost per HIV-positive case diagnosed for each site/session type. Costs incurred by the health system were collated, including: consult length, staff salary, government (Medicare) rebates, RHT kits, confirmatory laboratory HIV testing for reactive rapid tests and sexually transmitted infection testing. Costs of initial staff training were excluded. Weighted average HIV test positivity and RHT costs across all sites were calculated using numbers of MSM tested and confirmed HIV-positive cases at each site.
Results: Average HIV positivity was 1.01% among 8143 MSM tested across all sites (see table). RHT cost more per patient tested at community sites than SHC express sessions, but less than in SHC general and GPC sessions. Cost per positive case was lowest at the community temporary site, followed by central SHC express, GPC and community fixed site sessions. RHT delivery costs at community sites were comparable to or less than the weighted average for cost per patient and cost per positive case. Overall, costs were lower if nurses and peer workers delivered RHT during shorter consults.

Site (session)	Staffing	HIV positivity	Cost per patient*	Cost per positive case*
General Practice clinic	Doctor/nurse	1.57%	$198	$12589
Suburban SHC (general)	Doctor/nurse	0.74%	$134	$18146
Central SHC (general)	Doctor/nurse	0.94%	$130	$13745
Community temporary	Peer/nurse	2.06%	$122	$5931
Community fixed	Peer/nurse	0.89%	$114	$12900
Suburban SHC (express)	Nurse	0.74%	$108	$14661
Central SHC (express)	Nurse	0.94%	$105	$11163
Weighted average		1.01%	$123	$12190
SHC=sexual health clinic; *Australian dollars				

[Staffing, HIV positivity & costs by site]

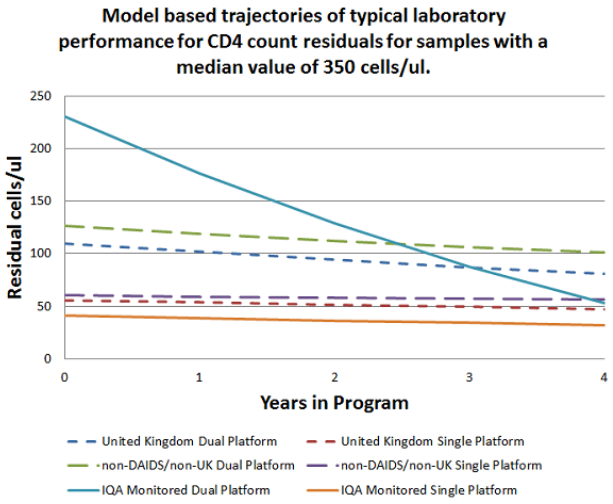
Conclusions: RHT cost per patient tested was lowest in SHC express sessions and community sites. Due to their higher observed HIV positivity, community-based and GPC sites compared favorably to SHCs regarding cost per positive case. These findings should inform decision-making regarding RHT implementation in other locations and services.

MOPED711

IQA/UK NEQAS EQA participation and accuracy of patient monitoring in clinical trial networks

J. Bainbridge[1], W. Rountree[1], R. Louzao[1], J. Wong[1], L. Whitby[2], T. Denny[1], D. Barnett[2]
[1]Duke University, Duke Human Vaccine Institute, Durham, United States, [2]UK NEQAS for Leucocyte Immuophenotyping, Sheffield, United Kingdom
Presenting author email: john.bainbridge@duke.edu

Background: United Kingdom National External Quality Assessment Service for Leucocyte Immunophenotyping Immune Monitoring Program (UKNEQAS), an ISO 17043 accredited proficiency testing program, provides external quality assessment (EQA) to non-U.S. laboratories affiliated with the NIH Division of AIDS (DAIDS) clinical trials networks. Such laboratories are required to participate in UKNEQAS with oversight, performance monitoring and remediation undertaken by Immunology Quality Assessment (IQA) staff, under DAIDS contract. Using data from November 2003 to September 2014, the first four years EQA participation of each of the 1242 laboratories was examined. Up to 65,297 data points were analyzed to determine if longer EQA participation was associated with improved laboratory accuracy.
Methods: Laboratory accuracy, defined as residuals from respective trial sample medians, was measured on four outcomes: CD4 counts (cells/ul) and percentages plus CD8 counts (cells/ul) and percentages. Three laboratory categories were defined: IQA monitored (n=149), United Kingdom/non-DAIDS (n=137), and non-DAIDS/non-UK (n=1035). Four longitudinal mixed models were fit with polynomials of program participation duration together with selected covariates. The fixed effects were used to generate trajectories for each of the four lymphocyte subset residuals in each laboratory category. For count outcomes, the groups were subdivided into single platform (SP) and dual platform (DP).
Results: Improvement in accuracy was found for all outcomes ($p < 0.0001$). IQA monitored laboratories (particularly IQA DP absolute counting users for counts) improved most ($p < 0.0001$) across the board. For percentage and DP count outcomes, UK laboratories performed best at entry into the program ($p < 0.05$). For SP count outcomes there was no difference at entry by laboratory category. SP laboratories did better than the DP laboratories ($p < 0.0001$) initially for count outcomes. Figure 1 shows increasing accuracy (decreased CD4 count residuals) for all groups, but the IQA DP group showed the greatest improvement ($p < 0.0001$).



[Figure 1]

Conclusions: EQA participation coupled with effective laboratory monitoring and remedial action is strongly associated with improved laboratory accuracy. Improvement in accuracy provides more reliable information to clinical trials facilitating better patient treatment decisions. UK laboratories (predominately SP) have high levels of accuracy at EQA program entry and therefore have limited room for improvement.

MOPED712

"I did not see a need to get tested before. Everything was going well with my health": a qualitative study of HIV testing in KwaZulu-Natal, South Africa

S. Tariq[1], S. Hoffman[2,3], G. Ramjee[4], K. Blanchard[5], J. Mantell[2], J. Phillip[4], T. Exner[2], S. Dawad[6]
[1]University College London, Research Department of Infection and Population Health, London, United Kingdom, [2]NYS Psychiatric Institute, HIV Center for Clinical and Behavioral Studies, New York City, United States, [3]Columbia University, Mailman School of Public Health, New York City, United States, [4]South African Medical Research Council, HIV Prevention Research Unit, Durban, South Africa, [5]IBIS Reproductive Health, Cambridge, United States, [6]The Presidency, PSPPD, Pretoria, South Africa
Presenting author email: shema.tariq.2@city.ac.uk

Background: KwaZulu-Natal has the highest prevalence of HIV in South Africa (SA) at nearly 40%. In 2010 the government launched a national HIV counseling and testing campaign (HCT), later raising the threshold for antiretroviral therapy (ART) initiation. Limited qualitative data exists on HIV testing in SA, including the impact of the HCT on decision-making. We describe barriers to and facilitators of HIV testing among participants in Pathways to Care, a cohort study of newly-diagnosed HIV+ adults in Durban, KwaZulu-Natal.
Methods: We conducted semi-structured interviews with 26 cohort participants (13 women, 13 men, median age=28 years), within one month of diagnosis, in 2012. Interview data were analyzed thematically and coded in NVivo. Coded text was compared across interviews to develop broader categories, and consensus was reached among the research team regarding the emergent explanatory framework.
Results: Less than half (n=12) of participants reported that they were aware of the HCT, and it was rarely cited as a major influence in decisions to test for HIV. Most participants (n=22) deferred testing until they had developed symptoms (many indicative of HIV), with only three directly seeking an HIV test when first developing symptoms. Instead, the majority of symptomatic participants consulted a variety of other medical professionals, local chemists, family members and traditional healers, which resulted in delayed HIV diagnoses.
Of the eleven symptomatic participants who made contact with medical services, only three reported that a healthcare professional offered or recommended an HIV test. Fear of death and HIV-related stigma were identified as other key barriers to testing. However, ART emerged as a fundamentally important motivator to test, offering the hope of health and normalcy.
Conclusions: Despite the large-scale 2010-2011 national HCT and the raised threshold for starting ART, most participants deferred testing until they had some symptoms. Efforts to encourage local health systems (including non-medical) to direct clients towards HIV testing, and continued expansion of HIV testing in medical services, may reduce testing delays. Future testing campaigns will benefit from a focus on the importance of testing when asymptomatic and the health-benefits of early ART.

MOPED713

Factors associated with low CD4+ count at diagnosis among patients enrolled in a prospective cohort study in KwaZulu-Natal, South Africa

S. Tariq[1], S. Hoffman[2,3], G. Ramjee[4], K. Blanchard[5], T. Exner[2], E. Kelvin[6], J. Phillip[4], N. Lince-Deroche[7,8], S. Dawad[9], J. Mantell[2], C.-S. Leu[2,3], R. Street[4], A. Gandhi[2]
[1]University College London, Research Department of Infection and Population Health, London, United Kingdom, [2]NYS Psychiatric Institute, HIV Center for Clinical and Behavioral Studies, New York City, United States, [3]Columbia University, Mailman School of Public Health, New York City, United States, [4]South African Medical Research Council, HIV Prevention Research Unit, Durban, South Africa, [5]IBIS Reproductive Health, Cambridge, United States, [6]CUNY, School of Public Health, New York City, United States, [7]IBIS Reproductive Health, Johannesburg, South Africa, [8]University of the Witwatersrand, Health Economics and Epidemiology Research Office, Johannesburg, South Africa, [9]The Presidency, PSPPD, Pretoria, South Africa
Presenting author email: shema.tariq.2@city.ac.uk

Background: At nearly 40%, KwaZulu-Natal has the highest HIV prevalence in South Africa (SA). Since the national government's April 2010-June 2011 HIV counselling and testing (HCT) campaign and the raising of the CD4+ threshold for antiretroviral therapy (ART) initiation to ≤350 cells/μl, there has been limited information on timing of HIV diagnosis in SA.
Methods: We analyzed data from Pathways to Care, a prospective cohort of 459 newly-diagnosed HIV-positive adults recruited from three public-sector clinics and interviewed between November 2010-May 2012. We restricted analysis to 282 (61.4%) participants who had a CD4+ blood draw within 4 months of HIV diagnosis, and self-reported the value of their first CD4+ count. Low CD4+ count was defined as CD4+ ≤350 cells/μl.
Results: Three-fifths (n=205) of participants were female; the median age was 30 years (interquartile range [IQR]: 18-52).
The majority of participants (60.9%, n=171) had not previously tested for HIV. Over 50% reported a CD4+ count ≤350 cells/μl at diagnosis; median CD4+ count was 318 cells/μl (IQR: 10-970). In multivariable analysis male sex and age ≥25 years were associated with late-stage diagnosis, whereas having ≥2 previous HIV tests was protective (Table 1).
Over the period of study enrolment, the proportion of participants presenting with low CD4+ count increased from 45.7% in the first 6 months (during the HCT) to nearly 70% in the last 6 months, after the HCT had ended (p=0.025). Over this same period, the proportion who had never previously tested for HIV increased from 51.6% to 73.7% (p=0.061).

Characteristic		Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI) adjusted for sex, age and recruitment clinic
Recruitment Period	Nov 2010 - Jun 2011	1	1
	Jul 2011 - Dec 2011	1.28 (0.75, 2.17)	1.22 (0.63, 2.38)
	Jan 2012 - May 2012	2.52 (1.26, 5.03)*	2.01 (0.91, 4.41)*
Sex	Female	1	1
	Male	1.77 (1.03, 3.03)*	1.80 (1.02, 3.17)*
Age	<25	1	1
	25-35	3.07 (1.59, 5.93)**	3.13 (1.60, 6.14)**
	>35	2.43 (1.13, 5.23)*	2.48 (1.13, 5.43)*
Previous HIV tests	None	1	1
	1	0.66 (0.36, 1.18)	0.79 (0.41, 1.50)
	≥2	0.34 (0.17, 0.65)**	0.36 (0.18, 0.72)**

CI, confidence interval; *p<0.05 **p<0.005

[Table 1: Factors associated with low CD4+ count]

Conclusions: Despite the recent implementation of more aggressive HIV prevention and control efforts in South Africa, over 50% of participants presented with CD4+ count ≤350 cells/μl.
Women and those who had ≥2 previous HIV tests were less likely to present late. The proportion presenting with low CD4+ count increased after the HCT ended, whereas the proportion reporting previous HIV tests declined. This may indicate that the HCT led to uptake of HIV testing by healthier individuals, but that this pattern was not sustained after the campaign ended. Continued testing campaigns and interventions, especially targeting men, are needed to encourage regular testing and prevent late diagnoses.

MOPED714

Increased counseling and testing visits are associated with remaining HIV uninfected

W. Wimonsate[1], S. Pattanasin[1], A. Sriporn[1], P. Luechai[1], K. Satumay[1], N. Tippanonth[1], N. Promda[1], T. Holtz[1,2], A. Chitwarakorn[3], E. Dunne[1,2]
[1]Thailand MOPH - U.S. CDC Collaboration, HIV/STD Research Program, Nonthaburi, Thailand, [2]Centers for Disease Control and Prevention, Division of HIV/AIDS Prevention, Atlanta, United States, [3]Ministry of Public Health, Department of Disease Control and Prevention, Nonthaburi, Thailand

Background: Voluntary counseling and testing (VCT) for HIV is provided for men who have sex with men (MSM) at the Silom Community Clinic @TropMed (SCC @TropMed) in Bangkok, Thailand. We assessed the number of VCT visits and other factors associated with remaining HIV uninfected over a nine-year period since the founding of the clinic.
Methods: At every HIV VCT visit at SCC @TropMed, MSM received a comprehensive counselling session, HIV transmission information, risk-reduction strategies, condoms and lubricants, and HIV and syphilis testing. Men had demographic information collected from self-registration and behavioral information collected by a counselor. We included MSM uninfected with HIV at baseline who received more than one HIV VCT from September 30, 2005 to August 30, 2014 in the analysis. Logistic regression was used to investigate factors associated with remaining HIV uninfected (having all HIV tests negative).
Results: There were 2,209 MSM for our analysis; the mean number of VCT visits was 3 (range 2-27 visits). Two-hundred-fifty-five men acquired HIV during the study period. In multivariable analysis, when adjusted for current residency, engagement in commercial sex work, and history of HIV testing, remaining HIV uninfected was associated with each additional VCT visit (Adjusted Odds Ratio [AOR] 1.8 for each visit, 95% Confidence Interval [CI] 1.6-2.1), repeating VCT within one year (AOR 2.3, 95% CI 1.8-3.1), being older (age ≥ 22 years old versus 14-21 years old) (AOR 1.8, 95% CI 1.3-2.6) and having a negative syphilis test result at first visit (AOR 2.5, 95% CI 1.6-3.9).
Conclusions: Characteristics of MSM remaining HIV uninfected and attending VCT provide insight into opportunities for HIV prevention. Because MSM with more and regular VCT visits, no syphilis infection, and older age were more likely to remain HIV uninfected, strategies to retain young MSM in comprehensive VCT, including STD testing and treatment, are needed.

MOPED715

Shaping care: a case study from Sierra Leone

A. Collins
Simon Fraser University, Faculty of Health Sciences, Vancouver, Canada
Presenting author email: alexandrab.collins@gmail.com

Background: The 'vertical' versus 'horizontal' debate to healthcare delivery and financing has been discussed globally, for decades. Over the past twenty years, research has detailed the negatives of a 'vertical' (i.e. disease-specific) approach, including program instability. Recently this delivery trajectory has shifted towards a 'diagonal' approach, which encourages gradual integration by strengthening the larger health system, while still working towards specific program goals. Current arguments suggest that 'diagonal' financing might be essential for maintaining HIV/AIDS treatment in low-income countries; however, donor conditionalities can create space for negative characteristics (i.e. instability) of 'vertical' programs, to manifest. This project critically analyzes donor expectations and conditionalities through an ethnographic account of HIV/AIDS programs and practices in Sierra Leone, focusing on the Global Fund, which provides 97% of the country's HIV/AIDS funding. The Global Fund has taken up Health Systems Strengthening (HSS) as a cross-cutting and 'diagonal' element to their funding approach. This move towards HSS in the global health community has simultaneously provoked a largely technocratic shift for programming efforts, with increased funding from donors to strengthen disease surveillance, data collection and reporting mechanisms.
Methods: Drawing on three months of multi-sited ethnographic fieldwork in Sierra Leone, I demonstrate how the realities of this technocratic push and conditionalities are challenging due to current infrastructure, increasing the administrative burden on HIV/AIDS program workers. From participant-observation in clinics, government agencies and multi-entity meetings, and semi-structured interviews with HIV/AIDS counselors and program officers, I show how donor expectations and stipulations have altered the perceptions and foci of many HIV/AIDS personnel, which can have detrimental outcomes.
Results: While recognizing the potential of 'diagonal' service delivery, the resulting technocratic push has shifted in-country focus to producing reports and digitizing data, rather than providing services. I argue that funding stipulations and expectations have transformed HIV/AIDS programs and practices into business-like transactions, limiting autonomous decision-making in Sierra Leone.
Conclusions: I conclude that closer examination needs to be paid to the 'friction' created between donor conditionalities and their implementation and influence on HIV/AIDS programs and practices using the particular Sierra Leonean context, encouraging more context-specific funding terms.

MOPED716

Trends in testing outside of traditional settings in England

L. Cieply, S. Collins, C. Penman, S. Mandal, S. Lattimore
Public Health England, Immunisation, Hepatitis and Blood Safety Department, London, United Kingdom
Presenting author email: lukasz.cieply@phe.gov.uk

Background: In 2012, it was estimated ~22% of people living with HIV were undiagnosed and 48% of adults were diagnosed late. BHIVA and BASHH guidelines highlight the importance of increasing HIV testing outside of traditional services. The sentinel surveillance of blood borne viruses collects data irrespective of test result, providing information on the population undergoing HIV testing at 15 sentinel laboratories.
Methods: Demographic and testing data for people tested for HIV between 2008 and 2012 were extracted in yearly testing cohorts. Duplicate records, reference testing, under 16's, and people tested via unknown locations were excluded. HIV positive individuals were excluded from analysis in subsequent years. GP services were linked to a dataset of all GP services across England to determine coverage.
Results: Overall 1,480,882 individuals were tested for HIV; of whom 0.9% tested positive. Half were tested in STI clinics (48.8%). Non-traditional settings accounted for a third of all testing (31.3%; n=463,827), with the number of individuals tested in NTS increasing 1.6-fold from 69,940 in 2008 to 112,033 in 2012, and the proportion positive declining from 1.1% to 0.8%. GP services accounted for one third (36.7%) of all NTS testing. Sentinel surveillance captures testing among 34% of all GP services, covering an estimated 20 million individuals. In 2008 48.8% of these GP services tested at least one individual for HIV, increasing to 54.6% in 2012. GP services tested 301 individuals per 100,000 population in 2008, increasing by two fifths to 425 by 2012. The greatest increase was in areas with a diagnosed prevalence of >2 per 1000 population, where testing rates increased by 49.4% (348 to 520 per 100,000 population) compared with 36.4% (288 to 393) in low prevalence areas, between 2008 and 2012. Despite an increase in testing among GPs, the proportion positive remained stable at between 0.5% and 0.6%.
Conclusions: Since 2008, there has been a 1.6-fold increase in HIV testing in NTS. Testing rates increased overall by one third across all GP services captured within the sentinel surveillance, mainly among those in high prevalence areas. These findings highlight the importance of HIV testing outside of traditional specialised sexual health services.

MOPED717

Impact of STOP HIV/AIDS program on HIV, hepatitis C and syphilis testing volumes in British Columbia

T.B. Consolacion[1], A. Yu[2], N.Z. Janjua[3,4], J. Wong[5], R. Barrios[6,7], J.S.G. Montaner[6,7], M. Krajden[2,8,9]
[1]British Columbia Centre for Disease Control, HIV/STI - Clinical Prevention Services, Vancouver, Canada, [2]British Columbia Centre for Disease Control, Hepatitis - Clinical Prevention Services, Vancouver, Canada, [3]British Columbia Centre for Disease Control, Vancouver, Canada, [4]University of British Columbia, School of Population and Public Health, Vancouver, Canada, [5]British Columbia Centre for Disease Control, Clinical Prevention Services, Vancouver, Canada, [6]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada, [7]University of British Columbia, Division of AIDS, Department of Medicine, Vancouver, Canada, [8]BC Public Health Microbiology and Reference Labratory, Vancouver, Canada, [9]University of British Columbia, Department of Pathology and Laboratory Medicine, Vancouver, Canada
Presenting author email: theodora.consolacion@bccdc.ca

Background: Diagnosing individuals living with HIV who are unaware of their HIV status provides an opportunity for health providers to engage clients into care, improving the outcomes for the client and reducing forward transmission. The STOP HIV/AIDS pilot was implemented in 2009, to increase population awareness of and testing for HIV. In 2013 the program was expanded province-wide. One of the indicators to assess the province's progress has been HIV testing volumes. Because of shared risk factors, HIV testing was expected to affect syphilis and hepatitis C (HCV) testing as well. We examine the trend in HIV, HCV and syphilis testing from 2006 (pre-STOP pilot) through 2014 in relation to the STOP implementation.
Methods: HIV, HCV, and syphilis testing data from 2006 to 2014 conducted at the Public Health and Microbiology & Reference Laboratory (PHMRL) in BC were analyzed. PHMRL conducts over 95% of HIV and HCV screening tests and over 99% of screening syphilis tests in BC. The data include tests where the resulting laboratory was PHMRL. A preliminary total of 1,838,765 HIV, 1,508,551 syphilis, and 1,387,123 HCV screening tests were included in the analyses.
Piecewise regressions were used to evaluate the trend in testing volumes before and after STOP implementation with calendar year and month predicting number of tests for each screening test type. The change points were estimated through the model.
Results: A significant change in testing trends for syphilis, HCV and HIV occurred between 2011 and 2012 based on model predicted change points. Preliminary analyses show that HIV testing increased significantly after the change point (unstandardized β=8.61, $p < .001$). Furthermore, significant increasing trends for both syphilis (unstandardized β=2.01, $p < .001$) and HCV (unstandardized β =3.35, $p < .001$) testing were noted after the change point. Annual percent increases in testing will be calculated since the implementation of STOP.
Conclusions: Significant increases in HCV and syphilis testing corresponded with increases in HIV testing, suggesting a simultaneous increase in awareness and testing of related infections. Roughly a 2 year lag is noted between the implementation year and change point estimated. Testing volumes continue to increase in 2014.

Monitoring and evaluation of treatment and care

MOPED718

Medication possesion ratio as a tool for assessing the adherence of antiretroviral therapy among HIV-infected Malaysians: a cross-sectional study

P. Raghavan[1,2], S.K. Chidambaram[3], C. Lee Kwok Choong[4], R. Mohamad Sani[5]
[1]Hospital Sungai Buloh, Pharmacy, Kuala Lumpur, Malaysia, [2]Hospital Sungai Buloh, Pharmacy, Infectious Disease Clinic, Sungai Buloh, Malaysia, [3]Hospital Sungai Buloh, Infectious Disease, Sungai Buloh, Malaysia, [4]Hospital Sungai Buloh, Infectious Disease, Selangor, Malaysia, [5]Hospital Sungai Buloh, Sungai Buloh, Malaysia

Background: Adherence to antiretroviral therapy (ART) is a predictor of virologic suppression, emergence of HIV drug resistance, disease progression and death. Monitoring of adherence is often necessary to identify patients at risk of poor clinical outcomes. One of the widely used measures to assess medication adherence is medication possession ratio (MPR). MPR is defined as the days of medications dispensed divided by the number of days between the first and last prescription refill. The aim of this study is to determine whether MPR can be a predictor of viral load outcome among patients who have failed first line ART.
Methods: A cross sectional study was carried out in Malaysia's National Tertiary HIV/AIDS referral hospital using computerized prescribing system between January 2008 and January 2013. We included 76 adult patients who have failed first line ART requiring a switch to second

line ART and compared with 77 adult patients on ART whom are virologically suppressed since 2008. MPR was computed and compared between the two groups using SPSS Statistics ver19. Adherence levels were categorized as: optimal (>95%) and suboptimal (< 95%).

Results: Mean duration of prescription days was 182 days. Mean MPR of patients virologically suppressed on ART and failed ART are 86.05% and 75.29% respectively. A significant percentage of patients (68%) who failed ART had suboptimal MPR (< 95%). Patients with suboptimal MPR had 3 fold odds of developing virological failure (VF) (p= 0.001, OR=3.944, 95% CI = 1.68 -6.8).We assessed the performance of two MPR threshold in predicting VF. When less than 95% MPR threshold was used, the sensitivity was 68%, specificity 61%, positive predictive value (PPV) 63% and negative predictive value (NPV) 66%. When MPR threshold was less than 80%, sensitivity was 44%, specificity 82%, PPV 71% and NPV was 60%.

Conclusions: This study proved that a significant association between MPR and virologic outcome exist in patients on ART. However, the suboptimal sensitivity and specificity of the MPR limits its utility as a sole predictor of VF.

MOPED719

Improving the provision of antiretroviral therapy (ART) using the community balance scorecard methodology in 8 districts of Malawi

D. Kuphanga
ActionAid Malawi, HIV and AIDS, Lilongwe, Malawi
Presenting author email: dkuphanga@yahoo.com

Background: Malawi, with funding from the Global fund, provides free Antiretroviral drugs to approximately 500,000 People living with HIV (PLHIV). Although this is the case, the provision of antiretroviral (ART) drugs has a lot of challenges including few trained ART technicians, stock outs and attitude of health care workers towards PLHIV.

ActionAid Malawi and the Coalition of Women Living with HIV in Malawi implemented the monitoring of HIV and AIDS services project whose objectives were to:

- Empower 240 PLHIV to monitor quality and availability of HIV/AIDS services using the balance scorecard 8 districts by 2014
- Increase participation of PLHIV in demanding quality services from service providers in 8 districts by 2014
- Increase national level engagement between representatives of PLHIV and policy makers by 2014.

Methods: The one year project which was implemented in 8 districts in Malawi used the community balance scorecard which is a monitoring methodology where trained people living with HIV develop simple scoring tools to score, monitor provision of ART and engage the service providers to demand solutions on the challenges.

240 PLHIV were trained in the community balance scorecard methodology while another 240 were trained in advocacy. 40 health facilities were monitored by the PLHIV who also held 40 engagements with service providers on the indicators which were identified.

Results: 75% of the health facilities reported no antiretroviral drugs stock outs during the period of the monitoring, 28% of the facilities reported of changes in the attitude of health personnel, 59% of the facilities reported an increase in the number of trained personnel in the administration of ART.

Conclusions: Monitoring of HIV and AIDS services by PLHIV increases the efficiency and accessibility of these services. To increase the efficiency and accessibility of ART, PLHIV should be empowered to identify challenges in the provision of ART and be able to engage service providers on the identified challenges.

MOPED720

Alcohol and depression: link with adherence and viral suppression in patients on antiretroviral therapy in rural Lesotho, Southern Africa

B. Cerutti[1], O. Faturiyele[2], M. Masetsibi[2], J. Bader[3], M. Motlatsi[2], T. Klimkait[3], L. Toti Mokoteli[2], C. Hatz[4], N.D. Labhardt[4]
[1]University of Geneva, Faculty of Medicine, Geneva, Switzerland, [2]SolidarMed - Swiss Organization for Health in Africa, Maseru, Lesotho, [3]University of Basel, Department of Biomedicine, Basel, Switzerland, [4]Swiss Tropical and Public Health Institute, Clinical Research Unit, Basel, Switzerland
Presenting author email: bernard.cerutti@unige.ch

Background: Alcohol use disorder and depression have been shown to be associated with poor adherence to antiretroviral therapy (ART), but only limited data are available regarding a possible association with viral suppression.

Methods: Within the context of a registered prospective multi-center study in rural Lesotho (NCT02126696), adult patients on ART ≥6 months were screened with the Alcohol Use Disorder Identification Test (AUDIT), using the thresholds recommended in the guidelines. Depression was monitored using the Patient Health Questionnaire (PHQ-9). Low adherence to ART was defined as a self-reported adherence <90% on a visual analogue scale. Viral suppression was defined as < 80copies/mL. Chi-square tests and logistic models were used to investigate the association between alcohol use, depression, adherence, and viral suppression.

Results: Out of 1,598 patients, 1,388 (86.9%) had fully documented AUDIT and PHQ scores. Main data, stratified by sex, are summarised in Table 1.

		Overall n=1'388	Women n=958	Men n=430	Odds-ratio (95% CI) Ref:men	p-value	p-value adjusted by age
Median age (Inter Quartile)		43.4 (34.5-53.5)	40.8 (32.4-51.4)	47.2 (38.5-56.3)		< 0.001	
Alcohol consumption	yes	268 (19.3%)	134 (14.0%)	134 (31.2%)	0.36 (0.27-0.47)	< 0.001	< 0.001
	no	1,120 (80.7%)	824 (86.0%)	296 (68.8%)			
Hazardous consumption (AUDIT ≥ 8)	yes	88 (6.3%)	42 (4.4%)	46 (10.7%)	0.38 (0.25-0.59)	< 0.001	< 0.001
	no	1,300 (93.7%)	916 (95.6%)	384 (89.3%)			
Alcohol Dependence (AUDIT ≥ 20)	yes	4 (0.3%)	3 (0.3%)	1 (0.2%)			
	no	1,384 (99.7%)	955 (99.7%)	429 (79.8%)			
Moderate to severe depression (PHQ-9 ≥ 10)	yes	400 (28.8%)	313 (31.7%)	87 (20.2%)	1.89 (1.45-2.49)	< 0.001	< 0.001
	no	988 (71.2%)	645 (67.3%)	343 (79.8%)			
Low adherence (≤ 90%)	yes	285 (20.9%)	204 (21.7%)	81 (19.1%)	1.16 (0.87-1.55)	0.308	0.146
	no	1,079 (79.1%)	736 (78.3%)	343 (80.9%)			
Viral suppression (≤80 copies/ mL)	yes	1,270 (91.5%)	883 (92.2%)	387 (90.0%)	1.31 (0.88-1.94)	0.187	0.107
	no	118 (8.5%)	75 (7.8%)	43 (10.0%)			

[Table 1]

Women with hazardous alcohol consumption were more likely to report low-adherence (42.5% versus 20.8%; OR: 2.8; 95%CI: 1.5-5.4, p=0.003) but had a similar rate of viral suppression (93.2% versus 91.5%; 1.3, 0.16-4.2, p=0.689). Similar results were found for men, with low-adherence rates of 28.6% and 18.4%
(1.8; 0.9-3.5, p=0.103), and viral suppression of 88.0% and 90.7% (0.8; 0.3-1.9, p=0.551) in hazardous- and non-hazardous drinkers, respectively.

Women with depression were more likely to report low adherence (25.7% versus 19.2%; 1.5, 1.1-2.0, p=0.020), but viral suppression rates were similar (93.0% versus 91.7%; 1.2, 0.7-2.0, p=0.471). Among men, 26.6% with depression and 18.0% without depression reported low-adherence (1.7; 1.0-2.8, p=0.068); rates of viral suppression were again similar with 92.6% and 89.9% (1.4, 0.6-3.3, p=0.413), respectively.

Conclusions: Positive screening for depression (31.7% of women, 20.2% of men) showed a higher prevalence than the general population, while the contrary was observed for hazardous drinkers
(4.4% of women, 10.7% of men).

Hazardous alcohol consumption and depression were significantly associated with lower self-reported adherence to ART among women, and to a lesser extent among men. However, for both no evidence of association was found with lower rates of viral suppression. This might suggest the existence of reporting bias regarding the adherence or the screening questionnaires.

MOPED721

Achieving viral suppression with antiretroviral treatment (cART) in an Eastern-European HIV population predominantly consisting of people who inject drugs (PWID)

P. Soodla[1], K. Huik[1], H. Rajasaar[1], M. Pauskar[1], E. Kallas[1], E.-L. Jõgeda[1], M. Maimets[2], I. Lutsar[1], R. Avi[1]
[1]University of Tartu, Faculty of Medicine, Department of Microbiology, Tartu, Estonia, [2]Tartu University Hospital, Department of Infectious Diseases, Tartu, Estonia
Presenting author email: pilleriin.soodla@gmail.com

Background: Estonia, an Eastern European country, has experienced "new" concentrated HIV epidemic among PWIDs, with transition to general population and increasing number of subjects receiving cART. As there is little data on treatment effectiveness in Eastern Europe, we aimed to define the proportion of subjects and factors associated with achieving viral suppression (VS).

Methods: Data were extracted from nationwide Estonian HIV Cohort Study (E-HIV) database. Subjects diagnosed HIV positive between 01.01.2000-31.12.2013, were included. All subjects ever received cART and at least two follow-up HIV-RNA plasma viral load (VL) measurements were eligible for analysis. VS was defined as two consecutive VL measurements of

< 75 copies/ml (significant VS) or < 1000 copies/ml (acceptable VS) within 360 and 720 days, regardless of type and adherence to cART. Gender, age, VL and CD4 count at treatment initiation and year of starting treatment were used as co-factors.

Results: Of 3764 patients in E-HIV diagnosed in 2000-2013, 3080 had ever received cART. There were 1772 and 2325 subjects eligible for the 360 day and 720 day analysis, respectively. In general, 55% were male, at the treatment initiation median age was 29 (IQR 25-35) years, median viral load was 5.0 $\log_{10}$ (IQR 4.0-6.0 $\log_{10}$) and median CD4 count was 218 (IQR 125-306) cells/µl. Significant VS during the 360 and 720 days was achieved in 751 (42%) and 1252 (54%) subjects, respectively and acceptable VS in 1218 (69%) and 1640 (70%) subjects, respectively. In univariate analyses VL and age, but not gender, CD4 cell count or year of starting treatment were associated with VS so that higher VL at treatment initiation decreased and older age increased the odds of VS (both p< 0.0001). These associations remained significant in multivariate analyses as shown in Table.

	Achievement of VS within 360 days, OR with 95%CI		Achievement of VS within 720 days, OR with 95%CI	
	HIV-RNA VL <75 copies/ml	HIV-RNA VL <1000 copies/ml	HIV-RNA VL <75 copies/ml	HIV-RNA VL <1000 copies/ml
HIV-RNA VL at treatment initiation (log10)	0.56 (0.51-0.63)	0.65 (0.58-0.73)	0.73 (0.67-0.8)	0.77 (0.7-0.86)
Age at treatment initiation in years	1.02 (1.01-1.03)	1.03 (1.01-1.04)	1.03 (1.02-1.04)	1.03 (1.02-1.05)
Gender, female vs male	1.09 (0.87-1.36)	0.95 (0.75-1.21)	1.08 (0.89-1.31)	1.01 (0.82-1.25)
CD4 count at treatment initiation	1.00 (1.00-1.00)	1.00 (1.00-1.00)	1.00 (1.00-1.00)	1.00 (1.00-1.00)
Year of treatment initiation	1.01 (0.96-1.06)	1.02 (0.96-1.07)	1.00 (0.95-1.04)	1.00 (0.96-1.05)

[Table. Factors associated with achieving VS]

Conclusions: In a typical Eastern European HIV population in Estonia, about half of the patients achieve significant and two third acceptable VS after the first and second year of cART, rates being slightly lower than in Western European cohorts. Older age and lower VL were associated with achievement of VS. Further and more detailed analysis is needed to fully understand all reasons of not achieving VS.

MOPED722

Using the Child Status Index (CSI) to measure changes in well-being in orphans and vulnerable children

N. Persaud[1], O. Onoh[2], E. Lee[3], Z. Kpamor[4]
[1]Management Sciences for Health, Technical Quality and Innovation, Arlington, United States, [2]Management Sciences for Health, Abuja, Nigeria, [3]Johns Hopkins, Bloomberg School of Public Health, Baltimore, United States, [4]Management Sciences for Health, Project Performance Management, Abuja, Nigeria
Presenting author email: zkpamor@msh.org

Background: Children orphaned and made vulnerable by the HIV/AIDS epidemic are vulnerable to sexual abuse, exploitation, illness, and homelessness. We sought to identify factors that determined changes in well-being of a cohort of orphans and vulnerable children (OVCs) who received support in six core areas (food and nutrition, shelter, legal and social protection, health, psychological care, and education) in Nigeria.

Methods: Using the Child Status Index (CSI), a standardized tool for assessing the well-being of OVCs, data were collected on 12 factors at enrollment and every six months from 12,417 OVCs who participated in a structured 18-month intervention. Composite scores were calculated for each OVC at baseline, six months, 12 months, and 18 months. Changes in status between baseline and each time period were calculated for the composite scores and for each factor and disaggregated by sociodemographic and caregiver characteristics. Differences in proportions were calculated using the chi-square test.

Results: Forty-nine percent of the OVCs were classified as extremely vulnerable at enrollment. Seventy-eight percent of the caregivers were females and 57% were aged 40 years or older. Fifty-seven percent of the OVCs improved during the first six months while 66% had improved by 12 months, and 72.7% had improved by 18 months (p=0.000). There were no significant differences in the proportion whose well-being improved related to the age of the caregiver or sex or age of the OVCs. There was a significant decline in the proportion of OVCs who showed no changes in well-being during the follow-up period (12.8% at six months compared to 5.5% at 12 months and 3.2% at 18 months; p< 0.05). Older OVCs were significantly more likely than younger OVCs to show no changes in well-being (P< 0.05). CSI scores for the 12 factors increased gradually over the 18 months. The slowest improvement was noted in nutrition and growth while rapid changes were found in school attendance, access to skills training, and access to health services.

Conclusions: Interventions for OVCs seem to show results if measured over a longer period. Despite receiving services a small group of OVCs showed no improvement in their well-being.

MOPED723

Transmitted HIV drug resistance survey in two provinces in Papua New Guinea

E. Lavu[1], N. Dala[2], A. Gurung[3], E. Kave[1], E. Mosoro[1], J. Markby[4], E. Aleksic[4], J. Gare[5], I. Elsum[4], G. Nano[6], M. Myatt[7], P. Kiama[8], S. Crowe[9], S. Bertagnolio[10], A. Hearps[4], M.R. Jordan[11]
[1]Central Public Health Lab, Port Moresby, Papua New Guinea, [2]National Department of Health, Port Moresby, Papua New Guinea, [3]WHO, PNG, Port Moresby, Papua New Guinea, [4]International Clinical Research Laboratory, Burnet Institute, Melbourne, Australia, [5]Institute for Medical Research, Goroka, Papua New Guinea, [6]Regional Medical Officer, Port Moresby, Papua New Guinea, [7]Brixton Health, Wales, United Kingdom, [8]Regional Medical Officer, Mount Hagen, Papua New Guinea, [9]Burnet Institute, Melbourne, Australia, [10]World Health Organization, HIV Department, Geneva, Switzerland, [11]Tufts, University School of Medicine, Boston, United States
Presenting author email: bertagnolios@who.int

Background: Surveillance of transmitted HIV drug resistance (TDR) amongst individuals accessing voluntary counselling and testing (VCT) services was conducted from May 2013 to April 2014 in two geographic regions of Papua New Guinea: Port Moresby, National Capital District and Mt Hagen, Western Highland Province.

Methods: Dried blood spots (DBS) were collected from HIV infected, ARV-naïve VCT attendees age <30 years; if female, nulligravid or primigravid. Genotyping was performed using previously described methods[1]. TDR was defined using the 2009 WHO Surveillance Drug Resistance Mutations List[2]. SLEAC classification[3] with floor and ceiling decision rules modelled to return probabilities of classification similar to those described for the original WHO TDR survey method,[4] classified TDR as low (< 5%), moderate (5-15%), or high (>15%).

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Results: In both regions, NNRTI TDR was classified as moderate. In contrast, NRTI and PI TDR were classified as low in both regions. The prevalence of NNRTI TDR in Port Moresby and Mt Hagen was 16.1% (95%CI 9.0%-27.2%) and 8.2% (95%CI 3.5%-17.8), respectively. The ratio of the NNRTI point prevalence estimate in Port Moresby to Western Highlands was 1.97 (95%CI=0.71-5.42); chi-square 1.81 (one-sided p=0.0896).

Conclusions: Using WHO classification, levels of NNRTI resistance in Port Moresby and Mt Hagen were moderate. The findings are concerning and threaten to limit the on-going effective use of NNRTIs as a component of national first-line ART. To assess the implications of these findings, nationally representative surveillance of HIV drug resistance among first-line ART initiators should be urgently implemented.

MOPED724

Declining mortality among HIV-positive Aboriginal people at a Vancouver inner-city health centre

P. Klakowicz[1,2], D. Tu[1,2], D. Moore[3,4], W. Zhang[3], G. Colley[3]
[1]Vancouver Native Health Society Medical Clinic, Vancouver, Canada, [2]University of British Columbia, Department of Family Practice, Vancouver, Canada, [3]British Columbia Centre for Excellence in HIV/AIDS, Vancouver, Canada, [4]University of British Columbia, School of Population and Public Health, Vancouver, Canada
Presenting author email: piotr.klakowicz@gmail.com

Background: We examined mortality rates of HIV-positive Aboriginal people and others at an Aboriginal-focused, inner-city primary-care health centre in Vancouver, Canada, over time when improvements were initiated based on a chronic care model approach to address high HIV-related mortality.

Methods: We conducted a retrospective cohort study of HIV-infected individuals at the clinic from 2007 to 2012, by linking clinical data with the provincial HIV treatment clinical registry. All-cause mortality and HIV-related mortality rates were calculated, for pre (2007-09) and post (2010-12), and factors associated with mortality were examined, with Aboriginal ethnicity as the primary explanatory variable.

Results: Of the 546 eligible study patients, 322 (59%) self-identified as Aboriginal. Overall, Aboriginal persons compared to others had higher all-cause mortality (14% vs 8%, p=0.035; 6.25 vs 4.02 per 100 person-years (PYRs), p=0.113, respectively) and higher HIV-related mortality (6% vs 2%, p=0.027; 2.50 vs 0.89 per 100 PYRs, p=0.063, respectively). Over time, from 2007-09 to 2010-12, we observed significant declines in all-cause mortality for both Aboriginal patients (10.0 to 5.0 per 100 PYRs, respectively; p=0.023) and others (7.2 to 3.0 per 100 PYRs, respectively; p=0.061). We also observed declines in HIV-related mortality for Aboriginal patients (5.56 to 1.80 per 100 PYRs, respectively, p=0.005).

Conclusions: Mortality declined for HIV-positive Aboriginal patients after the initiation of quality improvements in chronic disease management of HIV at the clinic. This highlights the effectiveness of both the chronic care model approach and the culturally-informed primary care at the clinic.

MOPED725

Analysis of ART clinical outcomes

M.T. Magoro[1], C. White[2], R. Pretorius[3], N. Ntuli[3], S.C. Makakole-Nene[4], P. Barron[5]
[1]National Department of Health, Monitoring and Evaluation, Pretoria, South Africa, [2]Clinton Health Access Initiative, CHAI, Pretoria, South Africa, [3]National Department of Health, Health Information Cluster, Pretoria, South Africa, [4]National Department of Health, Global Fund Cluster, Pretoria, South Africa, [5]National Department of Health, HIV and AIDS, TB and MCWH Branch, Pretoria, South Africa
Presenting author email: magoro@health.gov.za

Background: This study aim to describe loss to follow-up, retention on antiretroviral treatment (ART), viral load suppression and increase in CD4 counts data from adult patients on the ART programme between 2004/05 and 2013/14.
Methods: ART data was collected routinely through the TIER.Net database and exported to District Health Information System. Data was retrieved from the standardised clinical stationery and recorded into either TIER.Net in public health facilities providing ART.
Results: Data presented summarised clinical outcomes from 1,823 facilities and a total of 1,386,290 adult patients who started ART from April 2004 to March 2014. This represents 54% of total patient population.
The proportion of patients starting ART with CD4 count between 200-350 cells/µl increased from 6.5% of all patients starting ART in 2004/5 to 33.0% in 2013/14 while the proportion of patients with CD4 count below 100 decreased from 33.5% of all patients started in 2004/15 to 18.5 % in 2012/13. Retention of clients on treatment at 12 months was 87.9% for patients who started ART at any point in 2004/05 and 2005/06, while about 78.8% of patients started in 2011/12 were retained on ART at 12 months.
Data further demonstrates that at 12 months, 44.5% of adult patients had a viral load done and 79.7% of these results were <400 copies/µl, the proxy for viral load suppression. The 2004/05 cohort had 3.7% of adult patients lost to follow-up at 3 months whereas the 2012/13 cohort shows 10.2% lost to follow-up for the same period.
Conclusions: Adult patients who formed part of the 2004/05 cohort had superior retention prospects compared to all later cohorts. Loss to follow-up was higher in clients who were part of the later cohorts when compared with the 2004/05 cohort. Innovative interventions to improve patient retention are required.

MOPED726

Rate of ART initiation and time to ART initiation among HIV-infected participants in the Bangkok MSM cohort study, 2006-2014

A. Sriporn[1], W. Wimonsate[1], P. Luechai[1], S. Hengprasert[1], K. Satumay[1], N. Tippanonth[1], J. Tongtoyai[1], E. Dunne[1,2], A. Chitwarakorn[3], T. Holtz[1,2], T. Chemnasiri[1]
[1]Thailand MOPH - U.S. CDC Collaboration, HIV/STD Research Program, Nonthaburi, Thailand, [2]Centers for Disease Control and Prevention, Division of HIV/AIDS Prevention, Atlanta, United States, [3]Ministry of Public Health, Department of Disease Control and Prevention, Nonthaburi, Thailand

Background: To achieve the UNAIDS goal of zero deaths from HIV/AIDS, HIV-infected persons should be retained in care with antiretroviral treatment (ART).
We report the rate of follow-up with CD4+ cell count monitoring, ART initiation, and time to ART initiation of HIV-infected participants in the Bangkok Men who Have Sex with Men Cohort Study (BMCS).
Methods: Between 2006-2010, we enrolled participants into the BMCS and followed them every 4 months for 3-5 years. For HIV-infected participants, we provided post-test and antiretroviral therapy (ART) counselling, follow-up with CD4+ cell count monitoring every 4 months, and referral to ART services.
ART initiation was reported during follow-up visits. We conducted descriptive analysis of the data from follow-ups, including CD4+ cell count and ART initiation.
Results: We enrolled 1,744 men into the BMCS. As of 16 December 2014, 614 (35%) had been diagnosed with HIV infection. Of HIV-infected men, 482 (79%) had follow-up with CD4+ cell count.
At HIV diagnosis, the median CD4+ cell count was 438 cells/mm^3, and 141/482 (29%) were eligible for ART based on the 2011 Thailand HIV Guidelines -- having CD4+ cell count <350 cells/mm^3 and/or an AIDS-defining illness. During follow-up, 271/482 (56%) initiated ART. Among these, ART initiation occurred for 144 (53%) when their CD4+ cell counts were <200 cells/mm^3 and for 119 (44%) when their CD4+ cell counts were between 200-349 cells/mm^3.
The mean duration from HIV diagnosis to ART initiation was 2 years (IQR: 0.8-3.0 years).
The median annual CD4+ cell count of those who initiated ART (423 cells/mm^3, IQR: 334-518) was lower than that of those for whom ART was deferred (493 cells/mm3, IQR: 404-644) (p<0.001). In total, 186 (68%) of the 271 who reported initiating ART had an AZT- or d4T-based regimen.
Conclusions: In a sizeable fraction of HIV-infected BMCS participants, ART initiation was deferred despite low CD4+ cell counts and eligibility under 2011 guidelines. Efforts may be needed to ensure that HIV care providers incorporate updated information from the new Thai guidelines releases in 2014 which allow for ART initiation at any CD4+ cell count and include a preference for non-AZT/d4T-based regimen.

MOPED727

12-month costs of care of HIV-infected children initiating early antiretroviral therapy before the age of 2 years in Abidjan, Cote d'Ivoire, 2011-2014. The MONOD ANRS 12206 project

S. Desmonde[1], D. Avit[2], M. Amorissani-Folquet[2,3], C. Amani-Bosse[2], T. Eboua[2,4], V. Mea[2], S. N'Gbeche[5], S. Kouadio[2], E. Dainguy[3], M. Timite-Konan[2,4], V. Leroy[1], The MONOD ANRS 12206 Study Group
[1]Université Bordeaux, Institut de Santé Publique, d'Epidémiologie et de Développement, Bordeaux, France, [2]Programme PACCI - Site ANRS, Projet Monod, Abidjan, Cote D'Ivoire, [3]CHU de Cocody, Service de Pédiatrie, Abidjan, Cote D'Ivoire, [4]CHU de Yopougon, Service de Pédiatrie, Abidjan, Cote D'Ivoire, [5]Centre Pédiatrique de Prise en Charge, de Recherche et de Formation, Abidjan, Cote D'Ivoire
Presenting author email: sophie.desmonde@isped.u-bordeaux2.fr

Background: To determine the healthcare resource use and costs attributable to the care of HIV-infected infants on early antiretroviral therapy (EART) initiated < 2 years old.
Methods: We assessed the direct costs of care for all HIV-1 infected children < 2 years old, whose parents agreed to participate, without tuberculosis, included in an initial prospective cohort to receive an EART based on LPV/r in Abidjan. During the first 12-month on EART, we documented all severe morbid events (SME), leading to death or hospitalization and recorded drug prescriptions, ART and cotrimoxazole prophylaxis delivery, medical exams and consultations with specialists, hospital admissions and routine biological follow-up.
Results: We included 99 children, at a median age of 13.5 months (IQR: 6.8 - 18.6); 45% had reached WHO stage 3 or 4 at enrolment. Of these children, 5 (5%) died and 3 (3%) were lost to follow-up. During the first 12 months, 27 children presented 35 SME; the incidence rate was 36.77 per 100 child-years (IC95%: [35.55 - 37.99]). The mean cost of care per child-month reached 672.44 USD. Most of these expenses are borne by the Ivorian national AIDS program: ART (621.47 USD per child-month), cotrimoxazole prophylaxis (31.02 USD per child-month) and routine biological follow-up (6.24 USD per child-month). The additional healthcare resource use costs were 13.71 USD per child-month: 7.27 USD and 6.24 USD for drug prescriptions and medical exams, respectively. This mean cost of healthcare resource use per child-month was lower in children without SME compared to those who had (11.56 USD versus 18.66 USD, table 1). The mean cost of care per child-month of a SME was estimated 14.03 USD (IC95%: 9.45-18.60) in children who deceased and 8.03 USD in children who survived.

	Child-months of follow-up	Total cost (FCFA)	Mean cost per child-month (FCFA)	Mean cost per child-month (USD)	CI 95%
Total (N=99)					
Drug prescriptions	944.93	3878230	4104.27	7.27	[7.10 – 7.44]
Medical exams	773.47	2811440	3634.84	6.44	[6.26 – 6.62]
Medical imaging	773.47	732200	946.64	1.68	[1.59 – 1.77]
Laboratory exams	773.47	1441520	1863.71	3.30	[3.17 – 3.43]
Consultations with specialists	773.47	10000	12.93	0.02	[0.01 – 0.03]
Unknown	773.47	4000	5.17	0.01	[0.00 – 0.02]
Children with no severe morbidity (N =72)					
Drug prescriptions	706.27	2752940	3897.88	6.90	[6.71 – 7.10]
Medical exams	573.27	1509120	2632.48	4.66	[4.49 – 4.84]
Medical imaging	573.27	531100	926.44	1.64	[1.54 – 1.75]
Laboratory exams	573.27	969020	1690.34	2.99	[2.85 – 3.14]
Consultations with specialists	573.27	5000	8.72	0.02	[0.01 – 0.03]
Unknown	573.27	4000	6.98	0.01	[0.00 – 0.02]
Children with severe morbidity (N =27)					
Drug prescriptions	238.66	1125290	4715.03	8.35	[7.99 – 8.72]
Medical exams	200.20	1302320	6505.09	11.52	[11.05 – 11.99]
Medical imaging	200.20	201100	1004.50	1.78	[1.59 – 1.96]
Laboratory exams	200.20	472500	2360.14	4.18	[3.90 – 4.46]
Consultations with specialists	200.20	5000	24.98	0.04	[0.02 – 0.07]
Outside of an event (N=27)					
Drug prescriptions	186.42	1125290	6036.32	10.69	[10.22 – 11.16]
Medical exams	150.87	678600	4497.91	7.97	[7.52 – 8.42]
Medical imaging	150.87	201100	1332.94	2.36	[2.12 – 2.61]
Laboratory exams	150.87	472500	3131.84	5.55	[5.17 – 5.92]
Consultations with specialists	150.87	5000	33.14	0.06	[0.02 – 0.10]
Care of a severe event					
Deceased children (N=5)					
Drug prescriptions	2.57	20350	7918.29	14.03	[9.45 – 18.60]
Medical exams	2.1	0	-	-	-
Non-deceased children (N=22)					
Drug prescriptions	49.67	156680	3154.42	5.59	[4.93 – 6.24]
Medical exams	47.23	65000	1376.24	2.44	[1.99 – 2.88]
Medical imaging	47.23	8000	169.38	0.30	[0.14 – 0.46]
Laboratory exams	47.23	57000	1206.86	2.14	[1.72 – 2.55]

[Table1. Mean cost of care per child-month during the first 12 months of the MONOD trial]

Conclusions: Despite EART based on LPV/r, severe morbidity still occurs and represents a significant healthcare burden. The additional healthcare resource use costs, borne by patient families, remains substantial. In this resource-limited setting, it is crucial to include HIV-infected children earlier. Further research is needed to assess whether these costs are outweighed by the effectiveness of an earlier ART.

MOPED728

Third-line antiretroviral treatment: the Brazilian experience

C. Zaire[1,2], J. Paranhos[3], L. Hasenclever[3], B. Coriat[1]
[1]Paris XIII University, Centre d'Économie Paris Nord (CEPN), Paris, France, [2]Agence Nationale de Recherche sur le Sida et les Hépatites Virales (ANRS), Paris, France, [3]Federal University of Rio de Janeiro, Economics Institute, Rio de Janeiro, Brazil
Presenting author email: carlazaire@yahoo.fr

Background: Approximately 718 thousand people are infected with HIV in Brazil, among which 313,175 were in treatment in 2012. Third line antiretroviral drugs are indicated for the treatment of multi-resistant HIV/AIDS patients with virological treatment failure. Brazilian program distributes six third-line drugs: Darunavir (introduced in 2007), enfuvirtide (2005), étravirine (2010), raltégravir (2008), tipranavir (2010), maraviroc (2013), all patented and imported at very high prices. We aim to examine the Brazilian's situation regarding the supply of 3rd line antiretroviral: are there affordable? Is the price comparable to other countries?
Methods: The methodology for the study was based on a statistical work on Brazilian databases. We analyzed drug prices from 2010 to 2013 and calculated the price / patient / year, which is relevant to compare to other countries.
Results: Brazil regularly gets good discounts because of the annual and central purchase. Table 1 shows the annual values (price/ patient/ year) in dollars and the quantity purchased separately by year and by product. As we can compare, in 2012 according to data from MSF (2013), for raltegravir, Brazil paid less than Armenia (US$ 13 213), Georgia (US$ 13 225) and Paraguay (US$ 7 008). For etravirine, Brazil paid also less than Jamaica (US$ 6 570), Paraguay (US$ 7 782) and Ukraine (US$ 6 679).

	Price/patient/year (US$)	Purchased Quantity
Raltegravir 400mg tablet		
2011	$ 6 394.80	5 112 000
2012	$ 5 248.70	14 920 000
Etravirine 100mg tablet		
2010	$ 8 657.80	406 440
2011	$ 8 716.20	602 160
2012	$ 5 606.40	1 278 000
2013	$ 4 751.57	3 870 240

[Price/patient/year and purchased quantity]

Conclusions: When compared to other countries, Brazil has advantages in the final price, due to its population size and the quantity purchased. However, the fall in prices was, not always, proportional to the increase of the quantity purchased. One hypothesis for this, is that as it gets closer to the end of the monopoly (original patent) the negotiations becomes more flexible and overlap immediate interests (high price) in order to maintain good relations and maintain the sales after the patent expiration. Brazil has sustained the program courageously, but keep looking for ways to avoid increasing the budget share of third-line drugs. Since 2009, Brazil's strategy seems to be encouraging the local production with public-private partnership that, in the future, can stimulate the search for innovation.

MOPED729

UK healthcare providers' views on antiretroviral therapy in primary HIV infection

V. Parsons[1], S. Fidler[2], N. Fitzgerald[3], S. Collins[4], A. Phillips[1], R. Gilson[1], G. Hart[1], K. Porter[1], J. Fox[3]
[1]University College London, London, United Kingdom, [2]Imperial College London, London, United Kingdom, [3]Guy's & St Thomas' NHS Foundation Trust, London, United Kingdom, [4]HIV iBase, London, United Kingdom
Presenting author email: julie.fox@kcl.ac.uk

Background: UK HIV treatment guidelines advise starting before CD4< 350, and that treatment as prevention (TasP) is discussed, and offered, to all. We examined the attitudes of UK healthcare providers (HCP) towards antiretroviral therapy (ART) in primary HIV infection (PHI) and ascertained the scenarios in which it is recommended using an internet survey (December 2014).
Methods: PHI was defined as having a negative HIV antibody test within 6 months of positive, laboratory evidence of acute infection, or testing incident on a RITA assay. Logistic regression was used to test associations.
Results: 291 responses were received and 34 excluded (26 exited prematurely, 7 were not UK-HCP). Of the 257 remaining, 79% were from England (35% London), 4% Scotland, 2% Northern Ireland, 2% Wales and 13% unknown. 87% were clinicians, 9% nurses, 3% pharmacists and 1% health-advisors. 78%(200/257) of HCP had seen ≥1 PHI patient in the past year; median(IQR; range) was 3(2-5; 0-50). 81%(140/172) of clinicians had offered ART to ≥1 PHI patient in the past year; median number 2(1-4.5; 0-50). 89%(177/198) believed ART in PHI benefitted the immune system and 81%(174/216) believed there was individual benefit in starting ART in PHI versus deferring to CD4< 350. 33%(75/229) of HCP would recommend ART in PHI to an asymptomatic patient with CD4350-500, and 18%(40/226) would at CD4>500. 98%(217/221) of HCP would discuss TasP with PHI patients who reported having current sexual partners compared to 81%(174/216) for those reporting none. Clinicians with greater PHI caseload were more likely to recommend ART in PHI at CD4350-500 (OR per 5 patient increase 1.52; 95%CI 1.08-2.13; p=0.015) and at CD4>500 (1.83; 1.28-2.63; p=0.001). They were also less likely to believe it should only be offered according to UK guidelines (0.38; 0.22-0.67; p=0.001) and more likely to believe those starting in PHI are more likely to benefit from a functional cure (1.74; 1.13-2.68; p=0.011).
Conclusions: Most HCP believe there are health benefits of starting ART in PHI as opposed to deferring to CD4< 350. The majority, however, would not recommend ART for asymptomatic patients with CD4≥350. Clinicians with more PHI experience were more likely to recommend at CD4≥350.

MOPED730

Integrating HIVDR early warning indicators with quality improvement to minimize HIVDR occurrence, Thailand

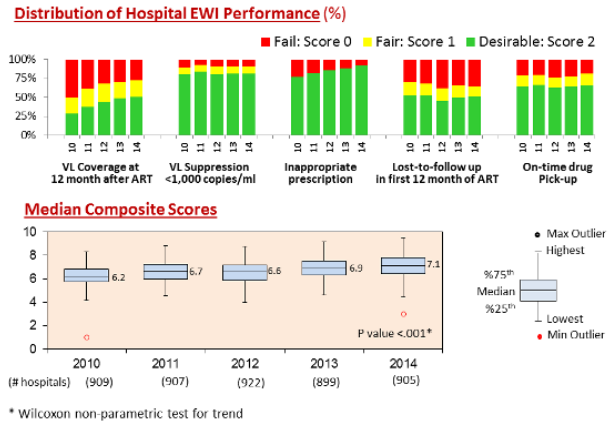
C. Lertpiriyasuwat[1], A. Teeraratkul[2], S. Bhakeecheep[3], N. Chatharojwong[2], K. Phokasawad[2], P. Yuktanon[1], N. Pattarapayoon[1], O. Sumet[1], S. Thanprasertsuk[4], T. Roels[2,5]
[1]Bureau of AIDS, TB and STI, Department of Disease Control, Thailand Ministry of Public Health, Nonthaburi, Thailand, [2]Thailand Ministry of Public Health-U.S. Centers for Disease Control and Prevention Collaboration, Global AIDS Program Thailand/Asia Regional Office, Nonthaburi, Thailand, [3]National Health Security Office, Region 1, Chiangmai, Thailand, [4]Department of Disease Control, Ministry of Public Health, Nonthaburi, Thailand, [5]U.S. Centers for Disease Control and Prevention, Center for Global Health, Division of Global HIV/AIDS, Atlanta, United States
Presenting author email: a.teeraratkul@gmail.com

Background: Managing optimal antiretroviral treatment (ART) is essential for program quality and to minimize occurrence of HIV drug resistance (HIVDR). Preliminary results from Thailand's experiences on implementing HIVDR "Early Warning Indicator (EWI)" which are ART site factors associated with emergence of HIVDR as a quality improvement (QI) tool are described.
Methods: Trends for five Thailand EWIs (T-EWI) were monitored during 2010-2014 including 1) viral load (VL) coverage (T-EWI1a), 2) VL suppression (T-EWI1b), 3) inappropriate ARV prescription (T-EWI2), 4) lost-to-follow up (T-EWI3), and 5) on-time drug pick-up (T-EWI4) (Table 1). Data were collected through an electronic, web-based information system, linked with the National Death Registry. Medical records of adults receiving ART under the national Universal Coverage Program have been used to quarterly generate standard reports for hospital, provincial and national levels. Weighted averages for hospitals of T-EWIs' of hospital performance were calculated. HIVDR-QI was first implemented in 2013 and hospital providers and regional and provincial coaching teams were trained. Individual scores for each of the five T-EWIs (0 for poor, 1 for fair and 2 for desirable) and median composite scores (with a maximum score of 10) were calculated to identify site-based QI priorities.

T-EWIs	Desirable target	2010	2011	2012	2013	2014	P value (Wilcoxon NP test for trend)
# ART sites	-	902	907	922	899	905	-
# Adults receiving ART	-	128,884	145,949	160,126	174,256	185,437	-
# Adults newly started ART	-	20,415	19,780	20,166	18,114	18,922	-
1) T-EWI1a: VL coverage	>90	54.8 (0-100)	65.5 (0-100)	73.1 (0-100)	77.3 (0-100)	80.4 (15.4-100)	<.001*
2) T-EWI1b: VL suppression	>90	93.5 (33.3-100)	93.3 (33.3-100)	92.8 (50.0-100)	92.7 (50.0-100)	93.0 (66.7-100)	0.848
3) T-EWI2: Mono-dual ARV	0%	0.3 (0-1.7)	0.2 (0-0.7)	0.1 (0-0.5)	0.1 (0-0.5)	0 (0-0.4)	<.001*
4)T-EWI3: Lost-to-FU	<5	7.5 (1.7-17.2)	7.4 (2.0-21.9)	8.9 (0.6-18.1)	8.1 (2.0-21.9)	7.9 (2.1-17.1)	0.039*
5) T-EWI4: On-time pick-up	>90	91.9 (78.7-99.0)	91.9 (81.1-97.8)	91.4 (73.3-98.1)	92.4 (74.4-99.5)	92.7 (77.4-97.8)	0.270

(1) T-EWI1a: % patients initiating with ART who had VL test at least once during 12 month (3-12 month) after initiation; (2) T-EWI1b: % patients whose VL at 12 month after ART was <1,000 copies/ml; (3) T-EWI2: % patients receiving ART were being prescribed with mono- or dual-regimen; (4) T-EWI3: % patients initiating with ART who lost to follow-up (missed appointment > 90 days) during 12 months after ART; and (5) T-EWI4: % patients receiving ART who returned for ARV pill pick up < 2 days after the ran-out date.

[Table 1: Monitoring of EWIs, Thailand, 2010-2014]



[Figure 1: EWI Composite Scores and Distributions of Hospital Performance National Patient Monitoring System, National Health Security Office, Thailand, 2009-2014]

Results: By September 2014, 185,437 persons were receiving ART at 905 hospitals. The 5-year trend for the individual EWI median percentages are shown in Table 1; Figure 1 shows the median EWI composite scores and the trends in hospital EWI performance. Key findings included significant improvement in T-EWI1a, though only 42% of hospitals met the desirable target in 2014; T-EWI1b remained >90%; T-EWI2 did not reach the desirable zero target; T-EWI3 significantly decreased from 8.9% in 2012 to 7.9% in 2014 though only 50% of hospitals met the desirable target; and T-EWI4 stayed >90%. The overall median composite score increased from 6.2 (1.0-8.3) in 2010 to 7.1 (3.0-9.5) in 2014 (p <.001).

Conclusions: EWIs have been used as a QI monitoring tool in Thailand. The results indicated areas for improvement and identified targeted site-based interventions for QI coaching. Priorities for hospitals to reach desirable performance are
1) increase VL screening,
2) reassess VL suppression, and
3) minimize lost-to-follow-up.

MOPED731

Benefits beyond the patient: a regression discontinuity analysis of the impact of adult antiretroviral therapy (ART) on childhood educational attainment in South Africa

J. Raifman[1,2], T. Baernighausen[1,2]
[1]Harvard School of Public Health, Department of Global Health and Population, Washington, United States, [2]Africa Centre for Health and Population Studies, Mtubatuba, South Africa
Presenting author email: juliargoldberg@gmail.com

Background: The human immunodeficiency virus (HIV) epidemic in sub-Saharan Africa has detrimental impacts beyond affecting the well-being and survival of those living with HIV, also affecting the educational attainment of children in communities with high HIV prevalence. Human capital accumulated through education plays a critical role in countries' long-run economic growth. Antiretroviral treatment (ART) may ameliorate the impact of HIV on education. We investigate the impact of ART on childhood educational attainment.

Methods: We combined longitudinal demographic surveillance data from KwaZulu-Natal, South Africa with data from the local, public HIV treatment and care program. South Africa adhered to the 2006 World Health Organization ART guidelines recommending that adults with CD4 counts below 200 cells per cubic millimeter begin ART until August 2011. We exploit this treatment threshold to conduct a regression discontinuity analysis estimating the impact of adult ART on child educational attainment. Whether patients fall just above or just below the treatment threshold should be random, meaning that the observed and unobserved characteristics of adults on treatment and the children with whom they lived should be equivalent and eliminating the problem of selection bias in estimating the causal impact of ART in the region around the cutoff. We compared children living with adults whose first CD4 counts were within 100 cells per cubic millimeter above and below the CD4 count cutoff. We were able to follow children for up to six years after adult CD4 count testing.

Results: The average age of children at the time of adult CD4 count testing was 11.0 years. When adults complied with the treatment threshold rule, living with an adult whose earliest CD4 count was just below the threshold increased childhood educational attainment by 1.17 years (p=0.036) relative to living with an adult whose CD4 count was just above the threshold. Adult ART increased childhood educational attainment by 0.30 years (p=0.017) among compliers and non-compliers. For children aged 16-20 years, adult ART increased educational attainment by 2.96 years (p=0.072) among compliers and by 0.64 years (p=0.022) among compliers and non-compliers.

Conclusions: We conclude that adult ART increases the educational attainment of children living in the same households.

MOPED732

Acceptability of internet and cell-phone messages to promote linkage to HIV care

R. Cabello[1], B. Magaly[2], I. Alva[3], P. Garcia[3], C. Diaz[4], A. Mühlbach[1], G. Mburu[5], V. Champion[1], D. Contreras[1]
[1]VIA LIBRE, Lima, Peru, [2]Universidad Peruana Cayetano Heredia., Lima, Peru, [3]Universidad Peruana Cayetano Heredia, Lima, Peru, [4]University of Miami, Miami, United States, [5]International HIV/AIDS Alliance, Hove, United Kingdom
Presenting author email: rcabello@vialibre.org.pe

Background: The Peruvian government has been providing free highly active antiretroviral therapy (HAART) since 2004. As of December 2013, Peru had an estimated 22,157 people on HAART, which represents 51% of those eligible.To improve linkage and retention to HAART, innovative and effective approaches are needed. The objective of this study was to assess the acceptability of receiving information about the National HAART Program via the internet and/or cell-phones to promote linkage to HIV care.

Methods: Between November and December 2014 we conducted a cross sectional survey at VIA LIBRE an HIV clinic that provides free HAART in Lima, Peru. During these months all participants who attended the clinic were invited to participate by completinga self-administered online questionnaire using tablets.

Results: 620 patients were eligible to participate in the survey, 41 declined and 30 did not complete the survey. Of the 549 surveyed , 513 were people living with HIV (453 male and 60 female) completed the questionnaire. The mean age was 37.9(18-65), 14% had finished high-school and 84.6% were studying at the university or have completed a degree. Both males and females (252(63.5%) males and 38(77.6%) females, (p=0.42) reported as important or very important (4 and 5 respectively on a scale of 1=not important and 5=very important) to receive information through SMS, 200(50.4%) males and 34(69.4%) females (p=0.11) preferredcell-phone voice messages and 177(44.6%) males and 23(46.9%) females (p=0.23) favoredsocial networks (Facebook). Additionally, 243(61.2%) males and 29(59.2%) females (p=0.11) believedthat it was important orvery important to receive information through emails, 207(52.2%) males and 24(49.0%) females (p=0.29) preferredwebpages, 195(49.1%) males and 26(53.1%) females (p=0.21) favoredchat and 176(44.3%) males and 21(42.9%) females (p=0.06) usinga blog.We did not find any significant difference in the acceptability of receiving messages through SMS, cell-phone voice messages, social network, chat, email, blog and webpages by gender.

Conclusions: The internet and/or cell phones were recognized as important ways to deliver information about the HAART Program in our study sample. SMS messages, followed by email, and cell-phone voice messages had the highest acceptability. These forms of ICT should be used to improvelinkage to HIV care among people living with HIV in Peru.

MOPED733

The effectiveness of compulsory addiction treatment: a systematic review

D. Werb, C. Rafful, M. Meacham
University of California, San Diego, Division of Global Public Health, San Diego, United States
Presenting author email: dwerb@ucsd.edu

Background: Drug addiction is a major source of HIV transmission. In many settings, compulsory treatment, wherein drug dependent individuals are mandated to receive addiction treatment, has been adopted as a strategy to address HIV transmission among this population. However, research on the effectiveness of this approach has yet to be systematically evaluated. We sought to conduct a systematic review of the effectiveness of compulsory addiction treatment.

Methods: We systematically reviewed and extracted findings from studies examining the outcomes of compulsory treatment. The primary outcome of interest was post-treatment drug use. The secondary outcome of interest was post-treatment recidivism. Two authors searched eight English-language databases (PubMed, PAIS International, Proquest, PsycINFO, Web of Science, Soc Abstracts, JSTOR, EBSCO/Academic Search Complete), one Spanish-language database (REDALYC), one Portuguese-language database (SciELO Brazil), the Internet (Google, Google Scholar), and article reference lists, from database inception to December 1st, 2014.

Results: Of an initial 430 potential studies identified, nine quantitative studies met the inclusion criteria. Studies evaluated compulsory treatment options including drug detention facilities, short (i.e. 21-day) and long-term (i.e., 6 months) inpatient treatment, community-based treatment, group-based outpatient treatment, and prison-based treatment. Three studies (33%) reported no significant impacts of compulsory treatment compared with control interventions. Two studies (22%) found equivocal results but did not compare against a control condition. Two studies (22%) observed negative impacts of compulsory treatment on recidivism. Two studies (22%) observed minor impacts of compulsory inpatient treatment on recidivism and drug use.

Conclusions: There is limited scientific literature evaluating compulsory addiction treatment and this literature does not suggest benefits of this treatment modality on drug use or recidivism. Given the known benefits of a range of voluntary approaches to treatment, such programs should be prioritized by policymakers seeking to reduce drug-related health and social harms.

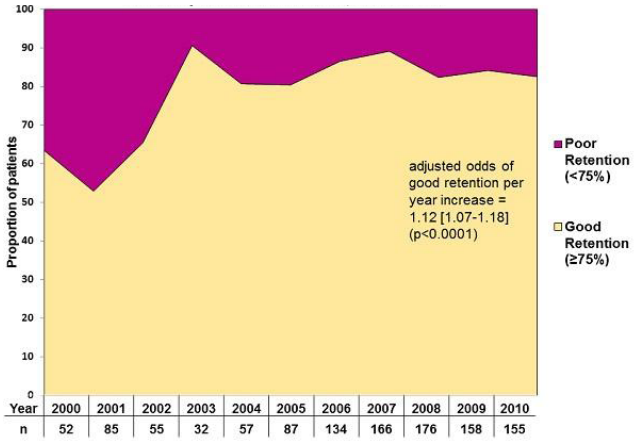
Monitoring and evaluation of HIV cascade

MOPED735

Early retention in care at an HIV outpatient clinic in Rio de Janeiro Brazil, 2000-2013

D. Silva[1], R.B. De Boni[2], J. Lake[1], S.W. Cardoso[2], S. Ribeiro[2], R.I. Moreira[2], J.L. Clark[1], V.G. Veloso[2], B. Grinsztejn[2], P.M. Luz[2]
[1]*University of California, Los Angeles, United States,* [2]*Instituto Nacional de Infectologia Evandro Chagas, Fundação Oswaldo Cruz, Rio de Janeiro, Brazil*
Presenting author email: dsilva@bu.edu

Background: In high-income settings, retention of people living with HIV (PLHIV) in early HIV care has been associated with improved survival and virologic outcomes. This study aims to characterize individual-level factors associated with early retention at an outpatient HIV clinic in Rio de Janeiro, Brazil.
Methods: We assessed early retention after initial linkage to HIV care among antiretroviral therapy (ART) naïve PLHIV ≥18 years old who presented to the outpatient HIV clinic at Instituto Nacional de Infectologia Evandro Chagas, Fundação Oswaldo Cruz (INI) between 2000-2011. Linkage within six months of cohort entry was defined by date of the first CD4+ T-lymphocyte count (CD4 count) or HIV viral load (VL), or ART start date, which ever occurred first. Early retention in the two years following linkage was defined by the proportion of six-month intervals with ≥ one CD4 count or VL measurement with the possible categories being 100%, 75%, 50%, 25%, 0%. Logistic regression quantified the association of socio-demographic and clinical factors with good retention (≥75%).
Results: The 1251 participants were 70% male, 48% non-white, median age was 35.02 years (IQR, 28.34-42.42), and 80% met criteria for good retention. Early retention improved over time (Figure 1). Compared to individuals < 30 years of age, older individuals were more likely to have good retention (30-40 years adjusted odds ratio (aOR)=1.58 [95% confidence interval,1.12-2.24]; 40-50 years aOR=2.87 [1.85-4.54]; >50 years aOR=2.48 [1.35-4.78]). Having >8 years of education (aOR=1.93 [1.40-2.67]) and starting ART ≤3 months after linkage (aOR=2.41 [1.49-3.95]) increased the odds of good retention. Unknown HIV transmission route (aOR=0.42 [0.25-0.74]) and unknown baseline CD4 count (aOR=0.44 [0.23-0.86]) decreased the odds of good retention. Sex, race, time-to-linkage, AIDS-defining disease, depression and metabolic disease were not significantly associated with good retention in multivariable analysis.



[Figure 1. Retention in early care of patients entering the HIV outpatient clinic at INI, 2000-2010]

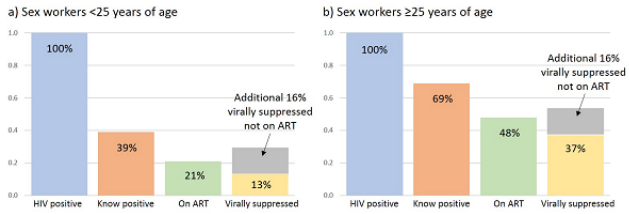
Conclusions: Retention in early HIV care in this urban Brazilian cohort is comparable to high-income settings. Increasing ART availability may partially account for improved early retention over time. Approximately 20% of persons linked to care have poor retention, and efforts to improve early retention should target younger and less educated patients. Further research may elucidate possible psychosocial and structural barriers to early retention in this population.

MOPED736

Engagement in HIV care among young female sex workers in Zimbabwe

S. Napierala Mavedzenge[1], E. Fearon[2], J. Hargreaves[2], P. Mushati[3], S. Mtetwa[3], T. Chiyaka[3], O. Mugurungi[4], D. Hanisch[5], K. Hatzold[6], A. Phillips[7], F. Cowan[3,7]
[1]*RTI International, San Francisco, United States,* [2]*London School of Hygiene & Tropical Medicine, London, United Kingdom,* [3]*Centre for Sexual Health and HIV/AIDS Research, Harare, Zimbabwe,* [4]*Zimbabwe Ministry of Health and Child Care, Harare, Zimbabwe,* [5]*United Nations Population Fund, Harare, Zimbabwe,* [6]*Population Services International, Harare, Zimbabwe,* [7]*University College London, London, United Kingdom*
Presenting author email: smavedzenge@rti.org

Background: Young sex workers (SW) are highly vulnerable to HIV, with data from Zimbabwe estimating HIV incidence at 10.8% among SW ≤25 years. The extent of young SW engagement with HIV services is unknown. In the baseline survey for a community-randomized trial of antiretrovirals for HIV prevention and treatment among SW in Zimbabwe (the SAPPH-IRe trial), we compared engagement in services and estimated the HIV care cascade among SW aged <25 compared with those ≥25 years.
Methods: We conducted the survey among 2722 SW recruited using respondent-driven sampling (RDS) in 14 sites. Eligible participants were ≥18 years and working as SW. A questionnaire was administered collecting data on demographics, sexual behaviour, sex work, HIV testing history and serostatus, uptake of HIV services and ART use. We collected dried blood spots for HIV testing, and if positive measured viral load (VL). Analysis used RDS-2 estimation pooling data across sites.
Results: Mean age was 31 years (range 18-65); 27% were <25 years. HIV prevalence was 56% overall, and was lower among those <25 (33% vs 64%, p<0.01). Among HIV- SW those <25 were moderately more likely to have tested in the last 6 months (75% vs 68%, p=0.08). However among HIV+ SW those <25 were less likely to know their status (39% vs 69%, p<0.01) and among those aware, less likely to report ART use (54% vs 69%, p=0.05). Both age groups reported high 100% ART adherence (83% vs 88%). However, only 62% of SW <25 reporting ART use had VL<1000 copies/mL, compared with 78% in SW ≥25 (p=0.06). Of all HIV+ SW <25 only 13% were on ART and had a VL<1000, compared with 37% in SW ≥25 (p<0.01; Figure). In both groups 16% reporting no ART use had VL<1000.



[Cascade of care for HIV+ female sex workers]

Conclusions: HIV prevalence was lower and recent testing common among SW <25, yet young HIV+ SW were less likely to know their serostatus. Fewer reported taking ART, perhaps reflecting more recent infection, and/or slower HIV progression. Despite high reported adherence, overall just 13% of young HIV+ SW on ART had VL<1000. Services need to be tailored to address the unique needs of young SW.

MOPED737

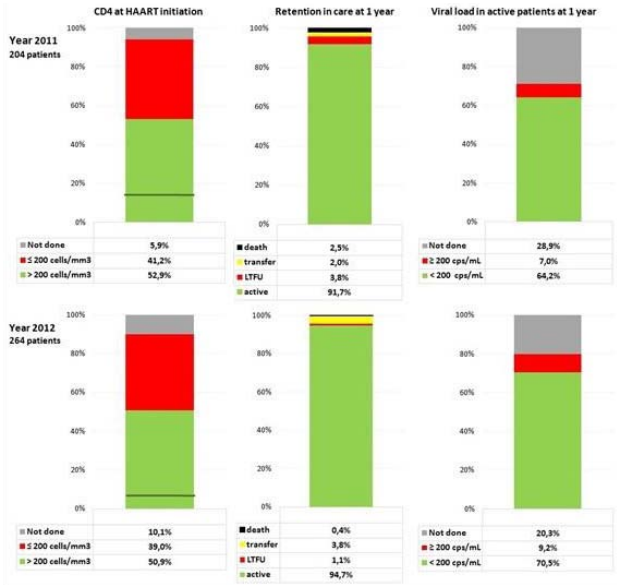
Evaluating the HIV cascade of care: model design, evaluation and results after implementation in one center for 2 consecutive years

M. Wolff[1], C.P. Cortes[1], M. Chiappe[1], D. Vera[2]
[1]*University of Chile, School of Medicine, Santiago, Chile,* [2]*San Borja Arriaran Hospital, Fundacion Arriaran, Santiago, Chile*
Presenting author email: marcewolff@yahoo.com

Background: The Cascade of Care (CoC) of the HIV epidemic implies many components, from a larger undiagnosed infected population to a minority successfully treated. The expanding access to antiretroviral therapy (ART) worldwide requires evaluating the whole process and its components; no standard method for that exists. Initial steps depend mainly in public health policies, the later ones in clinical performance at sites.
Objective: To validate, in a large AIDS care site, a proposed model for evaluating the CoC in the initial and advanced phases of the process, using simple, easily available parameters.
Methods: The 3 main model components are: Proportion of patients initiating ART with baseline CD4 cell count (CD4) > 200 cells/mm^3 in one calendar year (A1); proportion of patients retained in care (by drug pick up or medical visit) (B1) and proportion of active patients with viral load (VL) < 200 copies/mL (C1) both at one year ± 3 months. Secondary components of non-compliance in each main category were classified in: lower baseline CD4 (A2) and no data available (ND) (A3); abandonment (LTFU) (B2); transfer (B3) and death (B4) during year 1; VL

≥200 copies/mL (C2) and ND (C3) at one year. A1, B1 and C1 have each a maximal score of 100 points.

Results: The model was applied to 204 patients initiating ART during 2011 and 264 in 2012. In 2011 52.9% were A1 (CD4 >200 cells/mm^3); 41.2% were A2, and 5.9% A3. Retention (B1) was 91.7%; B2, 3.8%; B3, 2.0% and B4, 2.5%; C1 (VL < 200 copies/mL), 64.2%; C2, 7.0%; C3, 28.9%, respectively. In 2012 endpoints were: A1, 50.9%; A2, 39.0% and A3, 10.1%; B1, 94.7%; B2, 1.1%; B3, 3.8% and B4 0.4%; C1, 70.5%; C2, 9.2% and C3, 20.3%, respectively. (Figure). Retention was similar by drug pick up or medical visit evaluation. 2011 score was 207; 2012 was 216.



[Figure. Endpoints in the evaluation of the HIV cascade of care]
Dark green line: baseline CD4>350 cells/mm3. 2011 = 13.2%, 2012 = 6.8%

Conclusions: The model was easily implemented; gaps preventing optimal endpoints at initial and advanced steps of the CoC were defined. Tailored planning for improving outcomes can be made and standards for performance established. We propose that the model is helpful for evaluating the CoC and can be applied elsewhere.

MOPED738

Loss of HIV-positive patients in rural primary health care facilities in North West province, South Africa: a retrospective register audit

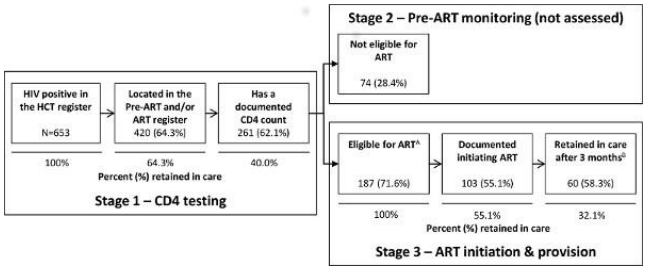
S. Galagan[1], J.M. Gilyvdis[1], S.A. Lippman[2], J. Grignon[3], S. Shade[2], E. Naidoo[4], E. Raphela[4], J. Tumbo[5], S. Barnhart[1,6], P.K. Kohler[1,7]
[1]*University of Washington, Global Health, Seattle, United States,* [2]*University of California San Francisco, Center for AIDS Prevention Studies, San Francisco, United States,* [3]*International Training & Education Center for Health, Department of Global Health, University of Washington, Pretoria, South Africa,* [4]*International Training & Education Center for Health, Pretoria, South Africa,* [5]*University of Limpopo, Department of Family Medicine and Primary Health Care, Medunsa, South Africa,* [6]*University of Washington, Department of Medicine, Seattle, United States,* [7]*University of Washington, Department of Psychosocial and Community Health, Seattle, United States*
Presenting author email: jgrignon@uw.edu

Background: Retention of patients in HIV care is a challenge among ART programs in South Africa. Clinic-based registers may provide a mechanism for tracing clients and assessing outcomes throughout the HIV care cascade, though typically clients are not identified and linked across registers.

Methods: As part of an overall health systems strengthening program in a rural area of North West Province, South Africa, a retrospective government register audit was conducted. Three months of HIV counseling & testing (HCT) and antenatal registers, and six months of Pre-ART and ART registers, were reviewed in twelve clinics. HIV-positive clients in HCT registers were traced to Pre-ART and ART registers. Documented CD4 counts, retention in care, initiation of ART, and referrals were assessed. Among HIV-positive clients identified in antenatal registers, proportions of clients with a documented CD4 result and initiating ART or PMTCT were calculated. Client charts were also accessed, but teams could not link the charts to register entries.

Results: Overall, 7,522 patients were identified accessing HCT services over three months; 653 (8.7%) patients were documented HIV-positive. Patients accessing HCT services were more frequently female (66.0%), adults (66.8%), and referred by health providers (55.9%). Four-hundred and twenty patients (64.3%) were successfully traced to Pre-ART or ART registers. Among those traced, 261 (62.1%) had a CD4 test result documented. Of those eligible for ART (N=187), 103 (55.1%) initiated ART and 60 (58.3%) of these patients had a documented visit to receive ART three months after initiation. Among HIV-positive clients in antenatal registers (N=177), 123 (69.5%) had a CD4 test result and 110 (62.1%) initiated ART or PMTCT.

Conclusions: HIV-positive clients were lost to follow-up at all steps of HIV care, underscoring the need for strategies to improve retention in care. Current documentation estimates a loss of 87.2% of patients between HIV diagnosis and ART provision three months after initiation. However, it is difficult to determine the relative contribution of lack of documentation, death, and clinic transfer compared to true loss of patients to HIV care. Improved identification and linkage of clients across registers would more readily identify losses to care and allow clinics to plan interventions accordingly.



[Retention in the HIV care continuum]

MOPED739

Treatment as prevention in Brazil: speeding up the pace to reach the 90-90-90 targets

A.R. Pascom, C. Habckost, F. Mesquita
Ministry of Health, STD, AIDS and Viral Hepatitis Department, Brasilia, Brazil
Presenting author email: ana.roberta@aids.gov.br

Background: The HIV continuum of care cascade framework allows efficient and effective monitoring of the fundamental needs of people living with HIV/AIDS (PLWHA). In 2014, WHO, UNAIDS, Latin America and Caribbean HIV Technical Cooperation Working Group (GCTH) and regional non-governmental organizations in Latin America stablished treatment targets to be reached by 2020, that were later incorporated by UNAIDS as global targets, the 90-90-90 targets. This study aims to present 2013 HIV continuum of care cascade and to foresee what Brazil still needs to do in order to achieve these targets.

Methods: Information was extracted from National HIV/AIDS databases. We defined four steps in the cascade framework: HIV infected (estimated from a statistical model based on the CD4 count at diagnosis); HIV diagnosed; on ARV treatment (ART); and virologically suppressed (VL < 1000 copies/mL). Based on this cascade, the 90-90-90 targets were estimated to Brazil. In our analysis we considered the amount of PLWHA that were incorporated during 2014 to estimate the number of people we have to include by 2020 to reach the 90-90-90 targets.

Results: Nearly 734,000 Brazilian residents were infected with HIV/AIDS in 2013. Out of them, 80% (589,000) were already diagnosed. Around 355,000 (48%) PLWHA were on ART and 293,000 (40%) had viral suppression. In 2014, we included 49,000 PLWHA on ART (excluding deaths and abandonment), meaning Brazil achieved 68% of its treatment target. Furthermore, we already achieved 63% of 90-90-90 targets related to the viral load suppression.

Conclusions: This study showed that in one year Brazil has achieved more than one fifth of its treatment and viral load suppression 90-90-90 targets. The adoption of treatment as prevention strategy in December 2013 appears to have accelerated the progress towards achieving these treatment targets. Brazil seems to be on the right track to reach the 90-90-90 targets, if it maintains the same rhythm observed in 2014.

MOPED740

National preventing mother to child HIV transmission program 2014, Thailand

S. Boonsuk[1], R. Lolekha[2], T. Naiwatanakul[2], C. Tonpudsa[1], B. Baipluthong[2], K. Tangjitrmaneesakda[3], S. Jirajariyavej[4], D. Teewanda[1], M. Martin[2]
[1]*Bureau of Health Promotion, Department of Health, Ministry of Public Health, Nonthaburi, Thailand,* [2]*Global AIDS Program (GAP) Thailand/Asia Regional Office, Thailand Ministry of Public Health-U.S. CDC Collaboration (TUC), Nonthaburi, Thailand,* [3]*Bangkok Metropolitan Administration, Department of Medical Services, Bangkok, Thailand,* [4]*Taksin Hospital, Bangkok Metropolitan Administration, Bangkok, Thailand*
Presenting author email: wutmd39ju@hotmail.com

Background: Approximately 800,000 women give birth each year in Thailand. In 2010, the national program to prevent mother-to-child HIV transmission (PMTCT) issued guidelines that recommended voluntary HIV counseling and testing for all pregnant women, promotion of couples HIV testing and counseling (CHTC) in antenatal care (ANC) settings, use of triple antiretroviral (ARV) for HIV-infected pregnant women regardless of CD4 count (Option B), ARV prophylaxis and infant formula for HIV-exposed infants, and linkage of HIV-infected women and

families to care. We describe the results of the national PMTCT program implementation in all public hospitals using the national PMTCT intervention monitoring system (PHIMS).

Methods: Aggregate data from ANC, delivery logbooks, counseling records, laboratory reports, and hospital data sources were summarized by hospital staff from ANC units, labor rooms, post-partum wards, and pediatric clinics. Data were compiled into a monthly report form and entered in the web-based PHIMS program. Standard national PMTCT reports were generated and used for analysis.

Results: From October 2013 to September 2014, 8,628 (79.0%) of 10,920 expected reports were received from 784 (86.2%) of 910 public hospitals in all 77 provinces. Among 513,631 women giving birth, 505,158 (98.4%) received ANC, 512,728 (99.8%) had HIV testing results, and 133,930 (26.1%) had received CHTC. Of women who gave birth and had HIV test results available, 3,164 (0.62%) were HIV positive, of whom 2,675 (84.6%) received CD4 count testing and 2,675 (84.6%) received triple ARV, 358 (11.3%) other ARV regimens, and 131 (4.1%) received no ARV. There were 3,182 infants born to HIV-infected mothers including 31 (0.97%) stillbirths, 599 (18.8%) low birth weight (< 2500 grams), and 355 (11.2%) preterm (< 37 weeks) infants. Among 2,689 HIV-exposed infants who received two HIV PCR tests during the reporting period, 60 (2.2%) were HIV infected and 49 (81.7%) of these infants were linked to HIV care.

Conclusions: We found high levels of ANC and HIV testing among pregnant women. Eighty-five per cent of HIV-infected expectant mothers received triple ARV and the mother-to-child HIV transmission rate was below 3%. Public health officials and providers should work to increase CHTC and linkage of HIV-infected infants to care.

MOPED741

Completeness and accuracy of data in Zimbabwe's national PMTCT program health facility registers: findings from a patient level data quality audit

E. Tachiwenyika[1], R. Musarandega[1], M. Murandu[1], M. Chideme[1], C. Muchuchuti[1], B. Mutede[1], I. Shabbir[2], R. Cathcart[2], A. Mahomva[1], L. Katirayi[3]
[1]Elizabeth Glaser Pediatric AIDS Foundation, Technical Department, Harare, Zimbabwe, [2]Elizabeth Glaser Pediatric AIDS Foundation, Strategic Information and Evaluation, Washington DC, United States, [3]Elizabeth Glaser Pediatric AIDS Foundation, Technical Department, Washington DC, United States
Presenting author email: lkatirayi@pedaids.org

Background: Prevention of mother-to-child transmission of HIV (PMTCT) remains a priority in Zimbabwe. Complete and accurate data are required to reliably monitor PMTCT targets. In 2014, the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) conducted a patient level data quality audit (DQA) of the national PMTCT program to measure completeness and accuracy of data in facility registers, which are used to measure PMTCT program performance.

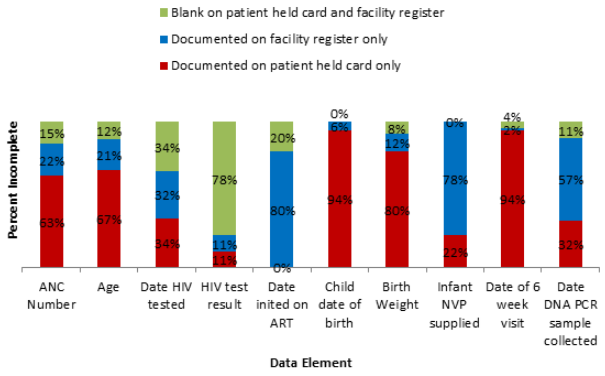
Methods: A descriptive cross-sectional study was conducted in 43 randomly selected health facilities. Patient level data for pregnant and lactating women and infants aged six weeks to six months were abstracted from patient-held medical cards and facility registers. In addition, exit interview findings with antenatal (ANC) and postnatal (PNC) women were compared with data on patient held cards. A data element for example age was complete if patient held card and facility register were documented, and accurate if documentation on the two sources were the same. Reasons for discordance were explored through interviews with healthcare workers (HCWs). Data were analyzed using STATA 12.

Results: Records for 292 ANC and 266 PNC women were reviewed. Table 1 summarizes average completeness and accuracy of data in facility registers by facility type. Overall completeness was 83% for ANC and 71% for PNC; overall accuracy was 75% for ANC and 66% for PNC. Completeness and accuracy of ANC data for clinics and rural hospitals were higher than referral facilities (mission, district and provincial hospitals). Incompleteness and inaccuracy were largely a result of health workers documenting on patient held cards only and not updating facility registers; largely due to multiple registers and high workload. Figure 1 summarizes contribution of documentation practices to incompleteness. Completeness based on data from patients' interviews and patients held cards was 100% for all data elements; accuracy was above 90%.

Conclusions: The variation in completeness and accuracy by facility type calls for targeted on-site mentoring and coaching of facility level health workers. Health worker documentation in patient held cards without updating facility registers was the major determinant of incompleteness and inaccuracy. There is need to ensure that health workers document in facility registers in order to accurately measure PMTCT service uptake.

Health Facility Type	Completeness of ANC data elements	Completeness of PNC data elements	Accuracy of ANC data elements	Accuracy of PNC data elements
Clinic	91%	69%	78%	63%
Rural Hospital	94%	65%	89%	60%
Mission Hospital	85%	76%	76%	72%
District Hospital	68%	74%	54%	66%
Provincial/Central Hospital	75%	70%	76%	67%
Average	83%	71%	75%	66%

[Completeness and Accuarcy of data by facility type]



[Reasons for incompleteness]

MOPED742

Are HIV-positive individuals more likely to engage with HIV care if someone else in the household is HIV-positive and in care?

B. Genberg[1], J. Wachira[2], B. Rachlis[2,3,4], H. Lee[5], C. Chen Bauer[5], V. Naanyu[6], M. Nyambura[2], E. Sang[2], J. Hogan[2,5], P. Braitstein[2,3,7]
[1]Brown University, Health Services, Policy & Practice, Providence, United States, [2]Academic Model Providing Access to Healthcare (AMPATH), Eldoret, Kenya, [3]University of Toronto, Dalla Lana School of Public Health, Toronto, Canada, [4]Ontario HIV Treatment Network, Toronto, Canada, [5]Brown University, Biostatistics, Providence, United States, [6]Moi University, School of Medicine, Eldoret, Kenya, [7]Moi University, College of Health Sciences, Eldoret, Kenya
Presenting author email: brachlis@gmail.com

Background: Our understanding of how household-level factors can influence engagement in HIV care is limited. We examined whether people living with HIV identified through home-based HIV testing (HBCT) were more likely to engage with care if there was already someone living with HIV and in care in the household.

Methods: The Academic Model Providing Access to Healthcare (AMPATH) program is one of Africa's largest HIV care providers and initiated HBCT in 2007. Electronic data from the care program (through June 2014) were merged with data from HBCT from 2009-2011 for one sub-county using probabilistic matching**.** We used adjusted prevalence ratios estimated from log-linear models with robust standard errors and Cox regression to measure the association between engagement in care (at least one visit with an HIV care provider) and having other HIV-positive household members in care for those previously known HIV-positive and the newly diagnosed, respectively. Models were adjusted for the number of HIV-positive members in the household, the total household size, and individual socio-demographic characteristics (i.e., age, sex, marital status, employment, income, education).

Results: A total of 2,355 individuals from 1,736 households were identified during HBCT as previously known HIV-positive, of whom 72%, 23%, and 5% had 1, 2, or ≥3 HIV-positive members in the household respectively. Compared with living in a household with no one engaged in care, having one (adjusted prevalence ratio (APR) = 1.63, 95% confidence interval (CI): 1.43, 1.85) or more (APR = 2.49, 95% CI: 1.96, 3.16) other household members engaged in care was associated with individual engagement in HIV care. Among 1,433 newly identified HIV-positive individuals from 1218 households, 70%, 26%, and 4% had 1, 2, or ≥3 HIV-positive members in the household, respectively. There was no association between household members' engagement in care and prospective linkage to HIV care among the newly diagnosed.

Conclusions: Including family members in intervention strategies may promote individual engagement in HIV care. Additional research is needed to understand the mechanism by which living in a household with at least one other person engaged in HIV care influences individual engagement in care.

MOPED743

Predictors of viral suppression and rebound among HIV-positive gay, bisexual, and other men who have sex with men in a large multi-site Canadian cohort

Z. Tanner[1,2], N. Lachowsky[1,3], S. Patterson[1,2], J. Raboud[4,5], E. Ding[1], H. Samji[1], M. Irick[1], A. Cescon[6], M. Hull[1,3], A. Bayoumi[7,8], M. Loutfy[8,9,10], A. Burchell[11], C. Cooper[12], M. Klein[13,14], N. Machouf[15], J. Montaner[2,3], C.M. Tsoukas[13], R. Hogg[1,2], the Canadian Observational Cohort (CANOC) Collaboration
[1]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada, [2]Simon Fraser University, Faculty of Health Sciences, Vancouver, Canada, [3]University of British Columbia, Faculty of Medicine, Vancouver, Canada, [4]University of Toronto, Dalla Lana School of Public Health, Toronto, Canada, [5]University Health Network, Division of Infectious Diseases, Toronto, Canada, [6]Northern Ontario School of Medicine, Sudbury, Canada, [7]St. Michael's Hospital, Centre for Research on Inner City Health, Toronto, Canada, [8]University of Toronto, Faculty of Medicine, Toronto, Canada, [9]Maple Leaf Medical Clinic, Toronto, Canada, [10]Women's College Research Institute, Toronto, Canada, [11]Ontario HIV Treatment Network, Toronto, Canada, [12]University of Ottawa, Ottawa Hospital Research Institute, Ottawa, Canada, [13]McGill University, Faculty of Medicine, Montreal, Canada, [14]McGill University Health Centre, Montreal Chest Institute, Montreal, Canada, [15]Clinique Medicale l'Actuel, Montreal, Canada
Presenting author email: ztanner@cfenet.ubc.ca

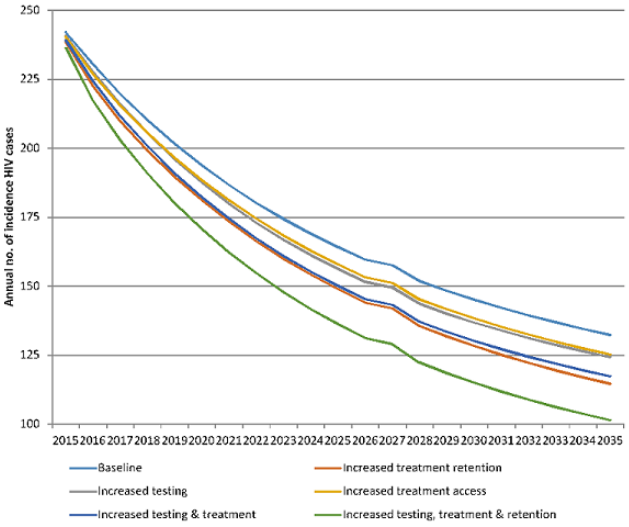
Background: Gay, bisexual, and other men who have sex with men (MSM) represent the largest HIV transmission category in Canada. However, there are limited pan-provincial data regarding HIV treatment outcomes after initiation of antiretroviral therapy (ART). We sought to identify socio-demographic and clinical correlates of viral suppression and rebound among MSM to inform treatment and retention strategies.
Methods: Our analysis included MSM participants in the Canadian Observational Cohort (CANOC), a multi-site cohort of HIV-positive adults from Canada's three most populous provinces, who initiated ART naïvely between 2000-2011. Accelerated failure time models analyzed time to viral suppression (≥2 consecutive measures < 50 copies/mL, ≥30 days apart within 1 year following treatment initiation) and rebound (≥2 consecutive measures >200 copies/mL, ≥30 days apart after achieving suppression), identifying key socio-demographic and clinical correlates.
Results: Within CANOC, 3180 participants were identified as MSM, of which 259 (8%) reported a history of injection drug use (IDU). At pre-ART baseline, the median age and CD4 count were 40 years (IQR=33-46) and 237 cells/uL (IQR=130-340), respectively. Viral suppression within 1 year of ART initiation was achieved by 2616 MSM (82.3%) in a median time of 5 months. Adjusted hazard ratios (HRs) of significant variables (p< 0.05) from the multivariate models are presented in Table 1. Independent predictors of viral suppression include more recent era of ART initiation, higher viral load testing rate, no IDU history, older age at baseline, lower baseline viral load, and prescription of a non-nucleoside reverse-transcriptase inhibitor (NNRTI) versus boosted protease inhibitor (PI) and unboosted PI. Independent predictors of subsequent viral rebound, experienced by 298 participants (11.4%) in a median time of 22 months, included less recent era of ART initiation, higher viral load testing rate, IDU history, younger baseline age, higher baseline CD4 count, and living in British Columbia versus Québec or Ontario.
Conclusions: Identifying predictors of suboptimal treatment outcomes is an important step towards improving HIV treatment and retention programs for MSM across Canada. Priority target groups include younger MSM with a history of IDU, who demonstrated a greater likelihood of treatment failure in our analysis.

MOPED744

Cost-effectiveness analysis alongside the cascade of HIV care: to seek, test, treat or retain? That is the question

B. Nosyk[1,2], J.E. Min[1], E. Krebs[1], R. Barrios[1], J. Montaner[1,3], STOP HIV/AIDS Study Group
[1]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada, [2]Simon Fraser University, Faculty of Health Sciences, Burnaby, Canada, [3]University of British Columbia, Division of Aids, Faculty of Medicine, Vancouver, Canada
Presenting author email: bnosyk@cfenet.ubc.ca

Background: Interventions to improve the cascade of HIV care at its various stages may vary substantially in their ability to deliver good value for money. There is an urgent need to maximize the value of health spending by prioritizing cost-effective interventions and more broadly, identifying an optimal mix of interventions given available resources. We consider hypothetical scenarios of increased uptake of HIV testing and treatment, and improved treatment retention to identify the most cost-effective public health strategy.
Methods: We used a previously-validated dynamic compartmental HIV transmission model to project the costs, benefits and epidemiological outcomes of the HIV/AIDS epidemic in BC from 2015 to 2035 under six hypothetical scenarios: (1) current practice, characterized using all available population-level epidemiologic and economic data; (2) a 10% increase in the HIV testing rate; (3) a 10% increase in treatment uptake; (4) a 25% decrease in the rate of treatment discontinuation; (5) interventions in scenarios (2)+(3); and (6) interventions in scenarios (2)+(3)+(4). Total HIV incidence, mortality, present-valued costs (in 2014$CDN) and quality-adjusted life years (QALYs) were estimated for each scenario, while incremental cost-effectiveness ratios (ICERs) were calculated against scenario (1), as well as the next-most resource intensive strategy in the interest of identifying the most efficient strategy. Analyses were executed from a third party payer (TPP) perspective.
Results: Scenarios (2) - (6) were all highly cost effective (< 1x GDP per capita) compared to actual practice. Strategies (3) and (4) were dominated by strategies (5) and (6) respectively. We found strategy (6) remained cost-effective compared to strategy (5), with an ICER of $30,351 per QALY gained. At an additional cost of $110M over the study timeframe (5.5M/year), jointly increasing HIV testing and treatment access and improving HAART retention resulted in 531 averted HIV cases, 115 averted deaths and an overall gain of 6,469 QALYs.
Conclusions: Despite significant investment and advances in HIV care in BC, we found interventions to further improve HIV testing and care were highly cost-effective. Further research is required to aid resource allocation decisions on the margin, and in real-time, using the observed effectiveness of such interventions as delivered within the province.



[Table 1. Estimated annual HIV incidence in British Columbia, Canada: 2015-2035, under hypothetical scenarios (1) - (6)]

MOPED745

Linkage to HIV care among Tebelopele voluntary counseling and testing clients, 2008 - 2012

N. Prata Menezes[1], P. Lekone[2], P. Loeto[2], R. Monnaatlala[3], M. Letebele[2], D. Ramaabya[4], E. Kim[5], A.C. Voetsch[5], T. Chebani[6], E. Fetogang[6]
[1]Association of Schools and Programs of Public Health/Centers for Disease Control and Prevention Allan Rosenfield Global Health Fellow, Atlanta, United States, [2]Centers for Disease Control and Prevention, Gaborone, Botswana, [3]Tebelopele Voluntary Counseling and Testing, Gaborone, Botswana, [4]Ministry of Health, Department of HIV/AIDS Prevention and Care, Gaborone, Botswana, [5]Centers for Disease Control and Prevention, Atlanta, United States, [6]Ministry of Health, Department of Health Policy Development, Monitoring and Evaluation, Gaborone, Botswana
Presenting author email: wyi0@cdc.gov

Background: Effective HIV treatment programs require successful referral of newly diagnosed clients. UNAIDS has set a goal of ensuring 90% of HIV-infected persons are diagnosed, 90% of those diagnosed are on antiretroviral therapy (ART), and 90% of those on ART achieve viral suppression. Estimated coverage of Botswana's HIV treatment program (Masa) among treatment eligible patients is 87%.
However, the proportion of HIV-positive clients identified through voluntary HIV counseling and testing and successfully referred to HIV care is unknown.
Methods: We used deterministic matching to identify individuals with HIV-positive test results at Tebelopele voluntary counseling and testing (TVCT) facilities that were in the Masa program database from 2008-2012. Individuals were matched by national identity number (Omang), name, birthdate, and gender. We analyzed demographic and clinical characteristics of individuals who were successfully linked to care. We used Masa treatment registration date as a proxy for entry into HIV care to calculate median days between first positive HIV result and entry into care.
Results: We identified 56,387 HIV-positive TVCT clients and 228,189 Masa patients. A total of 19,571 (34.7%) TVCT clients were linked to the Masa program. Overall linkage to care of HIV-positive individuals in TVCT was significantly higher (p< 0.001) among females (37.3%) than among males (31.0%). Among those linked to care, the proportion of TVCT clients linked to care within 6 months of HIV diagnosis increased from 31.0% in 2008 to 57.2% in 2012

(p< 0.001). Among those linked to care, median time from diagnosis to enrollment in care decreased from 423 days in 2008 to 42 days in 2012 (p< 0.001). Overall median CD4 cell count at enrollment increased from 171 cells/mm^3 in 2008 to 201 cells/mm^3 in 2012 (p< 0.001).
Conclusions: Documentation of successful referral from TVCT sites to Masa care and treatment services was available for one in three HIV-positive Tebelopele clients. Although speedy referral into Masa care improved, most TVCT clients who entered HIV care in 2012 had a CD4 count below national guidelines for ART initiation. Programs aimed at promoting earlier diagnosis and strengthening linkages to HIV care and retention are needed to reach the UNAIDS 90-90-90 goal in Botswana.

MOPED746

Linkage to care among HIV-infected infants in Botswana

G. Machao[1], P. Lekone[1], A. Lesego[2], E. Fetogang[3], N. Prata Menezes[4]
[1]Centers for Disease Control and Prevention Botswana, Global AIDS Program, Gaborone, Botswana, [2]International Training and Education Center for Health, Gaborone, Botswana, [3]Ministry of Health, Department of Health Policy Development, Monitoring and Evaluation, Gaborone, Botswana, [4]Centers for Disease Control and Prevention Atlanta, Atlanta, United States
Presenting author email: wyi0@cdc.gov

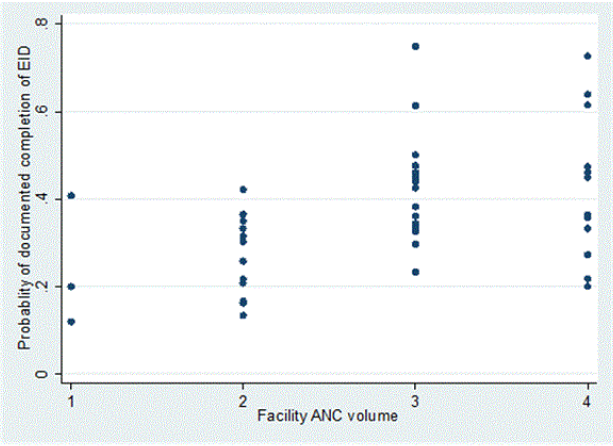
Background: HIV prevalence among pregnant women in Botswana is 30.4% with mother to child transmission estimated at < 4%. HIV-exposed infants are DNA PCR tested in the national Early Infant Diagnosis (EID) program. We assessed linkage of HIV-infected infants in the EID program to the ART program.
Methods: We de-duplicated the national EID database and the HIV care database. Demographic and clinical data for HIV-exposed infants were collected on lab requisition forms and sent with dried blood spot specimens for DNA PCR testing at referral laboratories in Botswana. Infant data and HIV results were captured in the EID database. Using deterministic matching we matched infants who tested HIV-positive from 2008 to 2012 to infants registered for ART using name, date of birth and gender for the same time period. We assessed median days to linkage and report on demographic and clinical characteristics of these infants.
Results: A total of 54,343 infants were PCR tested from 2008 to 2012 and 1,389 (2.6%) were identified as being positive for HIV. The HIV care database contained 228,189 unique individuals who were registered to receive HIV care from 2008 to 2012. Only 218 (15.7%) HIV-positive infant names were found in the HIV care database and were considered linked. Median time to linkage was 64 days and 52.3% of the infants were female. Of those linked to HIV care, 31.2% were infants tested by 8 weeks of age compared to 6.7% of infants tested at more than 12 months of age. Of the matched infants, 67.0% were linked to care within six months of being diagnosed. The percentage linked to care within 6 months was 70.6% in 2008, 70.9% in 2009, 68.3% in 2010, 52.9% in 2011 and 63.8% in 2012 (test for trend p=0.19).
Conclusions: Early infant diagnosis is intended to promptly identify and link HIV-positive infants to link to treatment and care for reduced morbidity and mortality. Our results indicate that less than 20% of HIV-positive infants were linked to care, with two-thirds linked within 6 months of being diagnosed. This most likely represents the worst-case scenario of linkage to care success.

MOPED747

A population-based estimate of documented completion of early infant diagnosis in Mashonaland East Province, Zimbabwe

K. Webb[1], V. Chitiyo[1], T. Ndoro[1], P. Nesara[1], S. Zizhou[2], N. Mahachi[3], B. Engelsmann[1], E. Geng[4]
[1]Organisation for Public Health Interventions and Development (OPHID) Trust, Harare, Zimbabwe, [2]Ministry of Health and Child Care, Mashonaland East Province, Marondera, Zimbabwe, [3]Ministry of Health and Child Care, National PMTCT Program, Harare, Zimbabwe, [4]University of California (UCSF), San Francisco, United States
Presenting author email: karen.myllynen.webb@gmail.com

Background: In Zimbabwe, information on health services received by HIV positive pregnant women and their exposed-infants across the PMTCT cascade is documented in multiple, paper-based registers at health sites. Summarizing individual completeness of service uptake can only be achieved by manual review and therefore the proportion of mother-baby pairs who uptake timely EID is not routinely reported. We conducted a population based survey in which individual HIV infected mother-baby pairs were followed through registers to better understand probability and determinants of completing EID.
Methods: We selected 45 of 193 health facilities in Mashonaland East Province using a modified probability proportional to size schema. Outcomes of all HIV positive mothers enrolled in ANC from 26-Apr-12 to 30-May-13 were traced through facility registers to determine documented uptake of EID for their HIV-exposed infant within three months of birth. We estimated the weighted probability of EID completion overall and assessed site-to-site variability. Influence of routinely collected facility and individual factors on documented completion of EID was analyzed using Poisson regression with robust standard errors to estimate risk ratios.
Results: We identified 2646 HIV positive women among a population of 18 065 attending ANC in 44 facilities (14.6%); 35.5% (n=939) had documented uptake of EID within three months (95%CI: 31.1%-39.9%). Average EID completion varied across ANC site volume (p< 0.01), but variability within groupings by site size was large and varied by more than 2-fold.



Volume categories women in ANC April 2012-May 2013:
1 = 1001-1500; 2 = 501-1000; 3 = 201-500; 4 = 0-200

[Figure. Proportion documented EID among HIV positive women in ANC by site volume]

After adjustment, gestational age at presentation (Risk Ratio [RR]: 0.97 per two weeks; 95%CI:0.95-0.99; p<0.01), later calendar time of ANC presentation (RR: 1.04 per 30 days; 95%CI:1.02-1.06, p<0.01) and smaller site volume were significantly associated with EID completion.

Variable ANC Volume	Risk Ratio	p-value	95% CI
High: 1001-1500 (referent)	1	-	-
Med-High: 501-1000	1.23	0.05	(1.00, 1.52)
Med-Low: 201-500	1.78	> 0.0001	(1.45, 2.19)
Low: 0-200	1.85	> 0.0001	(1.44, 2.38)
Poisson regression showing association of site ANC volume on the probability of documented EID completion. Association is adjusted for gestational age at presentation and calendar time.			

[Documented EID completion]

Conclusions: We observed low documented uptake for timely EID among a population-based sample of HIV positive women in ANC. While facility size had a strong influence on the probability of EID completion, dramatic variability within groupings by size indicate need for additional studies to understand facility characteristics related to size as well as local operational factors unrelated to size for effective service delivery. Future research should seek to trace and document true outcomes among mother-baby pairs with no documented uptake of timely EID.

MOPED748

Understanding gaps in service delivery through the HIV diagnosis-to-treatment cascade: findings from health facility surveys in six sub-Saharan countries

A. Wringe[1], K. Church[1], K. Machiyama[1], J. Nakiyingi-Miiro[2], A. Crampin[3], S. Oti[4], M. Mwangome[5], B. Zaba[1], C. Nyamukapa[6], A. Nyaguara[7], T. Lutalo[8], D. Michael[9], X. Gomez-Olive[10], J. Todd[1]
[1]London School of Hygiene and Tropical Medicine, Population Studies, London, United Kingdom, [2]MRC/UVRI Uganda Research Unit on HIV/AIDS, Entebbe, Uganda, [3]London School of Hygiene and Tropical Medicine, Infectious Disease Epidemiology/Karonga Prevention Study, Chilumba, Malawi, [4]African Population Health Research Center, Nairobi, Kenya, [5]Ifakara Health Institute, Dar es Salaam, Tanzania, United Republic of, [6]Manicaland HIV/STD Prevention Project, Harare, Zimbabwe, [7]Kenya Medical Research Institute, Kisumu, Kenya, [8]Rakai Health Sciences Program, Kampala, Uganda, [9]National Institute of Medical Research, Mwanza, Tanzania, United Republic of, [10]MRC/Wits Rural Public Health and Health Transitions Research Unit, Johannesburg, South Africa
Presenting author email: mia.crampin@lshtm.ac.uk

Background: Despite antiretroviral therapy (ART) roll-out, excess deaths occur across the diagnosis-to-treatment cascade. As part of a multi-country study to investigate HIV mortality in African health and demographic surveillance sites (HDSS), we conducted surveys in health facilities serving the study populations to describe the delivery and quality of HIV testing and counselling (HTC), and HIV care and treatment services.

Methods: Health facilities serving the population were purposively sampled in nine HDSS sites in Uganda, Tanzania, South Africa, Zimbabwe, Malawi and Kenya. Between October 2013 and May 2014, structured questionnaires were administered to the in-charge staff at each facility covering provision of HTC, prevention of mother-to-child transmission (PMTCT) and ART services. Data were entered at a centralised location and descriptive statistics were produced using Stata12.
Results: 139 facilities were surveyed ranging from 6 in Malawi to 36 in Zimbabwe. 65% of facilities were government-run, 27% were lower-level facilities (eg/dispensaries) and 10% were referral hospitals. HTC was available in some form at all facilities, though provider-initiated testing and counselling was not systematically provided in any site, even for attendees at antenatal care or family planning clinics. The availability of mobile HTC services ranged from 13% of 8 facilities in Kisesa (Tanzania) to 93% of 14 facilities in Rakai (Uganda).
Over 90% of facilities in all sites provided PMTCT-related services, while the proportion initiating patients on ART ranged from 39% to 100%. Task-shifting was common with over 50% of facilities in all sites allowing nurses to distribute ART refills. Stock-outs of HIV test kits and antiretroviral drugs in the past year occurred in facilities in all sites except South Africa. Between 6% and 40% of facilities per site reported senior staff member departures over the past year.
Conclusions: HTC and PMTCT service coverage was high across all sites, but there was variability in ART availability, decentralisation and task-shifting. Key challenges for all sites include staff turnover and supply issues demonstrating that poor service quality represents an important barrier to effective ART delivery. Future analyses comparing these findings with the mortality distribution of HIV-infected persons in each site will help explain the impact of programme differences on survival.

MOPED749

Linkage to TB treatment in Botswana among Tebelopele clients who screened positive for TB, 2008 - 2012

G. Machao[1], P. Lekone[1], T. Lere[2], B. Kgwaadira[2], P. Loeto[1], J. Kabomo[3], E. Fetogang[4], D. Voetsch[5], N. Prata Menezes[5], E. Kim[5]
[1]Centers for Disease Control and Prevention Botswana, Global AIDS Program, Gaborone, Botswana, [2]Ministry of Health, Department of Public Health, Gaborone, Botswana, [3]Tebelopele Voluntary Counseling and Testing, Gaborone, Botswana, [4]Ministry of Health, Department of Health Policy Development, Monitoring and Evaluation, Gaborone, Botswana, [5]Centers for Disease Control and Prevention Atlanta, Atlanta, United States
Presenting author email: xfw9@cdc.gov

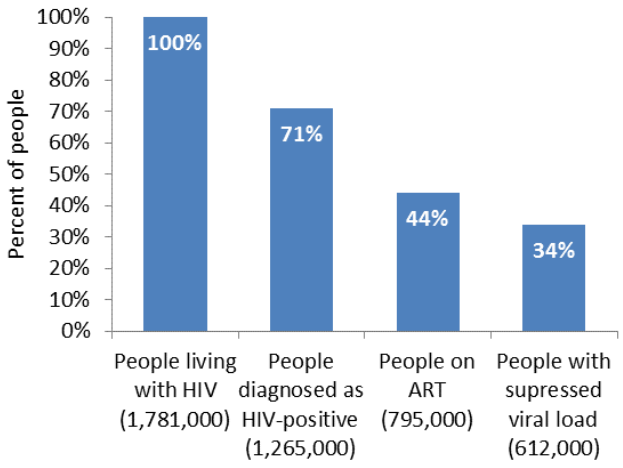
Background: The HIV prevalence in Botswana is 17.6%, while the tuberculosis (TB) case notification rate is 331 cases/100,000 population. The TB-HIV co-infection rate is estimated to be 65% (range 60-86%). In 2008, Tebelopele Voluntary Counseling and Testing (TVCT) began screening clients for TB symptoms. We assessed linkage between TVCT clients with TB symptoms and the Botswana National TB Programme (BNTP).
Methods: We identified unique client records in the 2008 to 2012 electronic TB register (ETR) and TVCT databases. TVCT clients age ≥15 screened positive for TB if they experienced cough lasting >2 weeks, fever, night sweats and unexplained weight loss. ETR only captures patients who are started on TB treatment and not all those that receive diagnostic evaluation. Using deterministic matching by Omang (national identification number), name, date of birth and gender we identified clients with a positive screen for TB in TVCT and were in ETR as having received TB treatment. We assessed median days to linkage, and other socio-demographic and clinical characteristics of these clients.
Results: Of the 425,157 TVCT clients, 28,542 (6.7%) screened positive for TB and of those, 63.4% were HIV negative. There were 25,968 individuals who received treatment in the BNTP. Among TVCT clients who screened positive for TB, 521 (1.8%) were linked to TB treatment in a median of 74 days. Among those linked, 84.8% were HIV-positive, 39.9% were females and 62.0% were linked within 6 months of TB screening. HIV-negative clients were more likely to be linked to treatment within 6 months than HIV-positive clients (75.9% vs. 59.5%, p<0.01). Linkage to TB treatment within 6 months increased from 48.0% in 2008 to 95.8% in 2012 (p-value=0.02).
Conclusions: Results indicate that <2% of individuals who screen positive for TB in VCT are diagnosed with TB and linked to treatment. With HIV-associated deaths accounting for 25% of all TB deaths globally, early identification and linkage to treatment among co-infected patients is crucial in reducing morbidity and mortality. More efforts are required to ensure that clients who screen positive for TB are evaluated and treated if diagnosed with active disease.

MOPED750

The care and treatment cascade and 2020 "90-90-90" targets in Latin America and the Caribbean: baseline 2013 estimates

G. Ravasi[1], M. Vila[2], M. Alonso[1], B. Gómez[3], E. Rodriguez[4], N. Jack[5], M. Ghidinelli[1]
[1]Pan American Health Organization/World Health Organization, Washington, United States, [2]Pan American Health Organization/World Health Organization, Buenos Aires, Argentina, [3]Pan American Health Organization/World Health Organization, Bogotá, Colombia, [4]Pan American Health Organization/World Health Organization, San Salvador, El Salvador, [5]Pan American Health Organization/World Health Organization, Kingston, Jamaica
Presenting author email: giovanni.ravasi@gmail.com

Background: In 2011, Latin America and Caribbean (LAC) countries reaffirmed their commitment to Universal Access to antiretroviral treatment (ART) (i.e. 80% ART coverage of people in need) by 2015. In 2014, new regional targets for 2020 were presented and endorsed at the Regional HIV Care and Treatment Forum held in Mexico City in May 2014 (90% diagnosed with HIV; 90% ART coverage of those in need; 90% viral suppression on ART; <10% late diagnosis with < 200 CD4+), based on the framework of the HIV care and treatment cascade.
Methods: We estimated a 2013 baseline for the 2020 targets and the care and treatment cascade for LAC, based on analysis of secondary data from UNAIDS estimates of people living with HIV, 2014 Global AIDS Response Progress Reporting (GARPR) data, reports from PAHO technical cooperation missions and other published secondary sources.
Results: For 2013, the baseline regional situation for the 2020 targets showed that 71% of all estimated persons with HIV were aware of their status (data from 13 countries representing 73% of all persons with HIV), 56% of persons eligible for treatment were on ART (based on GARPR data for LAC), and 77% of persons on ART had a viral load <1000 copies/ml (data from 21 countries representing 76% of all persons with HIV). In addition, 35% of new diagnosis were detected late with <200 CD4+ (data from 21 countries representing 76% of all persons with HIV). Based on 2013 data, the regional cascade of the continuum of care shows that 71% of people living with HIV were diagnosed (data from 13 countries), 44% were on ART (GARPR data) and 34% achieved viral load suppression (data from 21 countries).



[The 2013 care and treatment cascade for LAC]

Conclusions: In order for LAC to achieve the 90-90-90 targets by 2020, countries should increase efforts to expand HIV testing strategies for timely diagnosis prioritizing key populations based on epidemiological data,. Strengthening linkage and retention in care key to achieve ART coverage and viral suppression targets. The 90-90-90 targets are ambitious, but this analysis demonstrates they can be adequately monitored with available data to assess progress and challenges.

MOPED752

Improving engagement in care and viral suppression through health systems linkages and intensive case management: preliminary findings from a multi-city implementation project

M. Peng[1], R. Westergaard[1], C. Schumann[2], A. Meier[1], T. Hess[1], J. Vergeront[2]
[1]University of Wisconsin School of Medicine & Public Health, Department of Medicine, Madison, United States, [2]Wisconsin Division of Public Health, AIDS/HIV Program, Madison, United States
Presenting author email: rpw@medicine.wisc.edu

Background: To optimize antiretroviral treatment effectiveness, health systems must respond to diverse medical and social service needs of persons living with HIV/AIDS. The aim of this study was to evaluate the effect of an intensive case management program administered across multiple agencies by the Wisconsin AIDS/HIV Program. The program was designed to provide clients with the knowledge and skills necessary to maintain care engagement and achieve/ sustain viral suppression, and specifically targeted 3 groups:
(1) those newly-diagnosed with HIV,
(2) individuals being released from prison, and
(3) patients known to have HIV who have not consistently engaged in care.
Methods: This retrospective analysis compared clients enrolled in a time-limited, intensive case management intervention and propensity-matched controls selected from the Wisconsin HIV surveillance database. The study sample included 235 clients enrolled in intervention between 6/3/2013 - 8/26/2014 and a 1:1 matched control group. Engagement in care was defined as the presence of at least one HIV-specific laboratory test every 6 months since enrollment. Viral suppression was defined as a viral load ≤200 copies/ml at the time of the latest laboratory test during the follow-up period. Chi-square tests were used to assess differences between intervention and control groups.
Results: The intervention and control groups were similar with respect to median age (34), gender (80.4% male), and self-reported racial/ethnic group (24.3% white, 56.8% Black, 15.5% Hispanic/Latino, 3.4% Other). Compared to matched controls, a significantly higher proportion of intervention clients were engaged in care (75.3% vs. 49.8%, p<0.0001) and achieved viral suppression
(70.2% vs. 35.7%, p<0.0001). A subgroup analysis comparing only newly-diagnosed clients suggested there was no significant difference in care engagement between the intervention and control groups (78.7% and 74.5%, p =0.49); however, the proportion of newly-diagnosed patients achieving viral suppression was significantly higher for intervention clients (74.5% vs 58.5%; p = 0.02).
Conclusions: Intensive case management appears to be an effective strategy for improving care engagement and viral suppression among individuals with substantial barriers to HIV care. Future studies should investigate long-term treatment outcomes after discharge from the intervention in order to assess the sustained impact of the intervention among this patient population.

MOPED753

Characterizing retention in HAART as a recurrent event process: insights into 'cascade churn'

B. Nosyk[1,2], L. Lourenco[1], J.E. Min[1], D. Shopin[1], V. Lima[1], J. Montaner[1], STOP HIV/AIDS Study Group
[1]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada, [2]Simon Fraser University, Faculty of Health Sciences, Burnaby, Canada
Presenting author email: jmin@cfenet.ubc.ca

Background: The individual and public health benefits of highly active antiretroviral therapy (HAART) rely on continuous lifelong treatment retention. We aim to characterize HAART persistence and identify determinants of successive durations of HAART retention and non-retention over time.
Methods: We considered all ARV-naïve individuals initiating HAART during the period 1996-2012. We used linked population-level health administrative data to characterize durations of HAART retention and non-retention. We considered these durations separately, and used Cox proportional hazards (CPH) frailty models to identify demographic and treatment-related factors associated with durations of HAART retention and non-retention.
Results: A total of 6152 individuals were included in the analysis; 81.2% were male, 40.6% were people who inject drugs (PWID), and 42.8% initiated treatment with CD4< 200ppm^3. Overall 29% of the individuals sampled were continuously retained on HAART through the end of follow-up. HAART episodes were a median 6.8 months (interquartile range: 2.3, 19.5), while off-HAART episodes lasted a median 1.9 months (1.2, 4.5). In CPH frailty models, durations of HAART retention improved over time, while successive treatment episodes tended to decrease in duration among those with multiple attempts while off-HAART episodes remained relatively stable in duration. Younger age, earlier stages of disease progression and injection drug use were all associated with shorter durations of HAART retention and longer off-HAART durations.
Conclusions: Metrics to monitor HAART churn should be prioritized for HIV surveillance. There is an urgent need to develop clinical strategies and public health policies to improve HAART persistence, particularly among those at earlier stages of disease progression, the young, and PWID.

Monitoring and evaluation of health systems

MOPED754

The cost-effectiveness of population-level HAART expansion in British Columbia

B. Nosyk[1,2], J.E. Min[1], V. Lima[1,3], R. Hogg[1,2], J. Montaner[1,3], STOP HIV/AIDS Study Group
[1]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada, [2]Simon Fraser University, Faculty of Health Sciences, Burnaby, Canada, [3]University of British Columbia, Division of Aids, Faculty of Medicine, Vancouver, Canada
Presenting author email: jmin@cfenet.ubc.ca

Background: The cost-effectiveness of widespread HIV screening and facilitated access to antiretroviral treatment was first illustrated using mathematical models and since validated in a clinical trial setting. However, coordination and execution of a population-level response to HIV/AIDS is resource-intensive. Few examples of extensive evaluations of the public health and economic value of extant systemic responses are available. We capitalized on comprehensive data infrastructure to determine the cost-effectiveness of highly active antiretroviral therapy (HAART) scale-up witnessed in BC, Canada from 1997 to 2010 compared to hypothetical scenarios characterized by constrained treatment access.
Methods: Using linked population-level data, we populated a dynamic compartmental HIV transmission model to simulate the HIV/AIDS epidemic in BC from 1997 to 2010. HIV screening, transmission, risk behaviours, costs (in 2010$CDN) and quality-adjusted life years (QALYs) were estimated as a function of HIV risk group and disease progression. Incremental cost-effectiveness ratios (ICERs) were calculated from societal and third party payer (TPP) perspectives to compare actual practice (the true number of individuals accessing HAART) to scenarios of constrained expansion. Structural and parameter uncertainty was investigated in sensitivity analysis.
Results: We estimated that actual practice resulted in 263 averted incident cases compared to the 75% HAART access scenario, and 624 averted cases compared to the 50% access scenario. Within the study timeframe and using a TPP perspective, actual practice was costlier than scenarios of reduced treatment expansion, but led to substantially greater QALY gains, resulting in ICERs of $10,283/QALY compared to 75% expansion, and $11,153/QALY compared to 50% expansion. From a societal perspective, actual practice was cost-saving over the study horizon. Extending the time horizon to 2035 indicated that actual practice should lead to a (discounted) savings of $24.8M in total cumulative costs compared to the 75% access scenario, and a savings of $65.8M compared to the 50% access scenario.
Conclusions: The expansion of HAART in BC has resulted in substantial decreases in morbidity and mortality as well as a reduction in new HIV diagnoses. Resulting ICERs, derived within a limited timeframe, were well within the range of societal willingness to pay for an incremental QALY gain, and were cost-saving from a societal perspective.

MOPED755

Using the community score card approach to assess the quality of HIV/AIDS service delivery in public health facilities in Uganda

S. Kentutsi
National Forum of People Living with HIV/AIDS Networks in Uganda, Kampala, Uganda
Presenting author email: skent41@nafophanu.org

Background: The Community Score Card is a participatory community based monitoring and evaluation tool that enables citizens to assess the quality of public services including health. It is used to inform the citizens about the services they are entitled to, empowers them to monitor the quality, accessibility, availability and engage duty bearers to address concerns and gaps that may exist.
Methods: The Community Score Card approach used a phased methodology; in put tracking that involved physical observations, assessments and awarding marks using Focus Group Discussions and Key Informant Interviews, interface meetings with all stakeholders to jointly agree on marks given. The study was conducted in 12 health facilities in districts of Kitgum, Serere and Kalangala at Health Centre III and IV levels with a total of 472 (221Male, 251Female) respondents.
Results: The assessment was based on the thematic areas of the National HIV&AIDS Strategic Plan HIV of Prevention, Care&Treatment, Social Support and Systems Strengthening. The key areas for assessment was quality of service delivery in terms of eMTCT, HIV Counseling&Testing, Male Circumcision, blood transfusion, family planning, condom supply, ART&TB services, palliative care, nutritional services, home visits, paediatric and adolescent

HIV care. Provision of IEC materials, capacity building, rights awareness and psychosocial support services, staffing, equipment and infrastructure were assessed. Gaps revealed were drug and other supply stock outs, low staffing levels, lack of transport, absence of CD4 machines, limited knowledge on patients rights, staff absenteeism, fewer consultation rooms, fewer staff houses, poor patient-heath worker relationship, low uptake of family planning services and negative attitudes towards female condom use. Despite the gaps, the facilities were doing their best to serve the masses.

Conclusions: The health facilities serve the populace amidst several gaps. There is an urgent need to recruit more health workers to fill up the staffing gaps and reduce on the waiting time that patients take to see health workers and to ensure constant supplies of drugs, equipments and reagents including testing kits and condoms to reduce on frequent stock outs. Community sensitisation sessions on the national patient's charter as well as legal and human rights should be undertaken to empower citizens.

MOPED756

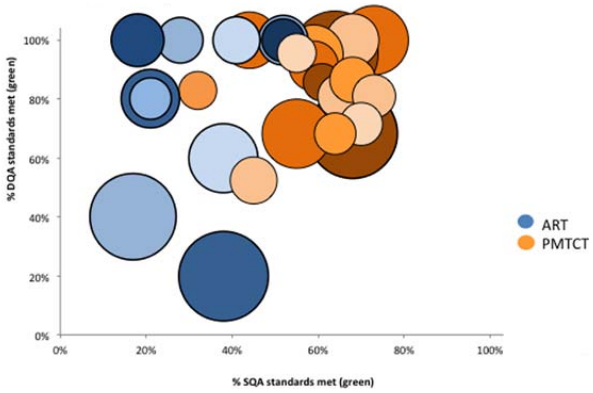
Assessment of data and service quality of the national PMTCT and ART programs in Cameroon

J.R. Lim[1,2], C. Keleko[2], D. Duncan[3], A. Cox[3], J. Amann[3], G.L. Ekali[4], J.J. Mosoko[2], O. Bolu[2]
[1]Association of Schools and Programs of Public Health/U.S. Centers for Disease Control and Prevention Allan Rosenfield Global Health Fellowship, Washington, United States, [2]U.S. Centers for Disease Control and Prevention, Yaounde, Cameroon, [3]U.S. Centers for Disease Control and Prevention, Atlanta, United States, [4]National AIDS Control Committee, Ministry of Public Health, Yaounde, Cameroon
Presenting author email: obb3@cdc.gov

Background: High quality prevention of mother-to-child HIV transmission (PMTCT) and antiretroviral treatment (ART) programs are necessary for HIV epidemic control. Program data and service quality must be monitored and strengthened to ensure that programs are optimized. The U.S. Centers for Disease Control and Prevention (CDC) provided technical assistance to the Cameroonian government to conduct a data quality and service quality assessment (DQA-SQA) in a sample of facilities in the Northwest and Southwest regions of Cameroon. The purpose was to measure data and service quality and to identify areas that need quality improvement. While the CDC through the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) currently only provides support to the PMTCT program, the activity served as a baseline for the newly-supported ART program.

Methods: Eighteen sites were selected based on a high volume of HIV-positive women receiving ARVs for PMTCT; 10 sites provided ART services; and 9 sites participated in an Option B+ pilot. A site assessment tool was developed in line with national guidelines to score facilities using a standardized scale to indicate site capacity. Assessment team members were trained to use the tool, and conducted the assessment through discussions with facility staff, review of national tools, and recreation of program indicators. Immediate written feedback was provided to facility staff and PEPFAR-funded partners to highlight strengths and challenges, provide recommendations, and facilitate remediation.

Results: DQA challenges included varying indicator calculation methods, incomplete national tools, and lack of data use for program management. The SQA identified gaps in patient care and management; where over 50% of sites needed improvement or urgent remediation. Although not a representative national sample, results demonstrate data and service quality are not always concordant by program area. While the PMTCT program data and service quality correlated, the data quality and quality of services at high-volume ART sites did not. (Figure)



[Figure. Distribution of sites by % of PMTCT (n=18) and ART (n=10) standards met for DQA-SQA, Cameroon. The area of the circle reflects the patient volume at the facility, and the saturation in colour is to distinguish each facility]

Conclusions: High quality data may not imply high quality services. Poor clinical documentation may impede patient care despite high quality program data. DQA-SQA methods can be used to inform strategic planning and program improvement. Synthesis of results provides context and understanding of the interaction between data and service quality.

MOPED757

M&E priority interventions: an assessment of M&E interventions that promote data quality in HIV care and treatment setting

D. Damba
Baylor College of Medicine Children's Foundation - Uganda, Strategic Planning, Monitoring and Evaluation, Kampala, Uganda
Presenting author email: ddamba@baylor-uganda.org

Background: With the global scale-up of treatment and care services, interventions to enhance data quality are inevitable. We implemented interventions to promote data quality in health facilities in Eastern Uganda including data validation, training, mentorship, financing, feedback meetings, computerisation, routine data quality assessment(RDQA) and supervision. This paper presents a before and after evaluation of these M&E strategic interventions.

Methods:
STUDY DESIGN: Before-and-after evaluation of the intervention.
POPULATION: 26 study sites were randomly selected from 78 ART sites in Eastern Uganda.
STUDY PERIOD: Records of 2010 (before intervention) and 2014 (after the intervention) were evaluated.
DATA COLLECTION: A standard RDQA tool was used to collect data on accuracy, completeness and timeliness of reports and other Monitoring and Evaluation (M&E) system dimensions such as structure, functions & responsibilities; use of appropriate tools; availability of data SOPs and reporting through a national system.
ANALYSIS: A report was considered accurate if the variance between the actual and reported data was less than 5%; complete if all fields filled and timely if submitted before 7th day. The M&E system dimensions was assessed using binary responses(YES/NO). A logistic regression model was fitted using SAS 9.2.

Results: Sixty percent of monthly reports were submitted by the study sites before compared to 91% after the intervention. The proportion of reports reviewed by supervisors was 51% before compared to 94% after the intervention. Compared to the period before, the odds were higher after intervention by 4.4 times (95%CI: 2.3-8.6) for an accurate report, 7.3 times (95%CI: 5.7-9.5) for a complete report and 7.3 times (95%CI: 5.7-9.5) for a timely report. Regarding the M&E dimensions, 92%(24) of sites had a well-established M&E system with defined roles and responsibilities and capable staff after intervention than before(42%). There was an increase in the proportion of sites using appropriate tools (from 60% to 89%), with SOPs (from 31% to 75%) and reporting through national system (from 61% to 100%).

Conclusions: Results in this study revealed strong evidence of strategic M&E interventions that yielded good quality data. Service providers and implementing partners need to prioritize and integrate them in in HIV care and treatment services.

MOPED758

Who accesses health services earlier than the other? Early lessons from an mHealth referral system in one of the 63 districts of Zimbabwe

P. Nesara
OPHID Trust, Harare, Zimbabwe
Presenting author email: nesarap@hotmail.com

Background: The mobile health (mHealth) system can be used to track and trace clients in hard-to-reach communities. Although referral systems have been in use in some resource-constrained settings[1], limited data are available on the number of days taken from date of referral to date of accessing health service. Our primary outcome of interest was number of days taken from date of referral to date of accessing services.

Methods: Three community referral facilitators, each based at a clinic, and 36 village health workers based in the community were each provided with a mobile phone to facilitate communication and data collection. Mobile phones were installed with secure templates to collect client details. Data were collected prospectively between 12 October 2014 and 8 January 2015 and analysed descriptively.

Results: Of the 56 clients, 14 (25%) were male and 42 (75%) were female. Modal age was 24 years. About. Female clients mostly accessed HIV testing (n=15), TB screening (n=10), ANC booking (n=8) and baby clinic (n=5). All male clients above 15 years (n=7) accessed TB screening only. Number of days taken to access a health service ranged from 0 to 33 days with a modal of 2 days. Clients referred for ANC or TB screening tended to delay by between 3 to 7 days. When outliers were removed from analysis (Figure 1), mean number of days was 1.25 (95% confidence interval [CI], 0.64-1.86) for male and 2.44 (95%CI, 1.69-3.20) for female.

Conclusions: Analysis of mHealth data helped to identify number of days clients take to access services. Reasons why women take relatively longer number of days than men following a referral needs to be investigated. Providing outreach services for ANC services and TB screening is recommended.

MOPED759

Leveraging mobile technology to send high quality ARV and HIV test kit consumption reports

E. Dias[1,2], L. Williams[1,2], A. Gopal[1,2], A. Soto[1], D. Lee[2], C. Endyke[1]
[1]FHI 360, Maputo, Mozambique, [2]Abt Associates, Maputo, Mozambique
Presenting author email: eunice_dias@chasssmt.com

Background: Avoiding stock outs of ARVs and HIV rapid test kits (RTK) are a pillar of any HIV care and treatment program. In Mozambique, health facility (HF) supply chain systems often rely on hand delivery and public transport to submit consumption reports from HF, then to the district, before reaching the provincial medications depot (PMD). To strengthen this logistics reporting system, the USAID-funded Clinical HIV/AIDS Services Strengthening (CHASS-SMT) project, in collaboration with the Mozambican MOH, began using mobile phones to send reports from HF to the PMD in order to improve access to quality consumption reports submitted in a timely fashion.
Methods: CHASS-SMT, in collaboration with MOH, delivered 115 mobile phones to 115 HFs with ART services. Training on how to complete consumption reports using the CommCare data management technology was provided to pharmacy technicians and the phones were programmed with data verification capabilities and sufficient network coverage to send the information to the provincial system.
Results: Following the implementation of this mHealth intervention, the number of days it took for the consumables report to reach the PMD was reduced from an average of 15 to 2 days. While this represents a successful reduction in reporting timeliness, a key lesson learned was the need for IT support to provide troubleshooting for technical problems. Despite training and potential effectiveness of the program, many staff in remote areas did not have the necessary background to respond to network connection problems.
Conclusions: Using simple technologies, such as mobile phones in rural areas, can be a reliable technology to strengthen supply chain reporting in resource constrained environments; however, the roll out of such programs needs to ensure sufficient maintenance, oversight and supervision. With proper support, mobile technology ensures timely reporting to help reduce ARV and RTK stock-outs by improving the process of communication between health facilities and health authorities. In addition to looking at completeness and timely reporting, continued research is necessary to measure the potential improvements this intervention had on data consistency as the CommCare reporting tool also incorporated simple validations to help users identify and correct inconsistencies.

MOPED760

The impact of social health insurance on HIV prevention and treatment: evidence from Kenya

L. Were[1], R. Wamai[2], O. Galarraga[1]
[1]Brown University School of Public Health, Health Services Policy and Practice, Providence, United States, [2]Northeastern University, African American Studies, Boston, United States

Background: Health systems in developing countries continue to face dwindling tax revenues, increasing healthcare costs, decreasing donor funding, and burdensome out-of-pocket payments especially for the poor. This situation is compounded by incidence and prevalence of HIV/AIDS with women disproportionately affected. Moreover, the HIV+ women continue to desire children, become pregnant, and give birth after knowing their HIV+ status. In such an environment, HIV+ women without access to effective and appropriate healthcare are likely to have lower economic productivity, experience negative health outcomes, and risk being caught in the cycle of poverty. As such Social Health Insurance (SHI) has been identified as a mechanism to enhance and diversify health financing, and provide access to healthcare. This paper adds to the literature by empirically analyzing the impact of the Kenya National Hospital Insurance Fund (NHIF) on the health outcomes of HIV+ pregnant women in Kenya.
Methods: We use electronic medical records (EMS) from the Academic Model Providing Access to Healthcare (AMPATH). We estimate patient level linear and logistic regressions with institutional delivery (Yes/No) and assisted by skilled birth attendant (Yes/No) as dependent variables for 16,000 HIV+ women . To make causal estimations, we implement propensity score methods including matching and inverse probability weighting. The models include a set of controls consisting of demographic, health, and economic variables.
Results: The causal estimates from matching indicate that NHIF members are 15% more likely to deliver at an institution and 14% more likely to have a skilled birth attendant at delivery. The IPW estimates also show that those with NHIF membership are 14% more likely to deliver at an institution and 20% more likely to have a skilled birth attendant at birth.
Conclusions: The findings shows that Kenya's NHIF does have positive and significant effects on the health outcomes of HIV+ pregnant women enrolled in the insurance scheme.This is important for at-risk populations like HIV+ pregnant women that need access to healthcare. NHIF's promise as it undergoes reforms is shown and the findings are informative to countries similar to Kenya that are exploring localized and sustainable mechanisms of financing HIV care that include SHI.

Tuesday 21 July

Oral Abstract Sessions

TUAA01 Survival of the Fittest: HIV Evolution and Adaptation

TUAA0101

Phylogenetically estimated HIV diversification rates reveal prevention of HIV-1 by antiretroviral therapy

J. Joy, R. Liang, R. McCloskey, T. Nguyen, C. Brumme, G. Colley, R. Hogg, J. Montaner, P.R. Harrigan, A. Poon
BC Centre for Excellence in HIV/AIDS, Vancouver, Canada
Presenting author email: jjoy@cfenet.ubc.ca

Background: Treatment of HIV infection with antiretrovirals reduces individuals' plasma viral loads to undetectable levels and in turn decreases the risk of transmission. Despite epidemiological evidence supporting the efficacy of 'Treatment as Prevention', quantifying this success remains a significant challenge. Phylogenetic analysis of viral sequence data can yield crucial insights into epidemic processes, including transmission dynamics. We sought to evaluate the impact of treatment on HIV transmission rates in British Columbia (BC), Canada using phylogenetic methods.
Methods: We recovered 27,296 anonymized HIV protease and RT sequences from 7,747 HIV patients in BC from the BC Centre for Excellence in HIV/AIDS database. Sequences were annotated with: sample collection date, treatment status at sample collection, date of first antiretroviral treatment, and risk factor (intravenous drug use (IDU), men having sex with men (MSM), heterosexual (HET)). Codons associated with known drug resistance were censored from the alignment prior to tree inference. We inferred a set of 1000 maximum likelihood phylogenetic trees. We calculated a lineage level phylogenetic branching rate for each HIV lineage in the trees, which provides an approximate measure of transmission rates. We stratified branching rates by treatment experience and risk factor. To assess the impact of treatment on onward transmission of HIV, we compared the mean HIV branching rate between treatment-experienced and treatment-naive lineages across the BC epidemic as a whole and among risk factors.
Results: Phylogenetic branching rates were significantly lower among treatment-experienced HIV lineages relative to treatment-naive lineages ($p < 0.001$), implying reduced rates of HIV transmission in the former. Importantly, treatment experienced lineages had significantly lower HIV branching rates irrespective of HIV transmission risk factor ($p < 0.001$ for IDU, MSM, and HET) or exposure to different antiretroviral drug classes ($p < 0.001$ NRTI, NNRTI, PI), suggesting these results are not driven by penetrance of health care into particular risk groups or therapeutic regimens.
Conclusions: Our results provide independent evidence that antiretroviral HIV treatment has limited the onward transmission of HIV to new hosts. These results are based on a lineage level measure, are measured phylogenetically rather than epidemiologically, and are replicated both across different risk exposure categories and different treatment regimens.

TUAA0102

Phenotypic properties influencing HIV-1 transmission fitness

K. Klein[1], A. Ratcliff[2], G. Nickel[2], I. Nankya[2], M. Lobritz[2], Y. Gao[2], R. Shattock[3], E. Arts[1]
[1]University of Western Ontario, Microbiology and Immunology, London, Canada, [2]Case Western Reserve University, Medicine, Cleveland, United States, [3]Imperial College London, Infectious Diseases, London, United Kingdom
Presenting author email: kklein5@uwo.ca

Background: Sexual HIV-1 infection requires penetration of the virus across the mucosal barrier and the establishment of infection in target cells. It is widely accepted that only one or a small number of HIV-1 clones is successfully transmitted from the donor to the recipient. However, little is known about the phenotypic properties of the transmitted virus and the influence the phenotype plays in the genetic bottleneck selection process. Here we evaluated possible phenotypic differences between acute and chronic HIV-1 that may effect transmission fitness.
Methods: We compared the genetic diversity of HIV-1 isolates from the female genital tract with isolates from the blood of the same donor by 454 pyrosequencing of the env region. Furthermore, we generated chimeric viruses from acute and chronic envelope genes using a yeast-based cloning strategy. The chimeric clones were then evaluated for host cell entry and receptor efficiency, sensitivity to entry inhibitors and for replication fitness in PBMCs, T cells and macrophages. Additionally we evaluated the transmission fitness across mucosal tissues by multi-virus competitions.
Results: Both, acute and chronic HIV-1 clones showed similar cell entry and receptor efficiency, sensitivity to inhibitors and replication fitness. Sequence analysis revealed that primary infection in the cervix resulted in a highly genetically diverse HIV-1 population, while only one or a few HIV-1 clones are in matched blood. Analysis of mixed competitions of acute and chronic HIV-1 env-clones in *ex vivo* tissue models revealed higher transmission fitness of acute isolates than chronic. We observed that higher transmission fitness was related to a reduced number of conserved N-linked glycans on the envelope of acute viruses.
Conclusions: Chronic HIV-1 isolates appear to stay and replicate in the mucosal tissue, while acute isolates are preferentially bound by tissue residing DCs/LCs and are subsequently transmitted to T cells. High levels of mannose binding proteins in tissue and lectins on epithelial cells may be responsible for a passive selection process of HIV-1 with fewer glycans for transmission due to reduced lectin binding.

TUAA0103

Population-level spread of immune-driven mutations in HIV-1 polymerase during the North American epidemic

N.N. Kinloch[1], D.R. Macmillan[1], A.Q. Le[1], L.A. Cotton[1], R. Mccloskey[2], D.R. Bangsberg[3], S. Buchbinder[4], M. Carrington[5], J. Fuchs[4,6], P.R. Harrigan[2], B. Koblin[7], M. Markowitz[8], K. Mayer[9,10], M.J. Milloy[2], M.T. Schechter[11], T. Wagner[4], B.D. Walker[3], J.M. Carlson[12], A.F.Y. Poon[1,2,11], Z.L. Brumme[1,2]
[1]Simon Fraser University, Faculty of Health Sciences, Burnaby, Canada, [2]British Columbia Centre for Excellence, Vancouver, Canada, [3]Ragon Institute of MGH, MIT, and Harvard, Cambridge, United States, [4]San Francisco Department of Public Health, San Francisco, United States, [5]Laboratory of Experimental Immunology, Frederick National Laboratory for Cancer Research, Frederick, United States, [6]University of California, San Francisco, United States, [7]New York Blood Center, New York, United States, [8]Aaron Diamond AIDS Research Center, New York, United States, [9]Fenway Community Health, Boston, United States, [10]Harvard Medical School, Cambridge, United States, [11]University of British Columbia, Faculty of Medicine, Vancouver, Canada, [12]Microsoft Research, Seattle, United States
Presenting author email: nkinloch@sfu.ca

Background: HLA-driven HIV-1 immune escape mutations that persist following transmission could gradually spread in the viral population, compromising host antiviral immunity over time. We investigate the extent and correlates of escape mutation accumulation in HIV-1 Polymerase (Pol) sequences in North America from 1979-present.
Methods: HIV-1 RNA Pol and HLA class I genotyping was performed on 338 Historic (1979-1989) and 278 Modern (2001- 2011) specimens from Boston, New York, San Francisco and Vancouver. HLA-associated polymorphisms were defined according to published lists. Historic and Modern datasets were also investigated for the presence for novel HLA-associated mutations using phylogenetically- informed methods. Ancestral reconstruction of the HIV-1 epidemic founder sequence was performed using BEAST and HyPhy.
Results: The estimated HIV-1 epidemic founder sequence dated to ~1969 and was near-identical to the modern subtype B consensus, suggesting no historic selective sweeps have occurred to shift the population consensus. No HLA-associated polymorphisms unique to the historic dataset were identified. Nevertheless, pairwise sequence diversity of modern HIV-1 sequences was ~twofold greater than historic sequences, with diversification predominating at HLA-associated sites ($p<0.0002$). N=20 published HLA-associated polymorphisms were investigated for spread over time. Overall, their median 'background' frequencies (in individuals lacking the restricting HLA) were 6.6% vs 16.8% in historic and modern eras respectively ($p=0.0004$); polymorphism frequencies in reconstructed pre-1979 ancestral sequences were also consistent with gradual spread ($p<0.01$). No correlation was observed between HLA allele frequency and relative spread of its associated polymorphisms ($r=-0.13$, $p=0.8$); rather, polymorphisms restricted by protective HLA alleles exhibited greater relative spread than those restricted by non-protective alleles ($r=-0.83$, $p=0.0047$). Despite these overall increases, the frequency of many polymorphisms (eg: B*51-associated RT-I135T) remained consistent throughout the eras. Moreover, at the whole-sequence level, the median extent of adaptation of the typical circulating modern HIV-1 Pol sequence to the average North American host remains 0%, indicating a low overall risk of acquiring HIV-1 harboring adaptations to one's HLA profile.
Conclusions: Immune escape mutations in HIV-1 Pol have spread significantly in the population since the genesis of the North American epidemic, however these changes are unlikely to herald immediate consequences for host antiviral immunity on this continent.

TUAA0104

Primary resistance against dolutegravir decreases HIV integration

T. Mesplède, K. Anstett, N. Osman, S. Hassounah, J. Liang, Y. Han, M. Wainberg
McGill University AIDS Centre, Lady Davis Institute for Medical Research - Jewish General Hospital, Montréal, Canada
Presenting author email: tibo_mes@hotmail.com

Background: Dolutegravir is an integrase inhibitor that has shown a high genetic barrier against the emergence of resistant strains. No resistance substitution has been observed in treatment-naïve individuals treated with this drug. In tissue culture experiments, we have identified the R263K resistance substitution as a signature substitution for HIV resistance against dolutegravir, an observation that was later confirmed in highly treatment-experienced individuals. Given the importance of DNA integration in the establishment of HIV persistence, we tested the ability of dolutegravir-resistant HIV strains to integrate within human DNA.
Methods: We used an Alu-mediated quantitative PCR to measure levels of integration of dolutegravir-resistant variants in primary human PBMCs. Levels of integration were normalized using the b-actin gene. These experiments were performed using subtype B and C viruses.
Results: Our results show that dolutegravir-resistant variants are impaired in their ability to integrate within human DNA. The integration levels of subtype B and C R263K variants were decreased by 30% and 40% compared to WT viruses, respectively. More important, the addition of several secondary substitutions failed to restore integration to a level comparable to WT and, in some cases, further lowered integration to only 20% of WT.
Conclusions: The relative inability of dolutegravir-resistant variants to integrate within human DNA may contribute to a progressive decrease in the viral reservoir of individuals who develop these substitutions.

TUAA0105

HIV-1 integrase variants retarget proviral integration and are associated with disease progression

J. Demeulemeester[1], S. Vets[1], R. Schrijvers[1], P. Madlala[1,2], M. De Maeyer[3], J. De Rijck[1], T. Ndung'u[2], Z. Debyser[1], R. Gijsbers[1]
[1]KU Leuven University, Pharmaceutical and Pharmacological Sciences, Leuven, Belgium, [2]University of KwaZulu-Natal, HIV Pathogenesis Program, Doris Duke Medical Research Institute, Nelson R Mandela School of Medicine, Durban, South Africa, [3]KU Leuven University, Chemistry, Leuven, Belgium
Presenting author email: rik.gijsbers@med.kuleuven.be

Background: Distinct integration patterns of different retroviruses, including HIV-1, have puzzled virologists for over 20 years. A tetramer of the viral integrase (IN) assembles on the two viral cDNA ends, docks onto the target DNA (tDNA) to form the target capture complex (TCC) and catalyzes viral genome insertion into the host chromatin.
Methods: We combined structural information on the Prototype Foamy Virus TCC with conservation in retroviral IN protein alignments to determine aa-tDNA base contacts. We generated HIV-1 variants based on the observed variability at these positions, assessed replication capacities and performed integration site sequencing to reveal their integration preferences. Finally, we examined their effect on disease progression in a chronic HIV-1 subtype C infection cohort.
Results: We identified retroviral IN amino acids affecting molecular recognition in the TCC and resulting in distinct local tDNA nucleotide biases. These residues also determine the propensity of the virus to integrate into flexible tDNA sequences. Remarkably, natural polymorphisms IN_{S119G} and IN_{R231G} retarget viral integration away from gene dense regions. Precisely these variants were associated with rapid disease progression in a chronic HIV-1 subtype C infection cohort.
Conclusions: Our findings reveal how polymorphisms at positions corresponding to HIV IN_{119} and IN_{231} affect both local and global integration site targeting. Intriguingly, these findings link integration site selection to virulence and viral evolution but also to the host immune response and antiretroviral therapy, since HIV-1 IN_{119} is under selection by HLA alleles and integrase inhibitors.

TUAA0106LB

HIV-1 specific IgG antibody levels correlate with presence of a specific HLA class II allele to impact acquisition and vaccine efficacy

H. Prentice[1], G. Tomaras[2], D. Geraghty[3], R. Apps[4], Y. Fong[3], P. Ehrenberg[1], M. Rolland[1], G. Kijak[1], W. Nelson[3], A. DeCamp[3], X. Shen[2], N. Yates[2], S. Zolla-Pazner[5], S. Nitayaphan[6], S. Rerks-Ngarm[7], P. Pitisuttithum[8], G. Ferrari[2], D. Montefiori[2], J. McElrath[3], R. Bailer[9], R. Koup[9], R. O'Connell[6], M. Robb[1], N. Michael[1], J. Kim[1], R. Thomas[1]
[1]US Military HIV Research Program, Walter Reed Army Institute of Research, Silver Spring, United States, [2]Duke University School of Medicine, Durham, United States, [3]Fred Hutchinson Cancer Research Center, Seattle, United States, [4]Leidos Inc., Frederick National Laboratory for Cancer Research, Frederick, United States, [5]New York University School of Medicine, New York, United States, [6]AFRIMS, Bangkok, Thailand, [7]Ministry of Public Health, Nonthaburi, Thailand, [8]Mahidol University, Bangkok, Thailand, [9]Vaccine Research Center, NIH, Bethesda, United States

Background: The RV144 trial had a vaccine efficacy of 31% and IgG antibodies to HIV-1 Envelope (Env) amino acid positions 120-204 were identified as a predictor of decreased risk of infection. The IgG responses were binding to scaffolded Env antigen comprising the variable loops 1 and 2, flanked by partial regions of the first and second conserved domains. Since HLA class II molecules are expressed on antigen presenting cells and modulate CD4 T cell stimulation of antibody production by B cells, we tested whether HLA allotypes influenced vaccine response and efficacy.
Methods: HLA-DRB1, DQB1, and DPB1 were genotyped in 760 individuals. Direct associations of 31 HLA class II alleles on Env (120-204)-specific IgG were compared using linear regression models. Interaction of HLA with IgG response to Env (120-204) was tested for an effect on acquisition by logistic regression.
Results: Higher levels of Env (120-204) IgG antibody directly correlated with the presence of DPB1*13 (P=0.002, q=0.05). Env (120-204)-specific IgG antibody levels also associated with decreased risk of HIV-1 infection only in the presence of DPB1*13 (OR=0.29 per 1-SD increase, P=0.006). Both of these findings were replicated with Env antigens across multiple viral subtypes. Vaccine efficacy increased to 71% among individuals that were DPB1*13+ and had higher levels of Env (120-204)-specific IgG levels relative to the placebos. To delineate the anti-Env antibody responses in DPB1*13+ individuals, we screened overlapping peptides to Env (120-204). Frequency and magnitude of IgG response specifically to Env peptide positions 119-133, which are involved in Env binding to CD4, associated with both presence of DPB1*13 and protection from HIV-1 acquisition among individuals with a DPB1*13 allele. Further evidence that immune responses induced by vaccination in individuals carrying DPB1*13 are different from those without DPB1*13, was apparent in significant viral sequence differences specifically in infected vaccine recipients with DPB1*13.
Conclusions: DPB1*13-associated immune responses to vaccination associate with decreased risk of HIV-1 acquisition. The specific differences in vaccine-induced responses elicited by individuals with HLA-DPB1*13 should be examined to determine the mechanism of protection of the vaccine. Understanding this HLA class II restricted mechanism will enable improved HIV vaccine design.

TUAA02 Hammer and Tickle: Targeting the Virus

TUAA0202

Zinc finger nuclease gene editing for functional cure in a nonhuman primate model of HIV/AIDS

C. Peterson[1], J. Wang[2], P. Polacino[3], M. Holmes[2], S.-L. Hu[3], P. Gregory[2], H.-P. Kiem[1,3]
[1]Fred Hutchinson Cancer Research Center, Seattle, United States, [2]Sangamo BioSciences, Richmond, United States, [3]University of Washington, Seattle, United States
Presenting author email: cwpeters@fhcrc.org

Background: Nuclease-mediated gene editing in hematopoietic stem cells (HSCs) holds great promise in the cure of HIV infection, but little information is available regarding the feasibility of this approach in large animal models. To better evaluate the function of HSCs following gene editing, we have engineered cells with disrupted CCR5 alleles and assessed engraftment following autologous transplant in the pigtailed macaque, *M. nemestrina*. Disrupted CCR5 alleles in this model should directly protect against infection with simian/human immunodeficiency virus (SHIV).
We are evaluating the extent to which CCR5-disrupted cell progeny engraft in macaques, and testing whether these cells impede infection by SHIV.
Methods: Zinc Finger Nucleases (ZFNs) are used to target the CCR5 locus in macaque HSCs. Engraftment and persistence of these autologous stem cells, and stem cell-derived lymphoid and myeloid cells, are measured *ex vivo* and *in vivo*. Animals are challenged with SHIV

virus containing an HIV envelope; to approximate the status of an HIV+ patient, three-drug combination antiretroviral therapy (cART) is initiated following viral set point. Animals reach undetectable levels of plasma viremia prior to autologous transplant with gene-edited cells.

Results: CCR5 targeting experiments yield up to 60% gene disruption in CD34+ cells *ex vivo*, translating to approximately 5% steady state bulk disruption *in vivo*. Gene-disrupted cells demonstrate long-term, multilineage engraftment in macaques, including comparable levels of disruption in CD3+, CD20+, CD14+, and granulocyte subsets. We also observe biallelic disruption of CCR5 in colony forming assays.

Importantly, this approach is equally feasible in SHIV-naïve and in SHIV-infected, cART-suppressed animals. During robust SHIV replication, our preliminary data suggest that CCR5-deleted cells undergo positive selection *in vivo*.

Conclusions: This is the first demonstration of successful long-term multilineage engraftment of ZFN-edited, CCR5-deleted HSCs in a NHP transplantation model. Our strategy results in robust levels of target gene disruption *in vivo*, yet does not impair HSC engraftment or differentiation. CCR5-deleted cells can undergo positive selection following challenge with SHIV. Our model enables the evaluation of novel therapeutic approaches not only in the context of acute HIV exposure, but also in the clinically relevant setting of pre-existing latent HIV infection.

TUAA0203

Crispr/Cas9 gene editing eradicates latent and protects cells against new HIV-1 infection

R. Kaminski[1], W. Hu[1], Y. Zhang[1], J. Karn[2], K. Khalili[1]
[1]Temple University, Neuroscience, Philadelphia, United States, [2]Case Western Reserve, Cleveland, United States
Presenting author email: kkhalili@temple.edu

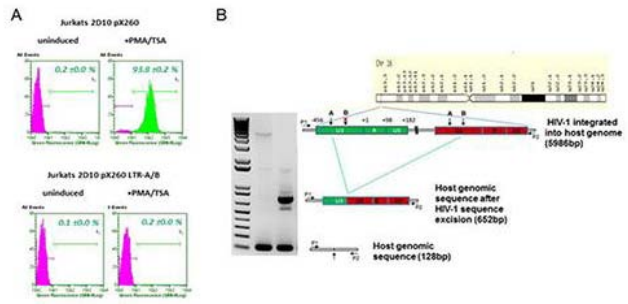
Background: A sterilizing cure for HIV-1/AIDS requires a strategy that eliminates all or at least some critical regions of the HIV-1 genome including the promoter positioned within the 5' LTR of the viral genome from cells serving as a stable reservoir for HIV-1, i.e. resting CD4+ T-lymphocytes, macrophages, and brain microglia, with no adverse impact on the host cells.

Methods: We have tailored CRISPR/Cas9 gene editing by bioinformatic screening, Surveyor assay, whole genome sequencing, and have successfully developed a series of guide RNAs (gRNAs) that, in complex with Cas9 nuclease, effectively and safely eliminate integrated copies of HIV-1 proviral DNA in several human cell culture models. We assessed the impact of our gene editing strategy on viral transcription and replication by measuring the level of a GFP reporter and viral p24, upon reactivation of virus from the latent stage by treatment with PMA and TSA.

Results: We demonstrated inactivation of HIV-1 gene expression and replication in latently infected T-lymphocytes and promonocytic human cell lines as well as microglial cells upon excising the proviral DNA fragment corresponding to the entire coding sequence of HIV-1 spanning the 5' to 3' LTRs from the host chromosome by the CRISPR/Cas9 approach.

Further, we demonstrate that the presence of LTR-specific multiplex of guide RNAs in cells expressing Cas9 acts as an efficient inhibitor blocking new HIV-1 infection.

Conclusions: Our findings suggest that the strategy involving the newly developed CRISPR/Cas9 serves as a promising platform that can be advanced for eradication of HIV-1 and a cure for AIDS



Eradication of HIV-1 DNA in latently infected cells.
A. Treatment of latently infected T-lymphocytes with PMA and TSA activates viral gene expression and expression of a GFP reporter in more than 93% of the cells. The presence of gRNAs (LTR A/B) and Cas9 dramatically prevented viral replication.
B. Examination of DNA by PCR and direct sequencing verifies removal of integrated proviral DNA from chromosome 16.

[Khalili_IAS_July2015_Fig1]

TUAA0204LB

Investigating the role of the immune checkpoint receptor TIGIT in T cells during HIV disease progression and as a target for immune restoration

G. Chew[1], T. Fujita[2], K. Clayton[3], N. Ishii[2], M. Abdel-Mohsen[4], T. Liegler[4], F. Hecht[4], M. Ostrowski[3], C. Shikuma[5], M. Maurer[6], A. Korman[6], S. Deeks[4], L. Ndhlovu[1]
[1]University of Hawaii, Manoa, Department of Tropical Medicine, Medical Microbiology, and Pharmacology, Honolulu, United States, [2]Tohoku University, Department of Microbiology and Immunology, Sendai, Japan, [3]University of Toronto, Department of Immunology, Toronto, Canada, [4]University of California, San Francisco, Department of Medicine, San Francisco, United States, [5]University of Hawaii, Manoa, Hawaii Center for HIV/AIDS, Honolulu, United States, [6]Bristol-Myers Squibb, Biologics Discovery California, Redwood City, United States

Background: HIV infection induces a series of phenotypic and functional changes to T cells that eventually results in a state of T cell exhaustion and failure to control viral replication. T-cell-Ig-and-ITIM-domain (TIGIT) is a recently described negative checkpoint receptor expanded on CD8+ T cells during LCMV infection in mice and inhibits anti-viral effector CD8+ T cell activity. We hypothesized that during progressive HIV infection, TIGIT surface expression will mark an expanded population of dysfunctional T cells, and that novel monoclonal antibodies targeting TIGIT would restore anti-HIV-specific T cell responses.

Methods: Surface expression of TIGIT and PD-1 on T cells were measured by flow cytometry from 103 HIV-infected participants [non-controllers (n=20), elite controllers (n=20), antiretroviral (ART) suppressed (n=39), acutely infected (n=24)] and 20 age and gender matched HIV-uninfected controls. Quantified cell associated HIV (CA-HIV) DNA and RNA from purified CD4+ T cells. Functional characterization of TIGIT+ T cells was performed and *ex-vivo* HIV-specific cytokine and proliferative responses were assessed in the presence monoclonal antibodies (mAb) targeting TIGIT and/or PD-1 pathways (anti-TIGIT mAb and anti-PD-L1 mAb).

Results: In controls a median of 28.05% of CD8+ T cells were TIGIT+ (IQR 24.43,39.15). In comparison, we found a significant expansion of TIGIT+CD8+ T cells during chronic (median 57.1%, IQR 42.6,63.45; p< 0.0001) and a non-significant trend in acute HIV infection (40.40%, 28.3,47.8; p=0.08). TIGIT expression remained elevated despite viral suppression and associated with CD4+ CA-HIV DNA. TIGIT+ and TIGIT+PD-1+ CD8+ T cells inversely correlated with CD4 count (p=0.0016, r=-0.658; p=0.0024, r=-0.385 respectively). TIGIT was expressed on >50% HIV-specific CD8+ T cells, however TIGIT+ T cells failed to produce cytokines in response to HIV antigens. Single blockade of TIGIT led to a significant increase of interferon gamma response to HIV Gag compared to no blockade (p=0.027). Co-blockade of TIGIT and PD-L1 lead to greater restoration of HIV-specific CD8+ T cell proliferative responses (4.10%, IQR 1.46,22.28) than single blockade of TIGIT (3.47, IQR 1.11,10.08; p=0.0078) or PD-L1 (3.945%, IQR 1.15,17.53; p=0.039).

Conclusions: These findings identify TIGIT as a novel marker of dysfunctional HIV-specific T cells and suggest TIGIT along with other checkpoint receptors may be novel curative HIV targets.

TUAA0205LB

Estrogen blocks HIV re-emergence from latency and points to gender-specific differences in HIV reservoirs

J. Karn[1], B. Das[1], C. Dobrowolski[1], E. Scully[2], S. Deeks[3], M. Gandhi[3], R. Johnston[4]
[1]Case Western Reserve University School of Medicine, Department of Molecular Biology and Microbiology, Cleveland, United States, [2]Brigham and Women's/Massachusetts General Hospital, Boston, United States, [3]UCSF School of Medicine, San Francisco, United States, [4]amfAR, The Foundation for AIDS Research, New York, United States

Background: Unbiased shRNA library screens have been used to identify novel genes and pathways that are required to maintain HIV latency and/or play an essential role in HIV transcription. One of the most prominent and robust "hits" was the estrogen receptor type 1 (ESR-1).

Methods: The activities of ESR-1 agonists, antagonists and estrogen on proviral reactivation were studied in transformed and primary cell models of latency and in patient cells.

Results: specific antagonists of ESR-1, such as Tamoxifen and Fulvestrant, are weak proviral activators but sensitize latently infected cells to very low doses of the proviral activators TNF-α (NF-κB inducer) and SAHA (HDAC inhibitor). By contrast, a selective ESR-1 agonist, propylpyrazoletriol (PPT) and the broader spectrum ESR-1 agonist diethylstilbestrol, strongly suppress both TNF-α and SAHA reactivation. In contrast to the ESR-1 antagonists, ESR-2 antagonists were not effective inducers of HIV expression in cell models. Co-activator 3 (SRC-3) is an upstream modulator of ESR-1, which also was identified as a hit in the shRNA screen. Blocking of SRC-3 by its inhibitor Gossypol also induces latent proviruses. Consistent with these results, specific knock-down of ESR-1 in Jurkat 2D10 cells with shRNA constitutively re-activates the latent provirus. In the HAART-treated patient samples there was a modest increase of spliced HIV env mRNA when resting memory cells were treated with the ESR antagonists Fulvestrant or Tamoxifen alone. Proviral reactivation by ESR antagonists was synergistically increased by SAHA. By contrast, β-Estradiol at concentrations in the physiological range led to dramatic reductions in proviral reactivation efficiencies. This is consistent with earlier observations that high levels of β-Estradiol can block HIV replication.

Conclusions: ESR-1 is a pharmacologically attractive target that can be exploited in the design of therapeutic strategies aimed at eradication of the latent reservoir. Our results show that drugs targeting ESR-1 can be used to either promote the re-activation of latent proviruses (antagonists) or limit their responses (agonists). The profound effects of β-Estradiol on HIV reservoir reactivation suggests there may be gender specific differences in HIV reservoirs and highlights the need to tailor latency reactivation strategies for both men and women.

TUAB01 ART: New Drugs, New Strategies

TUAB0101

Atazanavir/ritonavir 200/100 mg is non-inferior to atazanavir/ritonavir 300/100 mg in virologic suppressed HIV-infected Thai adults: a multicentre, randomized, open-label trial: LASA

T. Bunupuradah[1], S. Kiertiburanakul[2], A. Avihingsanon[1,3], P. Chetchotisakd[4], M. Techapornroong[5], N. Leerattanapetch[6], P. Kantipong[7], C. Bowonwatanuwong[8], S. Banchongkit[9], V. Klinbuayaem[10], S. Mekviwattanawan[11], S. Nimitvilai[12], S. Jirajariyavej[13], W. Prasithsirikul[14], W. Munsakul[15], S. Bhakeecheep[16], S. Chaivooth[16], P. Phanuphak[1], D.A. Cooper[17], T. Apornpong[1], S.J. Kerr[1,17], S. Emery[17], K. Ruxrungtham[1,3], LASA Study Group
[1]HIV-NAT, Thai Red Cross - AIDS Research Centre, Bangkok, Thailand, [2]Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand, [3]Division of Allergy and Clinical Immunology, Department of Medicine, Chulalongkorn University, Bangkok, Thailand, [4]Khon Kaen University, Khon Kaen, Thailand, [5]Prapokklao Hospital, Chanthaburi, Thailand, [6]Khon Kaen Hospital, Khon Kaen, Thailand, [7]Chiangrai Prachanukroh Hospital, Chiangrai, Thailand, [8]Chonburi Hospital, Chonburi, Thailand, [9]Rayong Hospital, Rayong, Thailand, [10]Sanpatong Hospital, Chiang Mai, Thailand, [11]Pranangklao Hospital, Nonthaburi, Thailand, [12]Nakhon Phatom Hospital, Nakhon Phatom, Thailand, [13]Taksin Hospital, Bangkok, Thailand, [14]Bamrasnaradura Infectious Disease Institute, Nonthaburi, Thailand, [15]Faculty of Medicine, Vajira Hospital, University of Bangkok Metropolitan Administration, Bangkok, Thailand, [16]National Health Security Office, Nonthaburi, Thailand, [17]Kirby Institute for Infection and Immunity in Society, University of New South Wales, Sydney, Australia
Presenting author email: torsak.b@hivnat.org

Background: Asian HIV-infected patients generally experience higher systemic exposure to HIV protease inhibitors (PIs). We compared the efficacy and safety of switching to lower vs standard dose of atazanavir/ritonavir (ATV/r) in virologically suppressed second-line patients.
Methods: Patients with plasma HIV-RNA (pVL) <50copies/mL, ALT<200 IU/L, and creatinine clearance (Crcl) ≥60mL/min while using PI-based regimens were randomized to ATV/r 200/100mg (A200) vs ATV/r 300/100mg (A300) once daily with 2NRTIs at 14 sites in Thailand. Patients were followed every 12 weeks until week 48. Virological failure (VF) was defined as had confirmed pVL >200copies/mL. Patients in ATV200 with VF resumed standard dose PI-based regimens. Treatment groups were regarded as non-inferior if the lower limit of the 95% confidence interval (95%CI) for the difference in VF was above -10% in an intention-to-treat (ITT) analysis at 48 weeks.
Results: 559 patients were randomized (ATV200; N=279 vs ATV300; N=280). At baseline, 85% used lopinavir/ritonavir, mean age was 42 years, body weight was 59 kg, CD4 was 539 cells/mm^3, and total bilirubin was 0.85 mg/dL.
At week 48, by ITT, the proportion of patients in ATV200 vs ATV300 with pVL<200copies/mL [difference, 95%CI] was 97.1% vs 96.4% [0.68, -2.29 to 3.65], the proportions with pVL<50copies/mL were 93.4% vs 91.7% [1.71, -2.67 to 6.09]. In per-protocol analyses the proportions with pVL<200copies/mL were 98.5% vs 99.2% [-0.72, -2.6 to 1.16]. Only one ATV200 recipient developed major resistance (I50L) to ATV.
Discontinuation from randomized therapy was 8 (2.9%) in ATV200 (1 death, 2 VF, 1 jaundice, 2 rash, 2 others) and 21 (7.5%) in ATV300 (2 deaths, 7 jaundice, 7 rash, 5 others) (p=0.01). At week 48, there was no difference between treatment arms in CD4, total cholesterol, triglyceride, and Crcl (all p>0.1). Comparing ATV200 vs ATV300, the number (%) of patients with total bilirubin >3.2mg/dL was 27 (10%) vs 46 (17%) respectively (p=0.017).
Conclusions: A lower dose of ATV/r-based regimens in Thais is non-inferior compared to standard dose ATV/r. Higher dose ATV was associated with higher rates of treatment discontinuation. ATV/r 200/100 mg can be recommended as part of routine care for Asian adults who have well-controlled HIV infection on a PI-based regimen.

TUAB0102

Switching from a tenofovir disoproxil fumarate (TDF)-based regimen to a tenofovir alafenamide (TAF)-based regimen: data in virologically suppressed adults through 48 weeks of treatment

T. Mills[1], J. Andrade[2], G. DiPerri[3], J. Van Lunzen[4], E. Koenig[5], R. Elion[6], M. Cavassini[7], J. Valdez Madruga[8], J. Brunetta[9], D. Shamblaw[10], E. DeJesus[11], C. Cohen[12], A. Plummer[13], Y. Liu[13], S. McCallister[13]
[1]Anthony Mills MD, Inc., Los Angeles, United States, [2]Hospital Civil de Guadalajara, Guadalajara, Mexico, [3]University Hospital Amedeo De Savoia, Turin, Italy, [4]Universitaetsklinikum Hamburg Eppendorf, Hamburg, Germany, [5]Instituto Dominicano de Estudios Virologicos IDEZ, Santo Domingo, Dominican Republic, [6]Whitman-Walker Health, Washington, United States, [7]Centre Hospitalier Universitaire Valdois, Lausanne, Switzerland, [8]Centro de Referencia e Treinamento Em DST/AIDS, Sao Paolo, Brazil, [9]Maple Leaf Research, Toronto, Canada, [10]La Playa Medical Group, San Diego, United States, [11]Orlando Immunology Center, Orlando, United States, [12]Community Research Initiative of New England, Boston, United States, [13]Gilead Sciences, Foster City, United States
Presenting author email: tmills@tonymillsmd.com

Background: Despite a favorable efficacy and safety profile, TDF-based regimens may be associated with renal toxicity and reduced bone mineral density (BMD). TAF is a novel tenofovir prodrug in which TFV plasma levels are 90% lower than seen with TDF, thereby reducing off-target side effects. Week 48 data in patients switching to a once-daily fixed dose combination regimen containing elvitegravir 150mg, cobicistat 150mg, emtricitabine 200mg, and TAF 10mg (E/C/F/TAF) are described.
Methods: Virologically suppressed adults (HIV-1 RNA < 50 copies/mL) with normal renal function taking one of 4 different TDF-based regimens for at least 48 weeks were randomized 2:1 to receive E/C/F/TAF or to retain their prior TDF-based regimen. Following randomization, all treatments were open-label.
Results: Of 1196 patients completing at least 48 weeks of treatment, 799 received E/C/F/TAF and 397 received their prior TDF regimen: E/C/F/TDF, 31.9%; EFV/FTC/TDF, 26.1%; ATV/RTV + FTC/TDF, 26.8%; ATV/COBI + FTC/TDF, 15.0%. Virologic success <50 copies/mL occurred in 95.6% on E/C/F/TAF and 92.9% on FTC/TDF + 3rd Agent (weighted difference: 2.7%; 95% CI: -0.3% - +5.6%), with virologic failure in 1.1% and 1.3% of patients, respectively. General safety was similar between the arms. The mean percent change (SD) in hip BMD: +1.95% (3.0) for E/C/F/TAF and -0.14% (3.0) for FTC/TDF+3rd Agent (p<0.001); the mean percent change (SD) in spine BMD: +1.86% (3.1) for E/C/F/TAF and -0.11% (3.7) for FTC/TDF+3rd Agent (p<0.001). There were no cases of Fanconi Syndrome on E/C/F/TAF and one case on FTC/TDF+3rd Agent. For patients on either a COBI or RTV boosted regimen prior to randomization, the estimated GFR increased 1.8 mL/min for E/C/F/TAF and decreased 3.7 mL/min for FTC/TDF+3rd Agent (p<0.001). As shown in the table, multiple measures of quantitative proteinuria, including tubular proteinuria, had statistically significant improvements for patients switching to E/C/F/TAF as compared with those retaining their prior TDF-based regimen.

Median % Change from Baseline to Week 48	E/C/F/TAF	FTC/TDF + 3rd Agent	Significance
Urine Protein: Creatinine (UPCR)	-18.5%	+9.4%	p<0.001
Urine Albumin: Creatinine (UACR)	-18.4%	+5.3%	p<0.001
Retinol Binding Protein: Creatinine (RBP:CR)	-32.9%	+15.7%	p<0.001
Beta-2-Microglobulin: Creatinine (B2MG:CR)	-49.2%	+14.4%	p<0.001

[Changes in Proteinuria & Tubular Proteinuria]

Conclusions: These 48 week data demonstrate that patients who switch from a TDF-based regimen to E/C/F/TAF maintain high efficacy, have statistically significant increases in BMD and have statistically significant improvements in multiple tests of renal function, as compared with patients remaining on their prior TDF-based regimen.

TUAB0103

Subjects with renal impairment switching from tenofovir disoproxil fumarate to tenofovir alafenamide have improved renal and bone safety through 48 weeks

S. Gupta[1], A. Pozniak[2], J. Arribas[3], F. Post[4], M. Bloch[5], J. Gathe[6], P. Benson[7], J. Custodio[8], M. Abram[9], X. Wei[8], A. Cheng[8], S. McCallister[8], M. Fordyce[8]
[1]Indiana University, Indianapolis, United States, [2]Chelsea and Westminster Hospital NHS Foundation Trust, London, United Kingdom, [3]Hospital La Paz, Madrid, Spain, [4]Kings College Hospital NHS Foundation Trust, London, United Kingdom, [5]Holdsworth House Medical Practice, Sydney, Australia, [6]Baylor College of Medicine, Houston, United States, [7]Be Well Medical Center, Berkley, United States, [8]Gilead Sciences Inc, Foster City, United States, [9]Gilead Sciences, Foster City, United States
Presenting author email: sgupta1@iu.edu

Background: Tenofovir (TFV) is renally eliminated, and the prodrug, tenofovir disoproxil fumarate (TDF) has been associated with renal toxicity and reduced bone mineral density (BMD). Tenofovir alafenamide (TAF) is a novel prodrug of tenofovir (TFV) that results in 90% lower plasma TFV levels as compared to TDF. The safety and efficacy of a once-daily single tablet regimen of elvitegravir, cobicistat, emtricitabine, and TAF (E/C/F/TAF) was assessed in HIV-1 infected patients with mild to moderate renal impairment.
Methods: Virologically suppressed adults with stable renal impairment ($eGFR_{CG}$ 30 to 69 mL/min) had their treatment switched from both TDF- and non-TDF-containing regimens to open-label E/C/F/TAF. Week 48 safety data by pre-switch TDF use are presented.
Results: Of 242 subjects switched to E/C/F/TAF [mean age 58 years (range: 24 - 82), 18% Black, 39% HTN, and 14% DM] 158 subjects (65%) were taking TDF-containing regimens prior to switch. At Week 48, the median (Q1, Q3) change from baseline for $eGFR_{C-G}$ was +0.2 (-5.8, 6.3) mL/min (p=0.81) and for eGFR-cystatin C was +2.7 (-6.2, 14.1) mL/min/1.73m2 (p=0.003). The following measures of renal tubular function improved significantly (p< 0.001 for all) for subjects switching from TDF-containing regimens to E/C/F/TAF: quantified proteinuria (UPCR, median [Q1, Q3] % change; -55 [-70, -28]), albuminuria (UACR, median [Q1, Q3] % change; -61 [-81, -27]), retinol binding protein (RBP:Cr, median [Q1, Q3] % change; -82 [-95, -55]), and beta-2-microglobulin (β-2-Mg:Cr, median [Q1, Q3] % change; -89 [-97, -61]). The prevalence of clinically significant proteinuria (UPCR > 200 mg/g) and albuminuria (UACR ≥ 30 mg/g) decreased from 48% to 13% and from 56% to 22%, respectively. Significant increases in mean % change in hip (+1.29%) and spine (+2.60%) BMD were observed at 48 weeks (p< 0.001 for both). Subjects taking non-TDF based regimens pre-switch (n=84) had no significant changes from baseline measures of renal function or BMD.
Conclusions: Subjects with mild and moderate renal impairment (eGFR 30 to 69 mL/min) who switched from TDF-containing regimens to once daily single-tablet E/C/F/TAF experienced improvements in multiple assessments of renal and bone safety through 48 weeks. These data support the safety of E/C/F/TAF in patients with impaired renal function.

TUAB0104

Efficacy and safety of doravirine 100mg QD vs efavirenz 600mg QD with TDF/FTC in ART-naive HIV-infected patients: week 24 results

J. Gatell[1], F. Raffi[2], A. Plettenberg[3], D. Smith[4], J. Portilla[5], C. Hoffmann[6], K. Arasteh[7], M. Thompson[8], D. Hagins[9], J. Morales-Ramirez[10], X. Xu[11], H. Teppler[11]
[1]University of Barcelona, Barcelona, Spain, [2]Hotel-Dieu University Hospital, Infectious Diseases Department, Nantes, France, [3]ifi-Institute for Infections, Hamburg, Germany, [4]Albion Centre, Sydney, Australia, [5]University Miguel Hernandez, Alicante, Spain, [6]ICH Study Center, Hamburg, Germany, [7]EPIMED/Vivantes Auguste-Viktoria-Klinikum, Berlin, Germany, [8]AIDS Research Consortium of Atlanta, Atlanta, United States, [9]Chatham County Health Department, Savannah, United States, [10]Clinical Research Puerto Rico, San Juan, Puerto Rico, [11]Merck & Co., Inc., Kenilworth, United States
Presenting author email: gatell@fundsoriano.es

Background: Doravirine (DOR), an investigational NNRTI with a novel resistance profile, was compared with efavirenz (EFV) in a double-blind, randomized, 2-part study in ART-naïve HIV-infected patients who also received tenofovir/emtricitabine (TDF/FTC). In Part 1 (dose selection), DOR at 25, 50, 100 and 200mg QD showed rates of virologic suppression similar to EFV 600mg QD; DOR 100mg was selected for ongoing evaluation. Part 2 enrolled additional patients to receive DOR 100mg or EFV. Using data from Parts 1+2 combined, DOR 100mg showed significantly fewer CNS AEs than EFV at week 8.
Methods: Week 24 efficacy and safety results were analyzed for all patients who received DOR 100mg or EFV in Part 1 (n=42 per group) and Part 2 (n=66 per group) combined. Patients were stratified at randomization by screening RNA ≤ or >100,000 copies/mL. Primary endpoints were the proportion of patients with HIV RNA < 40 c/mL (efficacy) and the proportion of patients with pre-specified CNS events (safety).
Results: Of the 108 patients randomized and treated per group, mean baseline RNA was 4.6 log_{10} c/mL in both the DOR and EFV groups, and mean CD4 counts were 432 and 448 cells/mm^3, respectively. Discontinuations in the DOR and EFV groups, respectively, were 4.6% and 12.0%.

Week 24 Efficacy, including subgroup responses by screening RNA ≤ or >100,000 c/mL

Endpoint	DOR† (N=108)	EFV† (N=108)	Difference [DOR-EFV] (95% CI)
HIV RNA <40 c/mL‡	72.2 %	73.1 %	-8.3 (-19.1, 2.4)
screening RNA ≤100K§ (n=66, 63)	83.3 %	85.7 %	-2.4 (-15.3, 10.6)
screening RNA >100K§ (n=38, 38)	60.5 %	65.8 %	-5.3 (-26.4, 16.4)
HIV RNA <200 c/mL‡	88.9 %	87.0 %	1.9 (-7.0, 11.0)
screening RNA ≤100K§ (n=66, 63)	92.4 %	92.1 %	0.4 (-9.8, 10.8)
screening RNA >100K§ (n=38, 38)	92.1 %	94.7 %	-2.6 (-16.5, 10.7)
Mean change in CD4 count§	154/mm^3	146/mm^3	8 (-37, 52)

† with TDF/FTC
‡ Non-completer = Failure (NC=F) approach to missing data.
§ Observed Failure (OF) approach to missing data.

Week 24 Clinical Adverse Event (AE) Summary & Primary Safety Analysis (CNS AEs)

Proportion of patients with:	DOR† (N=108)	EFV† (N=108)	Difference [DOR-EFV] (95% CI)
One or more AEs	75.9 %	84.3 %	-8.3 (-19.1, 2.4)
Drug-related AEs	27.8 %	55.6 %	-27.8 (-39.9, -14.8)
Serious AE	0.9 %	4.6 %	-3.7 (-9.6, 0.9)
Serious drug-related AEs	0 %	0.9 %	-0.9 (-5.1, 2.5)
Discontinued due to AEs	0.9 %	5.6 %	-4.6 (-10.8, 0.1)
One or more CNS AEs	26.9 %	46.3 %	-19.4 (-31.7, -6.6)*

† with TDF/FTC
* Prespecified safety hypothesis, p<0.001

[Tables]

The most common drug-related clinical AEs in the DOR and EFV groups, respectively, were nausea (7.4%; 5.6%), dizziness (6.5%; 25.0%), abnormal dreams (5.6%; 14.8%), nightmares (4.6%; 8.3%), and sleep disorder (3.7%; 6.5%). Drug-related AEs leading to discontinuation were hallucination for DOR (n=1) and dysesthesia, hallucination, drug eruption, dizziness, and disturbance in attention for EFV (n=5). The most common CNS AEs (all causality) were dizziness (DOR 9.3%; EFV 27.8%), insomnia (7.4%; 2.8%), abnormal dreams (6.5%; 17.6%), and nightmares (6.5%; 8.3%). Lab abnormalities of Grade 2 or greater were uncommon in both groups.
Conclusions: DOR 100mg qd demonstrated antiretroviral activity and immunological effect similar to EFV (each with TDF/FTC) and was generally safe and well tolerated during 24 weeks of treatment in ART-naïve, HIV-1 infected patients. Treatment-emergent CNS AEs through week 24 were significantly less common in the DOR group than in the EFV group.

TUAB0105

Raltegravir for prevention of mother-to-child transmission of HIV

M.-J. Trahan[1], V. Lamarre[1,2,3], M.-E. Metras[4], N. Lapointe[1,3,5], F. Kakkar[1,2,3]
[1]Université de Montréal, Faculté de Médecine, Montreal, Canada, [2]CHU Ste-Justine, Département des Maladies Infectieuses, Montreal, Canada, [3]Centre Maternel et Infantile sur le Sida, Montreal, Canada, [4]CHU Ste-Justine, Département de Pharmacie, Montreal, Canada, [5]CHU Ste-Justine, Département d'Immunologie, Montreal, Canada
Presenting author email: fatima.kakkar@umontreal.ca

Background: Raltegravir (RAL), though currently category C in pregnancy, and not recommended for use in newborns, has been used in exceptional cases for prevention of mother-to-child-transmission (PMTCT). We report on the outcomes of 14 infants exposed in utero to RAL, and the first newborn to be treated with RAL for 6 weeks for PMTCT.
Methods: Infants born to mothers treated with RAL during pregnancy from the Centre Maternel et Infantile sur le Sida (CMIS) mother-child cohort between 2010 and 2014 were included in the study. RAL levels were tested on the first available stored plasma sample after birth, and in the treated newborn, therapeutic drug monitoring was done at weekly intervals.
Results: In RAL-exposed infants, RAL was given to mothers at standard dosing of 400 mg BID, started at a mean GA of 30 weeks (range pre-conception-37.5 weeks). Indications for RAL included drug resistance and/or detectable viral load in the third trimester. Mean GA was 38.5 weeks (± 1.76), and mean birthweight was 3200 g (± 540). There were no clinical adverse events noted among RAL-exposed infants (mean follow-up time 119 weeks, range 48-144), and all were confirmed HIV negative. RAL levels tested in two exposed newborns at 16 and 30 hours of life were detectable at 0.9345 mg/L and 0.0381 mg/L, respectively, and undetectable in 6 other infants tested at days 4-14. RAL granules for suspension (Merck, special access) were obtained for prophylaxis of a term newborn (39 weeks GA) from a mother with multidrug-resistant virus, and started at 1.5 mg/kg BID, along with zidovudine and lamivudine at standard doses. RAL levels were consistently above the targeted trough for treatment (0.02 mg/L) (Table 1) for the duration of therapy. RAL was well tolerated and at follow-up, the infant was confirmed HIV negative.

Day of Life	Weight (kg)	Dose	mg/kg/ dose	Trough (hours)	Trough Level	Peak (hours)	Peak Level	Adjusted
6	3.115	5 mg BID	1.61	11.67	0.36	1.97	0.87	No
9	3.220	5 mg BID	1.55	11.25	0.75	1.25	0.15	No
20	3.565	5 mg BID	1.40	12	0.07	1.17	0.33	No
27	3.835	5 mg BID	1.30	11	0.06	1.15	0.02	Increased to 6 mg BID
40	4.275	6 mg BID	1.40	N/A	N/A	N/A	N/A	Stopped

[Table 1: Raltegravir Levels in a Treated Newborn]

Conclusions: RAL in late pregnancy had no adverse effects on infants exposed in utero. RAL treatment in the newborn at doses of 1.3-1.6 mg/kg BID was well tolerated and resulted in therapeutic drug levels. Given detectable levels of RAL in the first 30 hours of life in exposed infants, the timing and role of RAL in PMTCT should further be considered.

TUAB0106LB

Second-generation HIV-1 maturation inhibitor BMS-955176: antiviral activity and safety with atazanavir +/- ritonavir

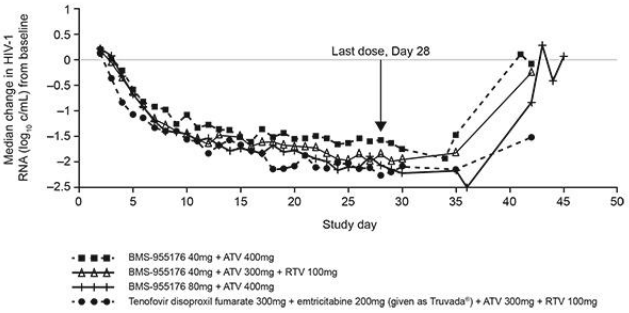
C. Hwang[1], D. Schürmann[2], C. Sobotha[2], M. Boffito[3], H. Sevinsky[1], N. Ray[1], P. Ravindran[1], H. Xiao[1], M. Krystal[4], I. Dicker[4], D. Grasela[1], M. Lataillade[4], for the BMS HIV Global Development Team

[1]Bristol-Myers Squibb, Research and Development, Princeton, United States, [2]Charité Research Organisation GmbH, Berlin, Germany, [3]St. Stephen's Centre, Chelsea and Westminster Hospital, London, United Kingdom, [4]Bristol-Myers Squibb, Research and Development, Wallingford, United States

Background: BMS-955176 is a second-generation HIV-1 maturation inhibitor that targets the HIV-1 Gag polyprotein, inhibiting the last protease cleavage event between capsid protein p24 and spacer peptide 1, resulting in the release of immature, non-infectious virions. Ten days of BMS-955176 monotherapy resulted in maximum median declines in HIV-1 RNA that plateaued at ~1.64 log_{10} c/mL at doses between 40mg and 120mg once daily (QD). Two drug combination studies *in vitro* demonstrated that BMS-955176 + atazanavir (ATV) had an additive effect. Due to the proximity of their sites of inhibition in the virus life cycle and the potential for synergy, we assessed the antiviral activity and safety of BMS-955176 with ATV±ritonavir (RTV) for 28 days in HIV-1-infected subjects.
In addition, this combination is being further evaluated to potentially serve as part of a booster-sparing and nucleot(s)ide-sparing strategy.
Methods: AI468002 (NCT01803074) was a Phase 2a, randomized, multipart trial. In Part B, 28 HIV-1 subtype B-infected subjects (HIV-1 RNA ≥5000 c/mL, CD4+ T-cell counts ≥200 cells/μL) were randomized 2:2:2:1 to 4 treatment groups (all QD): BMS-955176 40mg+ATV 400mg; BMS-955176 40mg+ATV 300mg+RTV 100mg; BMS-955176 80mg+ATV 400mg; and a standard-of-care (SOC) control of tenofovir disoproxil fumarate 300mg+emtricitabine 200mg (fixed-dose combination)+ATV 300mg+RTV 100mg.
Results: Median change in HIV-1 RNA at Day 29 was -1.66, -1.99, -2.18, and -2.22 log_{10} c/mL, and maximum median change in HIV-1 RNA from baseline to end of study/discharge (Day 42) was -1.86, -2.20, -2.23, and -2.39 log_{10} c/mL, for BMS-955176 40mg+ATV 400mg, BMS-955176 40mg+ATV 300mg+RTV 100mg, BMS-955176 80mg+ATV 400mg, and the SOC control, respectively (Table, Figure). There were no deaths, serious adverse events (SAEs), or AEs leading to discontinuation. Furthermore, the median bilirubin level was below the upper limit of normal for subjects receiving unboosted ATV with BMS-955176, in contrast to the level observed for subjects receiving BMS-955176 40mg+ATV+RTV or SOC.
Conclusions: In this study, BMS-955176 80mg+ATV and 40mg+ATV+RTV had similar maximum median declines in HIV-1 RNA compared with the SOC control. BMS-955176 with ATV±RTV was generally well tolerated. A Phase 2b study investigating BMS-955176 in a booster-sparing and nucleot(s)ide-sparing regimen in treatment-experienced patients will begin in Q2 2015.

	BMS-955176 (40mg QD)+ATV (400mg QD)	BMS-955176 (40mg QD)+ATV (300mg QD)+RTV (100mg QD)	BMS-955176 (80mg QD)+ATV (400mg QD)	Tenofovir disoproxil fumarate (300mg QD)+emtricitabine (200mg QD) (fixed-dose combination) +ATV(300mg QD) +RTV (100mg QD)
N	8	8	8	4
Maximum decline in HIV-1 RNA (log_{10} c/mL); median (min, max)	-1.86 (-1.49, -2.37)	-2.20 (-1.24, -3.52)	-2.23 (-1.87, -2.68)	-2.39 (-1.83, -3.04)
Median decline in HIV-1 RNA (log_{10} c/mL) on Day 29 (min, max)	-1.66 (-1.19, -2.04)	-1.99 (-1.04, -3.32)	-2.18 (-1.53, -2.68)	-2.22 (-1.83, -2.84)

[Changes in HIV-1 RNA from baseline]



[Median change in HIV-1 RNA (log10 c/mL) over time]

TUAB02 HCV: The Good News Continues

TUAB0201

A longitudinal analysis of liver fibrosis progression among NNRTI and PI users in the Canadian co-infection cohort study

L. Brunet[1], E.E.M. Moodie[1], J. Young[2], S. Walmsley[3], M. Hull[4], C. Cooper[5], M.B. Klein[6,7], Canadian Co-Infection Cohort Study Investigators

[1]McGill University, Epidemiology & Biostatistics, Montreal, Canada, [2]University Hospital Basel, Basel Institute for Clinical Epidemiology and Biostatistics, Basel, Switzerland, [3]University of Toronto, University Health Network, Toronto, Canada, [4]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada, [5]The Ottawa Hospital-General Campus, Ottawa, Canada, [6]McGill University, Medicine, Montreal, Canada, [7]McGill University Health Centre, Chronic Viral Illness Service, Montreal, Canada
Presenting author email: laurence.brunet@mail.mcgill.ca

Background: Both protease inhibitors (PI) and non-nucleoside reverse transcriptase inhibitors (NNRTI) have been associated with acute hepatotoxicity, but their long-term effect on liver fibrosis remains uncertain. We explored rates of change in liver fibrosis as measured by the aspartate-to-platelet ratio index (APRI) among HIV-hepatitis C (HCV) co-infected users of modern PI- or NNRTI-based regimens.
Methods: Data from a Canadian prospective multicentre cohort were analysed for 397 HCV PCR+ persons who initiated antiretroviral therapy in or after 2000, with regimens at cohort entry comprised of a backbone of either Tenofovir/Emtricitabine or Abacavir/Lamivudine with a PI or NNRTI as the anchor agent. The natural logarithm of the APRI score was the outcome of interest. Three multivariate linear regression analyses with generalized estimating equations were performed. Analysis 1 (intention-to-treat) used baseline exposure to PI or NNRTI; analysis 2 (per protocol) was restricted to persons with a viral load under 1000 copies/ml and censored participants when the class of anchor agent was changed; analysis 3 (as treated) allowed for changes in the class of anchor agent during follow-up.
Results: At cohort entry, 74% of participants were male, the median age was 44 years and 56% had used alcohol in the past six months. Therapy was started a median of 1.9 years before cohort entry (IQR: 0.3, 5.0), 70% used a PI and 69% were on a backbone of Tenofovir/Emtricitabine. PI use was associated with a median increase in APRI per 5 years of 16% (95% CI: 3%, 30%) in Analysis 1, 16% (95% CI: 0%, 32%) in Analysis 2 and 13% (95% CI: -1%, 27%) in Analysis 3. NNRTI use was not significantly associated with change in APRI in any of the three analyses, as shown in the table.

Analysis	APRI score at cohort entry, Median (IQR)	PI users (APRI units/5 years), Exp(β) (95% CI)*	NNRTI users (APRI unit/5 years), Exp(β) (95% CI)*
1. Intention-to-treat	0.63 (0.39-1.30)	1.16 (1.03, 1.30)	1.05 (0.90, 1.20)
2. Per protocol	0.60 (0.39-1.22)	1.16 (1.00, 1.32)	1.07 (0.89, 1.24)
3. As treated	0.63 (0.39-1.30)	1.13 (0.99, 1.27)	1.09 (0.93, 1.25)
*adjusted for baseline age, sex and time since HCV infection and updated alcohol use, CD4 cell count, viral load or virologic failure and number or type of previous regimens			

[Multiplicative median change in APRI per 5 years]

Conclusions: PI use seems to be associated with a faster progression of liver fibrosis, as measured by the median change in APRI score over five years. The consistency of estimates across the three analyses suggests that this is not the result of the type of patients using PI-based regimens, although we could not account for all patient characteristics influencing the choice of an anchor agent.

TUAB0202

Ledipasvir/sofosbuvir for 12 weeks in patients co-infected with HCV and HIV-1

S. Naggie[1], C. Cooper[2], M. Saag[3], J.C. Yang[4], L.M. Stamm[4], P.S. Pang[4], J.G. McHutchison[4], D. Dieterich[5], M.S. Sulkowski[6]
[1]Duke University Medical Center, Infectious Diseases, Durham, United States, [2]University of Ottawa, Ottawa, Canada, [3]University of Alabama at Birmingham, Birmingham, United States, [4]Gilead Sciences, Inc., Foster City, United States, [5]Mount Sinai School of Medicine, New York, United States, [6]Johns Hopkins University School of Medicine, Baltimore, United States

Background: Historically HIV co-infection was considered a negative predictor of HCV response to treatment with interferon/ribavirin (IFN/RBV). For sofosbuvir-based regimens, HIV/HCV patients have achieved similar sustained virologic response (SVR) rates as HCV mono-infected patients. We evaluated the safety and efficacy of the IFN-free, RBV-free, single tablet regimen of ledipasvir/sofosbuvir (LDV/SOF) in HCV genotype 1 or 4 patients co-infected with HIV-1 in the Phase 3 ION-4 study.
Methods: HCV treatment naïve and experienced HIV co-infected patients on stable, approved antiretroviral (ARV) regimens were enrolled and received LDV/SOF (90mg/400mg) once daily for 12 weeks. Patients with compensated cirrhosis were eligible. Permitted concomitant ARVs included tenofovir and emtricitabine (TDF+FTC) with raltegravir (RAL), efavirenz (EFV) or rilpivirine (RPV). Safety evaluations included adverse event (AE) and standard laboratory parameter monitoring in addition to enhanced renal toxicity monitoring, CD4 count and HIV-1 RNA levels. The primary efficacy endpoint was SVR12.
Results: 335 patients with GT1a (75%), GT1b (23%) and GT4 (2%) were enrolled; 82% were male, 61% were white, mean age was 52 (range 26-72), mean baseline HCV RNA was 6.7 log_{10} IU/mL (range 4.1-7.8), median baseline CD4 count was 662 cells/uL (Q1, Q3=469, 823), 20% had cirrhosis, 24% were *IL28B* CC genotype and 55% had not responded to prior HCV treatment. Patients were taking EFV (48%) or RAL (44%) or RPV (9%). The table shows SVR12 by ARV regimen. Overall, the SVR12 rate was 96% (320/335); 2 patients had on-treatment virologic failure likely due to non-compliance and 10 had virologic relapse after discontinuing treatment. SVR12 was similar among non-cirrhotic (96%) and cirrhotic (94%) patients and also among treatment naïve (94%) and treatment experienced (97%) patients. No patient had confirmed HIV virologic rebound (HIV-1 RNA≥400 copies/mL). No patients discontinued study drug due to an AE. AEs occurring in ≥10% of patients were headache (25%), fatigue (21%) and diarrhea (11%). No significant lab abnormalities were observed.
Conclusions: The IFN-free, RBV-free, single tablet regimen of LDV/SOF administered once daily for 12 weeks is highly effective and well tolerated in treatment-naïve and experienced, genotype 1 or 4 HCV-infected patients with HIV-1 co-infection, including those with cirrhosis.

Virologic Response	TDF+FTC+EFV (N=160)	TDF+FTC+RAL (N=146)	TDF+FTC+RPV (N=29)	Overall (N=335)
SVR12, n(%)	151 (94)	141 (97)	28 (97)	320 (96)
On-Treatment Failure, n (%)	1 (<1)	0	1 (3)	2 (<1)
Relapse, n (%)	8 (5)	2 (1)	0	10 (3)
Other, n (%) 0 3 (2) 0				3 (<1)

[SVR12 by HIV Regimen and Overall]

TUAB0203

High SVR rates in HCV/HIV-1 co-infected patients regardless of baseline characteristics

D. Wyles[1], J.J. Eron[2], J. Lalezari[3], C. Wang[4], P.J. Ruane[5], G. Blick[6], L. Bhatti[7], Y.B. Hu[8], M. Co[8], K. Gibbons[8], R. Trinh[8], M.S. Sulkowski[9]
[1]University of California San Diego, San Diego, United States, [2]University of North Carolina, Chapel Hill, United States, [3]Quest Clinical Research, San Francisco, United States, [4]Virginia Mason Medical Center, Seattle, United States, [5]Ruane Medical and Liver Health Institute, Los Angeles, United States, [6]CIRCLE CARE Center, Norwalk, United States, [7]AIDS Healthcare Foundation, Beverly Hills, United States, [8]AbbVie Inc., Chicago, United States, [9]Johns Hopkins University, Baltimore, United States
Presenting author email: dwyles@ucsd.edu

Background: The 3 direct-acting antiviral (3D) regimen of ombitasvir (OBV), paritaprevir (identified by AbbVie and Enanta; co-dosed with ritonavir; PTV/r), and dasabuvir (DSV) with ribavirin (RBV) is approved to treat HCV genotype 1 infection in patients with HIV-1 co-infection. In the TURQUOISE-I trial, response rates were 94 and 91% in this population when treated for 12 and 24 weeks, respectively. We report the week 12 post-treatment sustained virologic response rates (SVR12) by baseline characteristics.
Methods: Patients were randomized to receive OBV/PTV/r + DSV + RBV for 12 (N=31) or 24 weeks (N=32). Eligible patients in this open-label study were treatment-naïve or pegIFN/RBV-experienced with or without cirrhosis, had CD4+ count ≥200 cells/mm^3 or CD4+ % ≥14%, and plasma HIV-1 RNA suppressed while receiving a stable atazanavir- or raltegravir-inclusive antiretroviral (ART) regimen.
Results: Sixty-three patients were enrolled, of whom 92% were male, 24% black race, 19% with compensated cirrhosis, and 16% with a prior null response to pegIFN/RBV treatment. Two patients in the 12-week treatment group (1 withdrawn consent, 1 HCV relapse), and 3 in the 24-week treatment group (1 on-treatment virologic breakthrough, 2 post-treatment HCV re-infections) did not achieve SVR12. The patients with on-treatment breakthrough and relapse were both genotype 1a-infected with prior null response to pegIFN/RBV and had F4 fibrosis (cirrhosis). High SVR12 rates were achieved in patients with historically difficult-to-cure characteristics including those with IL28B non-CC genotype, high viral load, prior treatment failure, and advanced liver disease (Table). Lower baseline CD4+ T-cell counts did not negatively affect SVR12 rates. The regimen was well tolerated with no discontinuation due to adverse event or serious adverse event.
Conclusions: In HCV genotype 1 patients co-infected with HIV-1, OBV/PTV/r + DSV + RBV achieved high rates of SVR12 regardless of baseline host, viral, and disease characteristics whether treated with 12 or 24 weeks of therapy.

Characteristic	12-Week OBV/PTV/r + DSV + RBV	24-Week OBV/PTV/r + DSV + RBV
Overall	29/31 (94)	29/32 (91)
Black race Hispanic or Latino ethnicity	7/7 (100) 7/8 (88)	7/8 (88) 7/8 (88)
Age, ≥55 years	7/8 (88)	12/12 (100)
BMI ≥30	3/3 (100)	7/7 (100)
IL28B genotype CT TT	 16/16 (100) 8/10 (80)	 19/20 (95) 4/5 (80)
Prior pegIFN/RBV treatment experience Naïve Relapser Partial response Null response	 19/20 (95) 1/1 (100) 5/5 (100) 4/5 (80)	 20/22 (91) 3/3 (100) 2/2 (100) 4/5 (80)
Baseline HCV RNA ≥800,000 IU/mL Baseline CD4+ T-cell cells/mm3 <350 350 - <500	25/27 (93) 2/2 (100) 8/8 (100)	26/28 (93) 5/5 (100) 7/8 (88)
Baseline CD4+ T-cells/mm3 <350 350 - <500 Baseline fibrosis stage F2 F3 F4	 2/2 (100) 8/8 (100) 5/5 (100) 3/4 (75) 5/6 (83)	 5/5 (100) 7/8 (88) 5/5 (100) 1/1 (100) 5/6 (83)
SVR12, sustained virologic response at post-treatment week 12; OBV, ombitasvir; PTV, paritaprevir; r, ritonavir; DSV, dasabuvir; RBV, ribavirin		

[SVR12 rates by baseline characteristic, n/N (%)]

TUAB0204

Liver fibrosis regression after anti HCV therapy and the rate of death, liver-related death, liver-related complications, and hospital admissions in HIV/HCV co-infected patients with cirrhosis

J.L. Casado, S. Bañon, C. Quereda, A. Moreno, M.J. Perez Elías, S. Moreno
Ramon y Cajal Hospital, Infectious Diseases, Madrid, Spain
Presenting author email: smoreno.hrc@salud.madrid.org

Background: There are few data about the clinical outcome of hepatitis C (HCV)/HIV coinfected patients with liver cirrhosis after therapy, considering the possibility of fibrosis regression (FR).
Methods: We compared the incidence rate (IR), and the time to develop a liver complication and death, in 139 cirrhotic patients according to sustained virological response (SVR) or/and FR, as established by a confirmed 1-point decrease in Metavir score by transient elastography (TE).
Results: Overall, 42 patients reached SVR, and 23 of them (55%) had FR, in comparison with only 14 of the 91 (15%) without SVR. During a median follow up of 6.8 years (916.8 person-years), the IR of death, liver-related death, liver-related complications, and hospital admissions were significantly lower in patients with SVR/FR (Table). SVR patients without FR had a worse IR of death (5.36) and liver-related death (2.68) than non-SVR patients with FR (1.3, and 0.65, respectively; p< 0.01). In Cox multivariate analysis, only FR was associated with a lower risk of death (Adjusted Hazard Ratio, HR, 0.36; 95%CI 0.15-0.86), and liver-related death (HR 0.15; 95% CI 0.03-0.65), whereas both FR (HR 0.09; 95%CI 0.03-0.3, p< 0.01) and SVR (HR 0.24; 95% CI 0.07-0.87) decreased the risk of liver-related complications.

	SVR (42)			No SVR (91)		
	FR (23, 55%)	No FR (19, 45%)	p value	FR (14, 15%)	No FR (77, 85%)	p value
TE (Kpa)	7.1 (6.3-8.8)	17.5 (13.8-26.3)	<0.01	11.6 (6.3-11.2)	21.3 (17.2-45.4)	<0.01
Death (n, %) IR	4 (17%) 2.45	6 (32%) 5.36	0.01	2 (14%) 1.3	37 (48%) 7.6	<0.01
Liver-related death (n, %), IR	1 (4%) 0.61	3 (16%) 2.68	0.01	1 (7%) 3.65	29 (38% 5.9	<0.01
Liver-related complications (n, %) IR	1 (4%) 1.22	2 (11%) 1.78	0.2 0.15	5 (36%) 3.25	33 (43%) 6.81	0.01 <0.01
Hospital admissions (n,%) IR	2 (9%) 1.22	3 (16%) 2.68	0.7 0.13	4 (29%) 2.6	27 (30%) 5.6	0.2 0.04

[Table 1]

Conclusions: Fibrosis regression is frequent after anti-HCV therapy in HIV/HCV coinfected patients with compensated cirrhosis who achieve SVR, and it is associated with the highest reduction of death of any cause, liver-related mortality, liver-related complications, and hospital admissions.

TUAB0205

How generalizable are direct antiviral agents (DAA) trials for real world people co-infected with HIV/hepatitis C?

S. Saeed[1], K. Rollet-Kurhajec[2], E.C. Strumpf[1], M.B. Klein[2,3], the Canadian Co-Infection Cohort (CTN222)
[1]Department of Epidemiology, Biostatistics, and Occupational Health, McGill University, Montreal, Canada, [2]Department of Medicine, Division of Infectious Diseases/Chronic Viral Illness Service, Royal Victoria Hospital, McGill University Health Centre, Montreal, Canada, [3]CIHR Canadian HIV Trials Network, Vancouver, Canada
Presenting author email: sahar.saeed@mail.mcgill.ca

Background: Worldwide approximately 7 million people are co-infected with HIV-Hepatitis C (HCV). The most common risk factor for co-infection is injection drug use. HCV treatments have evolved at an unprecedented speed; Simpeprevir (SIM) and Sofosburvir (SOF) are among the latest DAAs approved for use. However clinical trials conducted with these agents have enrolled a small number of individuals, in ideal circumstances with strict inclusion/exclusion criteria. This provokes the question: how generalizable are their results?
Methods: We examined the study population characteristics (based on published inclusion/exclusion criteria) from the only two efficacy trials evaluating SIM (NCT01479868) and SOF (NCT01667731: PHOTON-1) for HIV-HCV co-infected patients and compared them to participants in the Canadian Co-Infection Cohort (CCC), a prospective cohort following 1383 co-infected people from across Canada (representing ~23% co-infected population in care).
Results: Due to eligibility criteria 30% (49/160) of screened subjects from 32 international study locations, and 29% (96/330) of screened subjects from 27 American sites were excluded from the SIM and SOF trials respectively. Of 1383 CCC participants, 1054 (76%) had evidence of chronic HCV (RNA+) at last visit; 699 (66%) infected with HCV genotype 1 and 887 (84%) infected with genotype 1,2 or 3 and therefore could have been eligible for these trials. After applying all the available trial inclusion/exclusion criteria, only 8.6% of genotype 1 (60/699) and similarly 8.6% (76/887) overall would have been eligible to participate. Active drug use within 12 months accounted for 46% of reasons for non-eligibility, restriction to specific antiretroviral therapies and liver fibrosis staging were also highly exclusive as described in table 1.

Exclusion Criteria (exclusive)	No (%) among Genotype 1 (n=699)	No (%) among Genotypes 1, 2 &3 (n=887)
Specific cART Regimens*	380 (54)	484 (55)
Active drug abuse within 12 months (excluding marijuana use)	320 (46)	402 (45)
HIV VL>50 copies/mL	175 (25)	225 (25)
HbA1c >10% (Used HOMA IR >2 as surrogate)	171 (24)	217 (24)
APRI** of <1 or ≥2	129 (18)	171 (19)
CD4 T-cell count <200 cells/mm3	106 (15)	136 (15)
Decompensated liver disease	23 (3)	27 (3)

*SOF trial: emtricitabine/tenofovir plus atazanavir/ritonavir; or darunavir/ritonavir; efavirenz; raltegravir; rilpivirine. SIM trial: excluded all boosted PIs and allowed only raltegravir, sustiva and ripilvirine

** Aspartate aminotransferase/platelet ratio index (APRI) <1 defined as non-cirrhotic or ≥2 defined as cirrhotic based on SOF trial

[Table1. Inclusion/Exclusion Criteria]

Conclusions: Limited population level data makes it difficult to examine external validity of clinical trials. However using data from the CCC we have illustrated that results obtained from clinical trials are not generalizable to the HIV-HCV patients in Canada and caution should be used when translating trial results in the real world.

TUAB0206LB

High efficacy of grazoprevir/elbasvir in HCV genotype 1, 4, and 6-infected patients with HIV co-infection: the phase 3 C-EDGE co-infection study

J.K. Rockstroh[1], M. Nelson[2], C. Katlama[3], J. Lalezari[4], J. Mallolas[5], M. Bloch[6], G. Matthews[7], M.S. Saag[8], P. Zamor[9], C. Orkin[10], J. Gress[11], M. Shaughnessy[11], S. Klopfer[11], H.L. Platt[11], M. Robertson[11], M. Sulkowski[12]
[1]Bonn University Hospital, Bonn, Germany, [2]Chelsea and Westminster Hospital, London, United Kingdom, [3]Université Pierre et Marie Curie, Paris VI and Hôpital Pitié-Salpêtrière, Paris, France, [4]Quest Clinical Research, San Francisco, United States, [5]Hospital Clinic-University of Barcelona, Barcelona, Spain, [6]Holdsworth House Medical Practice, Darlinghurst, Australia, [7]St Vincent's Hospital, Sydney, Australia, [8]University of Alabama at Birmingham, Birmingham, United States, [9]Carolinas Medical Center, Charlotte, United States, [10]Royal London Hospital, Bart's Health NHS Trust, London, United Kingdom, [11]Merck & Co. Inc., Kenilworth, United States, [12]Johns Hopkins University School of Medicine, Baltimore, United States

Background: The fixed-dose combination of grazoprevir (GZR, MK-5172, 100mg, an NS3/4 protease inhibitor)/elbasvir (EBR, MK-8742, 50mg, an NS5A inhibitor), an interferon-free, ribavirin-free, once-daily tablet has shown robust efficacy and safety in diverse populations. C-EDGE Co-infection is an on-going phase-III study evaluating GZR/EBR among treatment-naïve, HIV/HCV co-infected patients with GT1, 4, or 6.
Methods: Enrolled patients were on a stable antiretroviral (ARV) regimen (tenofovir or abacavir, and lamivudine or emtricitabine; and either raltegravir, dolutegravir or rilpivirine) with a CD4 >200 cells/mm^3 and an HIV RNA < 20 copies/mL, or were HIV treatment-naive with CD4 >500 cells/mm^3 and VL < 50,000 copies/mL. All patients received open-label GZR/EBR for 12 weeks. The primary efficacy endpoint was sustained virologic response at follow-up week 12 (SVR12). Adherence was assessed using electronic study medication diaries (eSMD) and pharmacokinetic (PK) assessment. All patients underwent testing for HCV resistance associated variants (RAVs) at baseline, and at failure and follow-up in those with virologic failure. Phylogenetic analysis was performed to distinguish relapse from reinfection.
Results: 218 patients were enrolled; 211 had suppressed HIV viremia; 7 were ARV-naïve. In the Full Analysis Set population, SVR12 was achieved by 207/218 (95%) patients, including 35/35 (100%) patients with cirrhosis (Figure 1). Of the 11 non-SVR12 patients, 4 failed for reasons other than virologic failure and 7 patients met criteria for virologic failure. Phylogenetic analysis of the 7 failures demonstrated 5 were relapses and 2 were reinfections (Table 1). Thus, 5/218 (2.3%) patients failed to clear HCV infection that was present pre-therapy. Of the 5 virologic relapses, two had baseline NS5A RAVs with >5x resistance to EBR *in vitro* (L31M, Y93S). Adverse events (AEs) were reported in 157/218 (72%) patients; serious AEs occurred in 2/218 (0.9%) patients. Adherence was >90% in the total population, including virologic failures. There was no difference in PK parameters in patients who achieved SVR12 vs. patients who did not achieve SVR12.
Conclusions: A 12-week regimen of GZR/EBR FDC was highly effective among HIV/HCV co-infected patients with GT1, 4 or 6 infection, with a favorable safety profile. SVR was high across all patient subgroups including African-Americans and those with cirrhosis.

	All Patients (N=128†)	GT1a (N=144)	Gt1b (N=44)	GT4 (N=28)
SVR12* n/N % 95% CI	207/218 95.0% 91.2, 97.5	136/144 94.4% 89.3, 97.6	42/44 95.5% 84.5, 99.4	27/28 96.4% 81.7, 99.9
LTFU or unrelated to VF**	4	3	1	0
Relapse‡	5	4	0	1
Reinfection	2	1	1	0

* HCV RNA assessed via COBAS TaqMan v2.0 [lower limit of quantitation <15 IU/mL]
†FAS (Full Analysis Set): all patients who received at least one dose of GZR/EBR
N = Number of subjects included in the analysis.
n (%) = Number of subjects who achieved SVR12 and the percentage calculated as (n/N)*100.
**Two subjects were lost to follow-up; one patient was discontinued for taking a prohibited concomitant medication, and one subject's FW12 visit was outside the analysis window
‡At baseline in the NS5A gene, 1 of the relapses had L31M/L RAV and 1 of the relapses had the Y93S RAV. The other 3 relapses had the WT NS5A gene at baseline.

[Table 1. SVR12 by Genotype]

TUAB0207LB

Daclatasvir plus sofosbuvir with or without ribavirin in patients with HIV-HCV co-infection: interim analysis of a French multicenter compassionate use program

K. Lacombe[1], H. Fontaine[2], C. Dhiver[3], E. Rosenthal[4], S. Metivier[5], T. Antonini-Michelle[6], M.A. Valantin[7], P. Miailhes[8], S. Harent[9], D. Batisse[10], G.-P. Pageaux[11], H. Aumaitre[12], S. Dominguez[13], J. Chas[14], T. Allegre[15], A. Lafeuillade[16], P. De Truchis[17], V. De Ledinghen[18], V. Leroy[19], E. Billaud[20], P. Sogni[2], F. Dabis[21], L. Wittkop[21], C. Duvivier[22], A. Filipovics[23], L. Fedchuk[23], Y. Bennai[23], D. Salmon[24]
[1]AP-HP, Hôpital Saint-Antoine, Inserm UMR-S707, UPMC - Paris VI, Paris, France, [2]Cochin Hospital, Paris, France, [3]Conception Hospital, Marseille, France, [4]Archet Hospital, University Hospital of Nice, Nice, France, [5]Purpan University Hospital, Toulouse, France, [6]Paul-Brousse Hospital, Villejuif, France, [7]Pitié Salpêtrière Hospital, Paris, France, [8]Lyon Civil Hospices, Lyon, France, [9]Bichat, Paris, France, [10]Georges Pompidou European Hospital, Paris, France, [11]Saint-Eloi University Hospital, Montpellier, France, [12]Saint-Jean Hospital, Perpignan, France, [13]Henri Mondor Hospital, Créteil, France, [14]UPMC Tenon Hospital, Paris, France, [15]Pays d'Aix Hospital, Aix-en-Provence, France, [16]Sainte-Musse Hospital, Toulon, France, [17]R Poincare Hospital, Garches, France, [18]Haut-Lévêque Hospital, Pessac, France, [19]Grenoble, Grenoble, France, [20]Hôtel-Dieu University Hospital, Nantes, France, [21]INSERM U897, Bordeaux, France, [22]Necker Hospital, Paris, France, [23]Bristol-Myers Squibb Research and Development, Rueil-Malmaison, France, [24]Saint Antoine Hospital, Department of Internal medicine and Infectious diseases, Paris, France

Background: All-oral regimen with daclatasvir (DCV; NS5A replication complex inhibitor)+sofosbuvir (SOF; NS5B polymerase inhibitor)±weight-based ribavirin (RBV) has demonstrated high sustained virologic response (SVR) rates in HCV mono-infected patients. This analysis reports SVR4 and SVR12 results from an ongoing multicenter compassionate use program (ATU) in France.
Methods: HIV-HCV co-infected patients with advanced liver disease from 221 centers have been included since March 2014. All patients received DCV+SOF QD for 12 or 24 weeks, with RBV added at the physician's discretion. Baseline characteristics, virological response rates and adverse events were collected through a standardized form.
We report interim SVR rates at 4 and 12 weeks after the end of treatment for patients who have completed treatment to date.
Results: Of 562 patients enrolled, 73.8% were males, median age was 52.3 years (30-74), 395 (71.0%) were cirrhotic and 460 (82.6%) were treatment-experienced. Child Pugh was A=85.4%, B=12.9%, C=1.7%. Genotype distribution was as follows: 387 GT1 (69.7%), 2 GT2 (0.4%), 72 GT3 (13.0%), 93 GT4 (16.8%) and 1 GT6 (0.1%), 7 missing data. Median HCV-RNA was 6.10 logUI/mL (1.08-7.97).
Combined antiretroviral therapy included: NRTI in 88%, PI in 36.4%, NNRTI in 23% and INI in 63.7% of the patients. Baseline median CD4 count was 551/mm^3 (0-1922). HIV-RNA was undetectable in 505 patients (98.4%).
RBV was added to DCV+SOF in 67 patients (12.0%). Treatment duration was 24W in 478 (85.1%) and 12W in 84 (14.9%) patients.
Overall, SVR4 was obtained in 90.2 % (148/164) and SVR12 in 95.9% (94/98) of the cases
Among patients treated with DCV+SOF for 12 or 24 weeks, 96.0% (24/25) and 95.1% (58/61) achieved an SVR12 respectively compared to 100% (6/6) and 100% (6/6) for patients receiving DCV+SOF+RBV. Neither duration of treatment nor cirrhosis status and genotype influenced the rate of SVR12 (Table 1).

Treatment duration			Genotype status					
	12 weeks	24 weeks	GT1 (all)	GT1 cirrhotic	GT3 (all)	GT3 cirrhotic	GT4 (all)	GT4 cirrhotic
SVR4 N= 164	41/49 (83.7%)	107/115 (93.0%)	104/116 (89.7%)	80/87 (92.0%)	13/15 (86.7%)	12/13 (92.3%)	26/28 (92.9%)	16/17 (94.1%)
SVR12 N= 98	30/31 (96.8%)	64/67 (95.5%)	66/68 (97.1%)	52/53 (98.1%)	11/11 (100%)	11/11 (100%)	14/15 (93.3%)	10/11 (90.9%)

[Efficacy of DCV+SOF±RBV regimens in HIV/HCV co-inf]

Treatment discontinuations occurred in 17 patients (3%) and were related to an adverse event (n=5), death (n=4, not related to treatment), patient decision (n=3), contra-indication (n=3) unknown reason (n=1) and patient lost to follow-up (n=1).
Conclusions: DCV+SOF±RBV regimen was well tolerated and demonstrated high SVR12 rate in HIV-HCV co-infected patients with advanced liver disease.

TUAC01 HIV and Behavioral Economics: Where the Money Is?

TUAC0101LB

Impact of conditional cash incentives on HSV-2 and HIV prevention in rural South African high school students: results of the CAPRISA 007 cluster randomized controlled trial

Q. Abdool Karim[1,2], K. Leask[1], A. Kharsany[1], H. Humphries[1], F. Ntombela[1], N. Samsunder[1], C. Baxter[1], J. Frohlich[1], L. van der Elst[3], S. Abdool Karim[1,2]
[1]CAPRISA, Durban, South Africa, [2]Columbia University, Epidemiology, New York, United States, [3]MIET Africa, Durban, South Africa

Background: Young women in southern Africa have high rates of sexually transmitted infections, including herpes simplex virus type-2 (HSV-2) and HIV. We investigated whether conditional cash incentives (CCIs) reduced the incidence of HSV-2 and HIV in rural high school students in South Africa.
Methods: An open-label, matched-pair, cluster randomised controlled trial (CAPRISA 007) was undertaken in 3,217 consenting male (n=1,517) and female (n=1,700) grade 9 and 10 students. A locally-developed HIV prevention program, *"My Life! My Future!"*, was actively implemented in all 14 schools. Seven schools (n=1,592 students) were randomly assigned to receive, in addition, cash incentives (maximum of $175 over 2 years) for fulfilling any combination of 4 conditions; annual HIV testing, performance in school tests, participation in "*My Life! My Future!*", and a written report on their community involvement project. HSV-2 and HIV serology was undertaken at baseline, 12 months and 24 months. In the intent-to-treat analysis, incidence rate ratios (IRRs) and p-values were adjusted for the matched-pair cluster design.
Results: HSV-2 prevalence at baseline was 9.0% in CCI schools and 7.3% in control schools. During follow-up, there were 319 new HSV-2 infections, with an incidence rate of 6.2 per 100 person-years in CCI schools compared to 8.7 per 100 person-years in control schools (IRR=0.70, 95%CI: 0.57 - 0.86; p=0.007). HSV-2 incidence was 7.1 per 100 person-years in the 760 students who received < $65, 6.3 per 100 person-years in the 304 students who received $65-$95, and 4.2 per 100 person-years in the 265 students who received >$95 (Trend test, p=0.12). The lower-than-anticipated overall HIV incidence rate of 1.6 per 100 person-years was similar in both groups of schools (IRR=1.26, 95%CI: 0.66 - 2.39; p=0.419). A four-fold larger study would be required for 80% power to observe a 30% HIV incidence reduction.
Conclusions: CCI schools had 30% lower HSV-2 incidence. Students who received larger cash incentives had lower HSV-2 incidence rates. The impact of CCI on HIV could not be adequately assessed as incidence was lower than expected, likely due to HIV lowering effects of both study-initiated and background community HIV interventions.

TUAC0102

The effect of conditional economic compensation and lottery-based rewards on uptake of medical male circumcision in Kenya: a randomized trial

H. Thirumurthy[1,2], S. Masters[1], S. Rao[3], K. Murray[2], E. Omanga[3], K. Agot[3]
[1]University of North Carolina at Chapel Hill, Department of Health Policy and Management, Chapel Hill, United States, [2]University of North Carolina at Chapel Hill, Carolina Population Center, Chapel Hill, United States, [3]Impact Research and Development Organization, Kisumu, Kenya
Presenting author email: hthirumu@email.unc.edu

Background: Low uptake of male circumcision has been a major challenge to scaling-up and maximizing the HIV prevention impact of voluntary medical male circumcision (VMMC) services in eastern and southern Africa. There is limited evidence on effective demand creation strategies for VMMC that address reported barriers to male circumcision. Building on insights from behavioral economics, we assessed whether providing compensation for opportunity costs of time or lottery-based rewards can increase VMMC uptake among men in Nyanza Province, Kenya.
Methods: Uncircumcised men aged 21-39 years were provided information on VMMC services and randomized in 1:1:1 ratio to two intervention groups or a control group. One intervention group was offered compensation of US$12.50 conditional on VMMC uptake. Compensation was provided in the form of food vouchers valid at shops in the study region. A second intervention group was offered the opportunity to participate in a lottery with high-value prizes upon undergoing circumcision. The primary outcome was VMMC uptake within 3 months.
Results: Among 903 participants enrolled, those randomized to receive compensation of US$12.50 had the highest VMMC uptake (8.4%, 26/308), followed by those receiving lottery-based rewards (3.3%, 10/302) and those in the control group (1.3%, 4/299). Logistic regression analysis showed that compared to the control group, the US$12.50 group had significantly higher VMMC uptake (Adjusted odds ratio (AOR) 7.1; 95% CI 2.4-20.8). Participants in the lottery-based rewards group were not significantly more likely to become circumcised than participants in the control group (AOR 2.5; 95% CI 0.8-8.1). The effect of providing compensation

of US$12.50 was largest among participants who were contemplating circumcision at the time of enrollment.

Conclusions: Providing conditional economic compensation was effective in increasing circumcision uptake among men in a short time period. The results are consistent with studies showing that small incentives can modify health behaviors by addressing barriers such as opportunity costs of time and present-biased decision-making. Contrary to findings from studies in high-income countries, lottery-based rewards did not significantly increase circumcision uptake. Testing economic interventions in other settings and applying them to different HIV behaviors can be useful for assessing the generalizability of the findings.

TUAC0103

Estimating the population-level effect of homelessness on HIV viral suppression among people who use drugs: an observational study

B.D.L. Marshall[1], B. Elston[1], S. Dobrer[2], J. Montaner[2,3], T. Kerr[2,3], E. Wood[2,3], M.-J. Milloy[2,3]
[1]Brown University, Department of Epidemiology, Providence, United States, [2]British Columbia Centre for Excellence in HIV/AIDS, Vancouver, Canada, [3]University of British Columbia, Department of Medicine, Vancouver, Canada
Presenting author email: brandon_marshall@brown.edu

Background: Homelessness has been identified as an important structural barrier to effective antiretroviral therapy (ART) utilization among HIV-infected people who use drugs (PWUD). However, the potential effect of reducing homelessness on viral suppression rates at the community level is unknown. We used an imputation-based marginal modeling approach to estimate change in the prevalence of viral suppression among HIV-infected PWUD, if homelessness were eliminated from the population.

Methods: We used data from a cohort study of community-recruited PWUD in Vancouver, Canada. Of note, HIV/AIDS treatment and care is provided free of charge in this setting. Persons were eligible to participate if they were HIV-infected and used an illicit drug in the month prior to enrollment. We assessed self-reported baseline housing status in the past six months. Viral suppression was defined as HIV RNA viral load < 50 copies per mm^3 at first study visit. We estimated the effect of homelessness on viral suppression using modified-Poisson regression, adjusting for demographics, socioeconomic characteristics, trauma history, depression, addiction treatment, and other confounders. Then, a marginal modeling approach was applied. First, we imputed the outcome probability for each individual while manipulating the exposure (homelessness) to never exposed, and then averaged these probabilities across the population. Bootstrapping was conducted to calculate 95% confidence limits.

Results: Of 718 eligible individuals enrolled between January 2005 and December 2013, the majority was male (66%), white race/ethnicity (55%), and had a history of injection drug use (94%). At baseline, 230 (32%) reported homelessness. The prevalence of viral suppression was 35% (95%CL: 31%-38%). Adjusted marginal models estimated a 14% relative increase (95%CL: 10%-24%) in viral suppression prevalence in the entire sample—to 40% (95%CL: 36%-45%)—if all homeless individuals were housed. Among those homeless at baseline, adjusted marginal models estimated that eliminating this exposure would increase viral suppression from 19% (95%CL: 14%-24%) to 37% (95%CL: 33%-42%).

Conclusions: Reducing homelessness among HIV-infected PWUD could have significant population-level benefits on outcomes in the HIV care continuum. Low threshold shelter and housing support programs should be considered as key components in comprehensive strategies to increase population-level viral suppression for people who use drugs.

TUAC0104

Applying principles of behavioral economics to ART adherence: discount rate, future expectations, and intrinsic motivation for adherence among ART initiates in Shinyanga region, Tanzania

N. Czaicki[1], P. Njau[2], S. Bautista-Arredondo[3], O. Simba[4], N. Padian[1], S. McCoy[5]
[1]University of California Berkeley, Epidemiology, Berkeley, United States, [2]Ministry of Health and Social Welfare, PMTCT, Dar es Salaam, Tanzania, United Republic of, [3]National Institute of Public Health, Department of Health Economics, Cuernavaca, Mexico, [4]Regional Medical Office, Shinyanga, Tanzania, United Republic of, [5]University of California Berkeley, Berkeley, United States
Presenting author email: nczaicki@berkeley.edu

Background: Behavioral economic theory suggests that understanding motivations and future preferences of people living with HIV infection (PLHIV) can inform the development of interventions supporting adherence to treatment and care. For example, PLHIV with high levels of intrinsic motivation to adhere to ART may require less external motivation, such as cash incentives. In addition, PLHIV who disproportionally value the present and heavily discount the future may be less likely to adhere to ART, a behavior with future benefits and present costs. We measured these constructs among antiretroviral therapy (ART) initiates at four HIV care and treatment clinics in Shinyanga Region, Tanzania.

Methods: We analyzed data collected from in-person interviews between December 2013 and December 2014 with food-insecure, HIV-infected adults who initiated ART in the past 90 days. Temporal discount rate, the rate at which individuals discount future costs and benefits, was measured using a bidding process to assess the acceptable percent increase of a hypothetical monetary offer they would receive in three months compared to a smaller amount received today. Future health expectations were assessed for one year from now, and intrinsic motivation for ART adherence was measured as the mean score (range: 0-3) on a Likert-scale using questions in the Treatment Self-Regulation Questionnaire.

Results: Overall, 511 food-insecure recent ART initiates were interviewed (mean age: 37, 64% female). Nearly all (99%) expected their health to be somewhat (55%) or much better (44%) one year from now. Excluding those who initiated treatment on the same day of the interview, mean internal motivation was 2.75 (standard deviation 0.36; n=423). Temporal discount rates (n=489) fell into four ranges: < 50% (8%), 50-100% (37%), 101-200% (54%), and >200% (2%).

Conclusions: These data indicate high levels of both intrinsic motivation for ART adherence and optimism towards future health among food-insecure ART initiates in Tanzania, suggesting that interventions designed to strengthen and sustain intrinsic motivation may be appropriate. The high discount rates indicate a greater focus on the present; thus, interventions aiming to overcome the short-term cost barriers to adherence and care (e.g. time, transport, competing needs) in order to achieve future gains may be highly effective among this population.

TUAC0105

Negative impact of South Africa's disability grants on HIV/AIDS recovery

N. Haber[1], F. Tanser[2], K. Herbst[2], D. Pillay[2], T. Bärnighausen[1,2],
Wellcome Trust Africa Centre for Health and Population Studies
[1]Harvard School of Public Health, Global Health and Population, Boston, United States, [2]Wellcome Trust Africa Centre for Health and Population Studies, Health Systems and Impact Evaluation, Mtubatuba, South Africa
Presenting author email: nhaber@mail.harvard.edu

Background: The South African disability grant (DG) has been theorized to incentivize poor recovery by tying grant receipt to AIDS sickness. Prior to 2008, many official guidelines defined qualifying AIDS disability as a CD4 count below 200mmHg, and this recommendation persists unofficially. We make two predictions:
1) The population distribution of CD4 counts will have an observable discontinuity with excess mass just below the CD4 qualification threshold of 200mmHg, and;
2) individuals receiving the grant will recover more slowly around this threshold than those who do not, due to threat of grant loss.

Methods: The analysis utilizes a two-stage panel regression methodology to absorb individual trends and identify differential recovery rates around the CD4 threshold of 200mmHg. The dataset for this analysis utilizes the Africa Centre Demographic Information System (ACDIS), an open cohort health and demographic monitoring program consisting mainly of annual surveys, individually matched with an HIV-focused clinical informatics system in rural KwaZulu-Natal, South Africa. Data are restricted to HIV+ individuals from 2004-2011 who have at least four observed CD4 counts, with at least one observed CD4 count above and below 200mmHg.

Results: The cohort for this analysis consists of 11,160 observations from 1,450 individuals. The distribution of CD4 counts shows clear excess mass just below a CD4 count of 200mmHg, with more pronounced for CD4 counts occurring in 2008 or earlier. Among observations around the threshold, the rate of recovery of those receiving DGs is 0.23mmHg/year lower (p=.020) than that of those not receiving DGs, controlling for individual recovery trends, age, education, time, household assets, and employment. Stratifying on gender, the effect is seen much stronger among women with a differential recovery rate of 58mmHg/year (p=.018). The effect is significantly larger for observations in 2008 or earlier.

Conclusions: This study finds that the South African disability grant system resulted in a modest but significant manipulation of CD4 counts in order to qualify for the grant. While policy changes have likely reduced the severity of the effect, policy makers should ensure that incentives from grants are aligned with health incentives to reduce poor outcomes, infectivity, and drug resistance.

TUAC0106LB

HPTN 068 conditional cash transfer to prevent HIV infection among young women in South Africa: results of a randomized controlled trial

A. Pettifor[1,2], C. MacPhail[3], A. Selin[4], X. Gomez-Olivé[5], J. Hughes[6], R. Wagner[5], W. Mabuza[5], I. Mokoena[5], S. Eshleman[7], E. Piwowar-Manning[7], R. Twine[5], A. Julien[4], C. Marcus[8], P. Andrew[9], J. Wang[6], Y. Xing[6], L. McKinstry[6], E. Hamilton[9], Y. Agyei[7], S. Allison[10], P. Sato[11], E. Townley[12], S. Tollman[5], K. Kahn[5], HPTN 068 Study Team
[1]University of North Carolina at Chapel Hill, Epidemiology, Chapel Hill, United States, [2]University of the Witwatersrand, School of Public Health, Johannesburg, South Africa, [3]University of New England, Armindale, Australia, [4]University of North Carolina, Carolina Population Center, Chapel Hill, United States, [5]University of the Witwatersrand, MRC/Wits Rural Public Health and Health Transitions Unit, School of Public Health, Johannesburg, South Africa, [6]University of Washington, Seattle, United States, [7]Johns Hopkins University, School of Medicine, Baltimore, United States, [8]University of North Carolina, School of Medicine, Chapel Hill, United States, [9]FHI360, Durham, United States, [10]National Institutes of Health, National Institutes of Mental Health, Division of AIDS Research, Rockville, United States, [11]National Institutes of Health, Office of AIDS Research, Bethesda, United States, [12]National Institutes of Health, National Institutes of Allergies and Infectious Diseases, DAIDS, Rockville, United States

Background: Young women in South Africa face a particularly high risk of HIV infection. Structural factors such as schooling, socio-economic status (SES) and financial dependence on partners contribute to this risk. Cash transfers have shown promise in reducing HIV risk in young women by addressing these factors. HPTN 068 is the first randomized trial to examine the impact of conditional cash transfers on HIV incidence among young women.
Methods: HPTN 068 is a phase III individually randomized trial to assess the impact of a conditional cash transfer on the acquisition of HIV among South Africa young women. Young women and their parent/guardian in the intervention arm received a monthly cash transfer conditional on 80% school attendance, which was verified using school attendance rosters. The intervention ran from April 2011 to March 2015.
Participants enrolled in the study were aged 13-20, in high school, not married or pregnant, and resident in the Agincourt Health and Demographic Surveillance System (AHDSS) site in rural Mpumalanga Province. Participants were seen at baseline, then annually for up to three follow-up visits, where HIV and HSV-2 testing were conducted and an interview was completed using Audio Computer Assisted Self Interviewing (ACASI). The interview assessed sexual behavior including partner specific details, schooling, mental health, SES and gender power dynamics. Participants were tested for HIV infection using two HIV rapid tests with Western blot confirmation. Stored samples from all participants at all visits were also tested at the HPTN Laboratory Center using assays that included an HIV antigen/antibody test and a qualitative HIV RNA test. To compare treatment arms, time to first HIV detection was analyzed using a Cox proportional hazards model
Results: We will present the impact of the conditional cash transfer on HIV incidence, unprotected sex, pregnancy, age difference with partners, number of sex partners, transactional sex, age of sexual debut and school attendance.
Conclusions: Cash transfers are increasingly being included as part of the package of prevention services that should be offered to young women to reduce HIV risk in sub-Saharan Africa. The evidence from this RCT will have important implications for HIV prevention policy and practice.

TUAC02 PrEP: Demonstration for Implementation

TUAC0201

The safety of HIV pre-exposure prophylaxis in the presence of hepatitis B infection

M.M. Solomon[1,2], M. Schechter[3], A.Y. Liu[4], V. McMahan[2], J.V. Guanira[5], R.J. Hance[2], S. Chariyalertsak[6], K.H. Mayer[7], R.M. Grant[2,8], iPrEx Study Team
[1]University of California, San Francisco, Division of Infectious Diseases, San Francisco, United States, [2]Gladstone Institutes of Virology and Immunology, San Francisco, United States, [3]Projeto Praça Onze, Hospital Escola São Francisco de Assis, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil, [4]Bridge HIV, San Francisco Department of Public Health, San Francisco, United States, [5]Investigaciones Medicas en Salud, Lima, Peru, [6]Research Institute for Health Sciences and Department of Community Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand, [7]Fenway Institute, Fenway Health, Beth Israel Deaconess Medical Center, and Harvard Medical School, Boston, United States, [8]University of California, San Francisco, San Francisco, United States

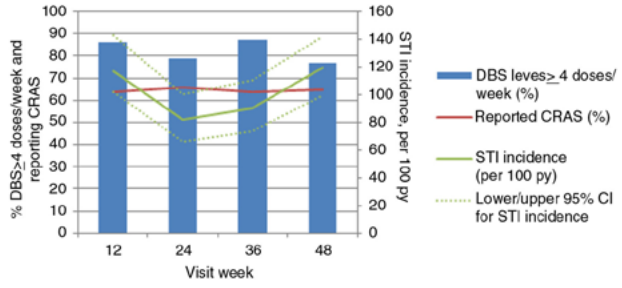
Background: Pre-exposure prophylaxis (PrEP) with daily oral FTC/TDF prevents HIV infection and is safe, but concern has been raised that PrEP could cause hepatitis B virus (HBV)-associated flares when discontinued by people with HBV infection, particularly among individuals with cirrhosis. The safety and feasibility of providing HIV PrEP in the setting of HBV infection was evaluated in the iPrEx study.
Methods: The iPrEx study randomized 2499 HIV-negative men and transgender women who have sex with men to once-daily oral FTC/TDF versus placebo. Hepatitis serologies and transaminases were obtained at screening and at PrEP discontinuation. Participants with a reactive hepatitis B surface antigen were enrolled if there was no clinical evidence of cirrhosis and transaminases were < 2.5 fold the ULN. HBV DNA was assessed by PCR and drug resistance was assessed by population sequencing (Abbott labs) at least once for individuals with evidence of HBV DNA. Vaccination was offered to individuals susceptible to HBV.
Results: Among 2499 enrolled participants, 12 (0.5%; including 6 randomized to FTC/TDF) had chronic HBV infection. After stopping study drug, 5 of 6 in the active arm had LFTs performed at follow-up. LFTs remained within normal limits at post-stop visits except for a Grade 1 elevation in 1 participant at post-stop week 12 (ALT=90, AST=61). There was no evidence of flares. PCR of stored samples showed that 4 had evidence of acute HBV infection at enrollment (2 in the active arm). Both had evidence of grade 4 transaminase elevations by week 4 with subsequent resolution. Overall, there was no evidence of TDF or FTC resistance among tested genotypes. Of 1633 eligible for vaccination, 1587 (97.2%) received at least one vaccine and 1383 (84.7%) received the complete series. Anti-HBs detection was 44.4% after one, 74.5% after 2, and 86.9% after 3 doses.
Conclusions: PrEP can be safely offered to persons with HBV infection if there is no evidence of cirrhosis or substantial transaminase elevation. As information is limited and treatment for HBV is complex, referral to a specialist is appropriate when available. HBV vaccination rates at screening were low globally, yet uptake and efficacy were high when offered.

TUAC0202

Adherence, sexual behavior and HIV/STI incidence among men who have sex with men (MSM) and transgender women (TGW) in the US PrEP demonstration (Demo) project

A. Liu[1,2], S. Cohen[1,2], E. Vittinghoff[2], P. Anderson[3], S. Doblecki-Lewis[4], O. Bacon[2], W. Chege[5], R. Elion[6], S. Buchbinder[1,2], M. Kolber[4], Demo Project Study Group
[1]San Francisco Department of Public Health, San Francisco, United States, [2]University of California, San Francisco, United States, [3]University of Colorado, Aurora, United States, [4]University of Miami, Miami, United States, [5]National Institutes of Health, Bethesda, United States, [6]Whitman-Walker Health, Washington, DC, United States
Presenting author email: albert.liu@sfdph.org

Background: Pre-exposure prophylaxis (PrEP) has demonstrated efficacy in reducing HIV acquisition in MSM and TGW. Little is known about adherence, sexual behavior, and HIV/STI incidence among those who elect to take PrEP in real-world settings.
Methods: The Demo Project is the first US multi-site open-label study assessing PrEP delivery in municipal STD (San Francisco, Miami) and community-health (Washington, DC) clinics. HIV-uninfected MSM/TGW were offered 48 weeks of PrEP. Tenofovir-diphosphate levels were measured in dried blood spots (DBS) in a random sample of participants (pts). Correlates of adherence were assessed using multivariable logistic regression. Sexual behaviors, PrEP discontinuations, and HIV/STI incidence are described.
Results: From 9/2012-1/2014, 557 pts enrolled, with 83% retained for the final visit (468.8 person-years (py)). Longitudinal drug levels, sexual behavior, and STI incidence are shown (figure). Among 147 pts with DBS testing, 65% had drug levels consistent with taking ≥4 doses/week at all visits, 3% always had DBS levels <2 doses/week, and 32% had an inconsistent pattern. Black pts, being self-referred to the PrEP program, and having a greater number of condomless anal sex (AS) partners were independently associated with DBS ≥4 doses/week (all p<0.05). Median AS partners in the past 3 months declined from baseline to week 48 (5 to 4, P<0.0008). Two-thirds reported condomless receptive AS (CRAS) at baseline, which remained stable during follow-up (p=0.96). Twenty pts chose to stop PrEP due to low self-perceived HIV risk, however 65% of these pts reported CRAS in the prior 3-6 months. Three participants were acutely infected at enrollment, and one seroconverted during follow-up (HIV incidence 0.21/100 py). This subject had DBS <2 doses/week at all prior visits. Overall, 27.5% had early syphilis, GC, or CT at screening, and 38% had ≥1 STI during follow-up; STI incidence was high (47.9, 42.8, and 12.6/100 py for CT, GC, and syphilis) but did not increase over time (p=0.87).



[Figure. Adherence, risk behaviour, and STI incidence over time in the demo project]

Conclusions: PrEP adherence was high and HIV incidence was low in this cohort at ongoing high sexual risk for HIV. STIs were common during PrEP use, highlighting the importance of screening and treatment. Strategies for counseling on appropriate PrEP discontinuation are warranted.

TUAC0203

Characteristics and oral PrEP adherence in the TDF2 open-label extension in Botswana

F. Henderson[1], A. Taylor[1], L. Chirwa[2], T. Williams[1,3], C. Borkowf[1], M. Kasonde[4], R. Mutanhaurwa[4], O. Matlhaba[4], K. Hageman[1], P. Casillas[4]
[1]Centers for Disease Control and Prevention, Atlanta, United States, [2]Centers for Disease Control and Prevention, Francistown, Botswana, [3]ICF Macro, Atlanta, United States, [4]Centers for Disease Control and Prevention, Gaborone, Botswana
Presenting author email: inh3@cdc.gov

Background: The TDF2 Study was a randomized, double-blind, placebo-controlled trial of daily oral coformulated tenofovir disoproxil fumarate (300 mg)/emtricitabine (200 mg) (TDF/FTC) for pre-exposure prophylaxis of HIV infection (PrEP) among young heterosexual adults in Gaborone and Francistown, Botswana. TDF2 completed follow-up in 2011, demonstrating 62% overall protective efficacy.
We describe final results of a 12-month open-label extension (OLE).
Methods: Between February and May 2013, former TDF2 participants were screened and offered 30-day supplies of TDF/FTC for up to 12 months. OLE exclusion criteria included HIV infection, pregnancy/breastfeeding, and abnormal serum creatinine clearance or phosphorus. Demographic and sexual behavior data were collected at baseline. Dual rapid fingerstick HIV testing, sexual behavior questionnaires, and self-reported adherence measures were conducted monthly. Dried blood spots (DBS) were collected monthly.
Tenofovir levels were measured from DBS for a subset of 30 randomly selected participants at months 1, 3, 6, 9 and 12.
Results: Of 1219 TDF2 participants, 736 were contacted, and 229 (Male: 55.5%) were eligible and started drug. 71.2% were single, and 23.9% were married/cohabitating. 60.3% of participants completed at least 10 monthly visits. Across all visits, 71.2% reported 1 sex partner in the prior 30 days; 8.7% reported 2 partners, and 2.4% reported ≥ 3 partners. For the prior three days, 87.8% reported taking TDF/FTC daily, while 5.5% reported taking it 1-2 times and 6.7% reported taking none. Overall, 58.3% reported 'very good' adherence in the prior 30 days, and 32.3% reported 'good' adherence.
Of the 30 participants (Male:77%) selected for DBS testing, the overall proportion with detectable mean tenofovir levels (>25ng/mL) was 94%. At months 1, 3, 6, 9, and 12, the proportion with detectable mean tenofovir levels were 93%, 93%, 100%, 93%, and 90%, respectively.
After starting drug, no HIV infections were observed during the study.
Conclusions: In this open-label study of TDF/FTC for oral PrEP, we observed high self-reported 3-day medication adherence, high percentage of detectable DBS tenofovir levels, and no HIV infections. These findings lend support to efforts to expand availability of PrEP in the context of generalized epidemics in resource-limited settings. Further work is needed to define longer-term adherence for such populations.

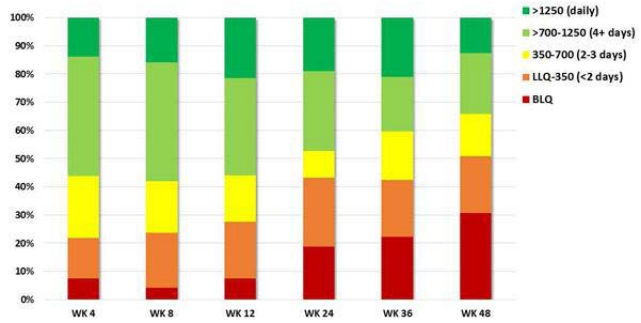
TUAC0204LB

An HIV pre-exposure prophylaxis (PrEP) demonstration project and safety study for young men who have sex with men in the United States (ATN 110)

S. Hosek[1], B. Rudy[2], R. Landovitz[3], B. Kapogiannis[4], G. Siberry[4], N. Liu[5], B. Rutledge[5], J. Brothers[1], J. Rooney[6], C.M. Wilson[7], Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN)
[1]Stroger Hospital of Cook County, Psychiatry, Chicago, United States, [2]New York University Medical Center, New York, United States, [3]University of California Los Angeles, Los Angeles, United States, [4]NICHD/MPIDB, Bethesda, United States, [5]Westat, Rockville, United States, [6]Gilead Sciences, Foster City, United States, [7]University of Alabama at Birmingham, Birmingham, United States

Background: Young men who have sex with men (YMSM), particularly racial/ethnic minority YMSM, are a key population for implementation of domestic PrEP interventions. This open-label PrEP study examined uptake and adherence to PrEP and assessed sexual risk behavior among a diverse sample of YMSM in 12 US cities.
Methods: ATN110 combined PrEP with evidence-based behavioral risk reduction interventions along with frequent sexual health and adherence promotion counseling. Eligible participants were 18-22 year old HIV-uninfected MSM who reported HIV transmission risk behavior in the past 6 months. Participants were recruited and screened for preliminary eligibility through venue-based outreach, community presentations, and online advertising. Laboratory screening determined final eligibility.
Study visits occurred at baseline, monthly through week 12, then quarterly through week 48. Dried blood spots (DBS) were serially collected for the quantification of tenofovir diphosphate (TFV-DP) blood levels.
Results: Between March and September 2013, 2186 individuals were approached, 277 (13%) were preliminarily eligible, and 200 were enrolled (mean age=20.2; 54.5% Black, 26.5% Latino). Eleven (4%) had undiagnosed HIV infection at screening and 2 acute HIV infections were diagnosed at baseline. Diagnosis of STIs at baseline was high (22%) and remained high across visits. Most participants (98%) chose to take PrEP. Figure 1 shows TFV-DP levels. At week 4, 56% of participants had TFV-DP levels consistent with ≥4 pills/week. By week 48, 34% of participants had TFV-DP levels consistent with ≥4 pills/week, with a noticeable drop-off occurring at Week 24. Four HIV seroconversions occurred on study (3.29/100 person-years); all had TFV-DP BLQ at diagnosis. Condomless sex was reported by >80% of participants throughout the study and condomless anal sex with last partner was associated with higher TFV-DP levels.

Tenofovir diphosphate levels (fmol/punch) and PrEP dosing estimates as measured by dried blood spot assay



[Figure 1]

Conclusions: ATN110 enrolled a diverse sample of YMSM vulnerable to HIV. PrEP uptake was high with the majority achieving protective drug levels during initial monthly visits. As visits decreased in frequency, so did adherence, while reported sexual risk behavior remained constant.
Given the frequency of STI diagnoses, HIV infections may have been higher without PrEP. YMSM in the US may need access to PrEP in youth-friendly settings with tailored adherence support and potentially augmented visit schedules.

TUAC0205LB

Pre-exposure prophylaxis (PrEP) uptake and associated factors among MSM and TGW in the PrEP Brasil demonstration project

B. Hoagland[1], V.G. Veloso[2], R.B. De Boni[2], J.V. Madruga[3], E.G. Kallas[4], N.M. Fernandes[2], R.I. Moreira[2], A.Y. Liu[5], B. Grinsztejn[2], PrEP Brasil Study Team
[1]Fundação Oswaldo Cruz, IPEC, Rio de Janeiro, Brazil, [2]Fiocruz, Rio de Janeiro, Brazil, [3]CRT, São Paulo, Brazil, [4]USP, São Paulo, Brazil, [5]Bridge HIV | San Francisco Department of Public Health, San Francisco, United States

Background: In Brazil, men who have sex with men (MSM) and transgender women (TGW) are the populations most heavily affected by the AIDS epidemic. Although the WHO recommends PrEP for these populations, the feasibility and interest in this prevention strategy in real world settings in low and middle-income countries are unknown. This study aims to describe PrEP uptake and associated factors in Brazil.
Methods: PrEP Brasil is a demonstration project to assess the feasibility of implementing PrEP provided at no cost to high risk MSM and TGW within the Brazilian public health system. The project was advertised through social and other media. Participants were assessed for PrEP eligibility at FIOCRUZ-RJ, CRT-SP and USP-SP. At USP, 100% participants were self-referred, while at Fiocruz and CRT they were either self-referred or assessed for participation during HIV-testing or post-exposure prophylaxis provision. Predictors of PrEP uptake were assessed using a Poisson regression model.
Results: Of 986 MSM/TGW approached between April/2014 - April/2015, 798 were potentially eligible and 409 were enrolled. PrEP uptake was 51.25%. Median age at enrollment was 29 years (IQR 25-35); 93.5% had ≥12 years of education; 83.9%, 8.8% and 5.9% identified themselves as homosexual, bisexual or TGW, respectively (Table); syphilis prevalence, rectal *Chlamydia* and *Gonorrhea* detection were 21.3%, 8.2% and 4.7%, respectively. In multivariate analysis, factors associated with PrEP uptake were: recruitment at CRT-SP (aRR 1.27; 95% CI 0.99-1.62) or USP-SP (aRR 1.72; 95% CI 1.33-2.24) vs. FIOCRUZ; having a steady partner (aRR 1.45, 95% CI 1.18-1.78); having an HIV-test within the last 12 months (aRR 1.33, 95%CI 1.01-1.74); prior PrEP awareness (aRR 1.27, 95%CI 1.0-1.59); and having ≥ 2 male condomless anal sex partners within the last 12 months (aRR 1.65, 95% CI 1.32-2.05).
Conclusions: This is the first PrEP demonstration project for MSM and TGW in a middle-income country. Overall, PrEP uptake was high. The higher uptake among those at higher risk and with an existing awareness of PrEP emphasizes the importance of establishing strategies to improve HIV risk perception and PrEP awareness in the MSM and TGW communities in Brazil.

	Approached (1) N(%)	Potentially Eligible (2) N(%)	Included (3) N(%)	Declined(4) N(%)	Percent of PrEP uptake*	p-value**
Overall	986	798	409	365	51.25	
Site location (5)						<0.001
FIOCRUZ	622 (63.08)	455 (57.02)	175 (42.79)	262 (77.26)	38.46	
CRT-SP	225 (22.82)	216 (27.07)	135 (33.01)	57 (15.62)	62.5	
USP-SP	139 (14.1)	127 (15.91)	99 (24.21)	26 (7.12)	77.95	
Age						0.26
18-25 years	335 (33.98)	266 (33.33)	127 (31.05)	128 (35.07)	47.74	
26-35 years	435 (44.12)	358 (44.86)	189 (46.21)	165 (45.21)	52.79	
36-45 years	160 (16.23)	124 (15.54)	62 (15.16)	57 (15.62)	50	
>45 years	56 (5.68)	50 (6.27)	31 (7.58)	15 (4.11)	62	
Sexual Identity						0.04
Homosexual	823 (83.55)	658 (82.56)	343 (83.86)	293 (80.49)	52.13	
Bisexual	99 (10.05)	87 (10.92)	36 (8.8)	47 (12.91)	41.38	
Transgender woman	44 (4.47)	36 (4.52)	24 (5.87)	14 (3.85)	66.67	
Other	19 (1.93)	16 (2.01)	6 (1.47)	10 (2.75)	37.5	
Color/Race						0.05
White	455 (46.15)	399 (50)	219 (53.55)	161 (44.11)	54.89	
Non-white	531 (53.85)	399 (50)	190 (46.45)	204 (55.89)	47.62	
Schooling						0.06
<12 years	89 (9.03)	66 (8.27)	26 (6.36)	42 (11.51)	39.39	
>12 years	897 (90.97)	732 (91.73)	383 (93.64)	323 (88.49)	52.32	
Steady partner						<0.001
Yes	472 (47.87)	385 (48.25)	223 (54.52)	149 (40.82)	57.92	
No	514 (52.13)	413 (51.75)	186 (45.48)	216 (59.18)	45.04	
Perceived likelihood of getting HIV in the next year						<0.001
0-25%	569 (57.71)	437 (54.76)	189 (46.21)	237 (64.93)	43.25	
50-100%	417 (42.29)	361 (45.24)	220 (53.79)	128 (35.07)	60.94	
Previous HIV test (last 12 months)						<0.001
Yes	657 (66.63)	575 (72.06)	334 (81.66)	219 (60)	58.09	
No	329 (33.37)	223 (27.94)	75 (18.34)	146 (40)	33.63	
Prior PrEP awareness						<0.001
Yes	594 (60.43)	498 (62.64)	296 (72.55)	183 (50.41)	59.44	
No	389 (39.57)	297 (37.36)	112 (27.45)	180 (49.59)	37.71	
# Male condomless anal sex partners (last 12 months)						<0.001
<2	512 (51.93)	370 (46.37)	143 (34.96)	222 (60.82)	38.65	
2 or more	474 (48.07)	428 (53.63)	266 (65.04)	143 (39.18)	62.15	
Anal sex with HIV-positive partners(12 months)						<0.001
Yes	346 (35.09)	324 (40.6)	208 (50.86)	104 (28.49)	64.2	
No	211 (21.4)	87 (10.9)	41 (10.02)	44 (12.05)	47.13	
I do not know	429 (43.51)	387 (48.5)	160 (39.12)	217 (59.45)	41.34	
STD diagnosis (12months)						0.01
Yes	138 (14)	128 (16.04)	79 (19.32)	39 (10.68)	61.72	
No	848 (86)	670 (83.96)	330 (80.68)	326 (89.32)	49.25	

(1) All individuals approached for pre-screening who were age 18 or older, male at birth, lived in the State, self-reported HIV negative status and reported having at least one male sexual partner in last 12 months

(2) Includes all individuals approached at pre-screening(1) who: a) reported 2 or more male condomless anal sex partners OR anal sex with HIV positive partner OR STD diagnosis in last 12 months ; and b) had a negative HIV test result

(3) Individuals who enrolled the study

4) Decline represents the sum of refusals in all steps. Individuals who agreed to participate but did not show up at the screen or enrollment visit were considered as declining

(5) FIOCRUZ-RJ: Fundação Oswaldo Cruz, located in Rio de Janeiro; CRT-SP: Centro de Referência e Treinamento em DST e AIDS, located in São Paulo; USP-SP: Universidade de São Paulo.

*% uptake= # included/# Potentially eligible at pre-screening

**chi-square for bivariate analyses

[Study population characteristics and PrEP uptake]

TUAC0206LB

Pharmacokinetics and pharmacodynamics of tenofovir reduced-glycerin 1% gel in the rectal and vaginal compartments in women: a cross-compartmental study with directly observed dosing

G. Nair[1], J.E. Justman[2], J. Piper[3], M. Marzinke[4], C. Hendrix[4], J. Dai[5], J. Pan[5], B. Galaska[6], L. Levy[7], J. Shwartz[8], I. McGowan[9], C. Dezutti[10]

[1]Centre for AIDS Programme of Research in South Africa (CAPRISA). University of KwaZulu Natal, Durban, South Africa, [2]Columbia University, ICAP at Columbia, New York, United States, [3]NIAID/DAIDS, Bethesda, United States, [4]Johns Hopkins University, Baltimore, United States, [5]FHCRC-SCHARP, Seattle, United States, [6]Microbicides Trial Network, Pittsburgh, United States, [7]FHI 360, Washington, United States, [8]CONRAD, Arlington, United States, [9]University of Pittsburgh, Magee-Womens Research Institute, Pittsburgh, United States, [10]Microbicide Trials Network, Pittsburgh, United States

Background: Tenofovir (TFV) gel, when used consistently as a vaginal microbicide, prevents HIV infection. As unprotected anal intercourse is prevalent amongst heterosexual women, data on TFV concentrations and anti-HIV activity in the rectal compartment following vaginal application, and vice versa, are needed.

Methods: MTN-014 is a phase 1 cross-over, randomized trial comparing the pharmacokinetics of TFV reduced-glycerin (RG) 1% gel following 14 days each of daily rectal versus vaginal directly observed dosing (DOD), with a 6-week washout period in between each phase. Vaginal and rectal tissue and fluid and blood samples were collected 24 hours after the end of each phase and analysed for TFV and TFV-diphosphate (TFV-DP) concentrations. Vaginal and rectal fluids were tested for HIV inhibition using a TZM-bl assay.

Results: Fourteen HIV-uninfected women, mean age 34 years, were enrolled at the Bronx Prevention Center in New York City and 13 completed all study procedures. Of the 392 expected doses, 91% were DOD, 2 (0.5%) were missed and the remaining doses were reported as used. Mean plasma TFV concentrations were similar after 14 days of either dosing route (Table). Rectal concentrations of TFV and TFV-DP were detectable after vaginal dosing in only 1/13 and 2/13 tissue samples, respectively, while vaginal concentrations of TFV and TFV-DP were detectable after rectal dosing in 6/14 and 3/14 samples, respectively. Rectal and vaginal dosing phases each resulted in markedly lower levels of tissue TFV and TFV-DP concentrations in the opposite compartment, with at least 1.7 log 10 differences between mean concentrations in the two compartments.

After vaginal dosing, inhibition of HIV increased by 42% in vaginal fluid, but no change was found in rectal fluid. No change in HIV inhibition in vaginal or rectal fluid was noted after rectal dosing.

Compartment	Vaginal Use Phase				Rectal Use Phase		
	Mean (standard deviation)	number of samples with detectable drug	Median, IQR		Mean (standard deviation)	number of samples with detectable drug	Median, IQR
Plasma							
TFV (ng/ml)	0.99(1.27)	10/14 (71%)	0.58 (0,1.31)		1.19 (1.74)	10/14 (71%)	0.82 (0,1.22)
Vaginal Tissue							
TVF (ng/mg)	45.8 (72.6)	12/13 (92%)	8.5 (1.0,44.8)		0.09 (0.12)	6/14 (43%)	0 (0,0.16)
TFV-DP (fmol/mg)	1945 (4105)	12/13 (92%)	166 (37,2377)		13 (30)	3/14 (21%)	0 (0,0)
Rectal Tissue							
TFV (ng/ml)	0.02 (0.06)	1/13 (8%)	0 (0,0)		12.2 (27.1)	12/14 (86%)	3.0 (0.7,10.9)
TFV-DP (fmol/mg)	10.48 (25.81)	2/13 (15%)	0 (0,0)		710 (1306)	10/14 (71%)	196 (0,550)

[Compartmental Pharmacokinetics of Tenofovir gel]

Conclusions: Cross-compartmental concentrations of TFV and TFV-DP were low in this study comparing rectal and vaginal DOD TFV RG 1% gel and pharmacodynamics activity was noted only in the vaginal fluid compartment. Whether these low tissue concentrations are protective remains to be determined.

TUAC03 MSM: The Global Perspective

TUAC0301

Worsen epidemic of early HIV infection among men who have sex with men in China: implication for real time action

J. Xu[1], W. Tang[2], H. Zou[1], T. Mahapatra[3], Q. Hu[1], G. Fu[4], Z. Wang[5], L. Lu[6], M. Zhuang[7], X. Chen[8], J. Fu[9], Y. Yu[1], J. Lu[1], Y. Jiang[1], W. Geng[1], X. Han[1], H. Shang[1]

[1]The First affiliated Hospital of China Medical University, Shengyang, China, [2]University of North Carolina, Project-China, Guangzhou, China, [3]University of California at Los Angeles, Epidemiology, Los Angeles, United States, [4]Jiangsu Provincial Center for Disease Control and Prevention, Nanjing, China, [5]Henan Provincial Center for Disease Prevention and Control, Zhengzhou, China, [6]Yunnan Provincial Center for Disease Prevention and Control, Kunming, China, [7]Shanghai Center for Disease Prevention and Control, Shanghai, China, [8]Hunan Provincial Center for Disease Prevention and Control, Changsha, China, [9]Shangdong Provincial Center for Disease Prevention and Control, Jinan, China

Presenting author email: xjjbeijing@gmail.com

Background: Recent upsurge of new HIV infections among men who have sex with men (MSM) is a major concern in China. Paucity of national-level information regarding the burden and predictors of this progressive epidemic of new infections called for a multi-centric, comprehensive investigation.

Methods: Mixed methods were used to recruit MSM (Engaged in sex with men (oral and/or anal) within the last one year, aged 18 years or older and agreed to provide written informed consent) from seven cities (Shanghai, Nanjing, Changsha, Zhengzhou, Ji'nan, Shenyang and Kunming) in different regions of China between 2012 and 2013. Early and established HIV infections were determined by Western Blot and BED HIV-1 capture enzyme immunoassay. Syphilis and herpes simplex virus-2 (HSV-2) were also tested. The study process and content were approved (No. 2011(36)) by the Ethics Committee of The First Affiliated Hospital of China Medical University.

Results: A total of 4496 eligible MSM were recruited. The majority was aged ≤35 years (77·5%), migrants (60·3%), never married (69·8%), and played receptive role in anal sex (70·5%). The HIV prevalence was 9·9%, and 41·9% were recently infected, with HIV incidence of 8·9/100 Person-Years. The prevalence of HSV-2 and syphilis were 12·5% and 8·5%, respectively. Early HIV infection was associated with having multiple male partners (aOR=1·4, 95%CI 1·1-1·9), recreational drug use (aOR=2·2, 95%CI 1·6-3·0), anal bleeding (aOR=2·1, 95%CI 1·4-3·0), circumcision experience (aOR=2·0, 95%CI 1·3-3·1), syphilis infection (aOR=2·8, 95%CI 1·9-4·3) and HSV-2 infection (aOR=2·3, 95%CI 1·5-3·3).

Conclusions: HIV epidemic among Chinese MSM was worsening with an alarming number of recently infected HIV patients along with high burden of STIs. High rate of early HIV infection is potentially resulting in progressive deterioration of the overall HIV epidemic among MSM

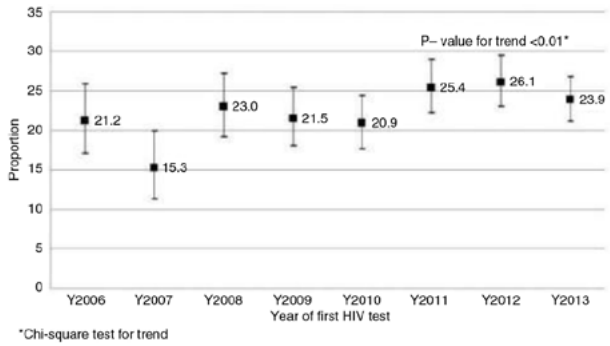
in China. Interventions specifically targeting high-risk MSM especially those having high-risk behaviors (especially multiple partners and recreational drug use), syphilis or HSV-2 infection and anal bleeding were urgently required for efficient control of HIV among MSM in China.

TUAC0302

Repeat HIV voluntary counseling and testing within one year among men who have sex with men, Bangkok, Thailand 2006-2013

W. Wimonsate[1], S. Pattanasin[1], A. Sriporn[1], P. Luechai[1], K. Satumay[1], N. Tippanonth[1], N. Promda[1], T. Holtz[1,2], A. Chitwarakorn[3], E. Dunne[1,2]
[1]Thailand MOPH - U.S. CDC Collaboration, HIV/STD Research Program, Nonthaburi, Thailand, [2]Centers for Disease Control and Prevention, Division of HIV/AIDS Prevention, Atlanta, United States, [3]Ministry of Public Health, Department of Disease Control and Prevention, Nonthaburi, Thailand

Background: Current Thailand Ministry of Public Health (MOPH) recommendations state that men who have sex with men (MSM) should repeat HIV testing every 6-12 months. We investigated the proportion and trend of repeat HIV voluntary counseling and testing (VCT) within 12 months among Thai MSM attending Silom Community Clinic @TropMed.
Methods: Silom Community Clinic @Trop Med has been located in downtown Bangkok since late 2005, with easy access and convenient operating hours for MSM. It provides free-of-charge, confidential and rapid HIV VCT by MSM-friendly staff. We advertise the clinic via website, Facebook, outreach, and friend referrals. For first-time testers, we recommend that they repeat VCT every 6-12 months. For this analysis, we included men with an initial HIV test who had visited the clinic for ≥12 months and had a baseline HIV-negative result; the first VCT visit occurred between 2006- 2013 with follow-up period through October 2014. On a yearly basis, we looked at the number and proportion of first-time testers who had another VCT visit within the next 12 months. We used chi-square test for trend to test changes in the proportion of repeat testing within 12 months by calendar year.
Results: Between 2006-2013, 9,345 MSM were tested by our testing services and 4,597 met the criteria above and were included in this analysis. Most (67.1%) were 25 years and older, and most (87.9%) lived in Bangkok or nearby provinces at time of first test. Among these MSM, 2,016 (43.9%) repeated VCT. The number of new testers increased annually from 340 men in 2006 to 880 in 2013. The proportion of MSM who repeated VCT within one year varied between 15.3% to 26.1% by calendar year (mean = 22.2%) and there was a statistically significant increasing trend from 2006-2013 (p<0.01) (Figure).



[Figure. Proportion of clinic attendees with initial HIV test who repeated testing within one year, Thailand, 2006-2013]

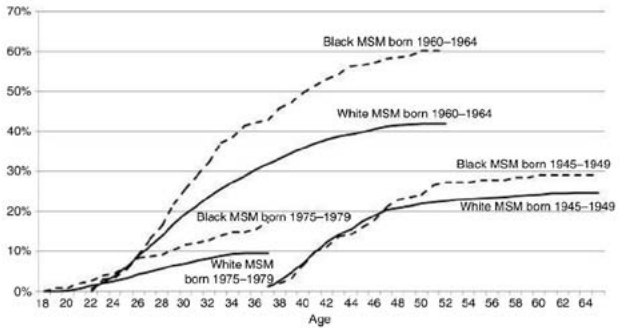
Conclusions: Between 2006-2013, the number of new testers doubled, and the proportion of men who repeated VCT significantly increased. Given that roughly one-fifth of MSM repeated VCT within 12 months, counseling to emphasize repeating VCT according to Thailand MOPH recommendations should be strengthened and systematic strategies to retain testers should be implemented.

TUAC0303

Dramatic declines in lifetime HIV risk and persistence of racial disparities among men who have sex with men (MSM) in King County, Washington, USA

G. Chan[1], A. Bennett[2], S. Buskin[2,3], J. Dombrowski[1,2], M. Golden[1,2]
[1]University of Washington, Department of Medicine, Seattle, United States, [2]Public Health - Seattle & King County, Seattle, United States, [3]University of Washington, Department of Epidemiology, Seattle, United States

Background: In the US, HIV disproportionately affects MSM, who account for >60% of new cases. Although recent data suggest HIV incidence is declining nationally, rates in MSM are stable, and the proportion of cases occurring in black MSM is increasing. Because sexual mixing is largely age-assortative, using life tables to estimate risk within birth cohorts may be useful in assessing and anticipating trends in the population's risk.
Methods: We constructed life tables for the period 1982-2012 to estimate the cumulative risk of HIV diagnosis among MSM in King County born 1940-1994. We used U.S. Census data to define the size of the white and black male populations of King County, Washington, national and local survey data to estimate the proportion of men who are MSM, and local surveillance data to define the number of HIV diagnoses in MSM each year.
Results: We estimated that 6% of the local male population was MSM. Age-specific risk of HIV diagnosis increased in birth cohorts from the 1940s until the mid-1960s and thereafter declined, plateauing among cohorts born after the mid-1970s (Figure).



[Cumulative Risk of Acquiring HIV Among MSM in King County]

This trend occurred in both white and black MSM. In the peak risk cohort, MSM born 1960-64, >40% of white and >60% of black MSM had been diagnosed with HIV by age 50. A dramatic decline in this risk was evident when comparing the percentage of MSM diagnosed with HIV in different birth cohorts. Among white and black MSM born 1960-1964, the cumulative risk of HIV diagnosis by age 35 was 29% and 42% respectively, while among MSM born 1975-1979, this risk decreased to 9% and 15%, respectively. However, as absolute risk of HIV diagnosis decreased overall in younger cohorts, relative differences between white and black MSM appear to increase. Throughout the period and across birth cohorts, cumulative HIV risk was 18% to 84% higher among black vs. white MSM.
Conclusions: Comparing birth cohorts, cumulative HIV risk among MSM in King County has declined approximately 65% in those born after the mid-1960s, although racial disparities persist. Our findings highlight the importance of evaluating HIV risk within birth cohorts and demonstrate remarkable local progress in HIV prevention.

TUAC0304

Ethical considerations for inclusion of men who have sex with men under the age of 18 in epidemiological research: evidence from six sub-Saharan African countries

A. Grosso[1], S. Stahlman[1], T. Mothopeng[2], N. Taruberekera[3], G. Ouedraogo[4], O. Ky-Zerbo[5], V. Pitche[6], S. Anato[7], B. Sithole[8], X. Mabuza[9], N. Ceesay[10], D. Diouf[11], G. Trapence[12], E. Umar[13], S. Baral[1]
[1]Johns Hopkins University, Center for Public Health and Human Rights, Baltimore, United States, [2]Matrix Support Group, Maseru, Lesotho, [3]Population Services International, Johannesburg, South Africa, [4]Institute de Recherche en Sciences de la Sante, Ouagadougou, Burkina Faso, [5]Programme d'Appui au Monde Associatif et Communautaire, Ouagadougou, Burkina Faso, [6]Conseil National de Lutte contre le SIDA du Togo, Lomé, Togo, [7]Arc en Ciel, Lomé, Togo, [8]University of Stellenbosch, Department of Health Sciences, Stellenbosch, South Africa, [9]Rock of Hope, Manzini, Swaziland, [10]UNAIDS, Banjul, Gambia, [11]Enda Sante, Dakar, Senegal, [12]Center for the Development of People, Blantyre, Malawi, [13]Malawi College of Medicine, Blantyre, Malawi
Presenting author email: grossoas@gmail.com

Background: In many settings, laws or institutional review board policies require parental permission for youth < 18 years to participate in research. Individual and social risk factors for HIV acquisition often occur before age 18. Youth may be unwilling to participate in HIV epidemiological research requiring parental consent due to the sensitive nature of risk factors such as sexual behaviors and experiences of violence. Young men who have sex with men (MSM) are at especially high risk for HIV acquisition and are often unwilling or unable to disclose their sexual orientation or practices to their parents. In sub-Saharan Africa, where HIV prevalence among MSM is high and sex between men is criminalized or highly stigmatized in many countries, epidemiologic research on this vulnerable population of young MSM is particularly relevant and sparse. One strategy for assessing the potential size of the population of young (< 18) MSM is to ask adult MSM retrospective questions about the age at which they first had anal sex with a man.
Methods: MSM aged 18 or older were recruited using respondent-driven sampling in Burkina Faso, Togo, Lesotho, Malawi and Swaziland. MSM aged 15 and above were recruited using snowball sampling in The Gambia. Participants completed a survey that included a question asking how old they were when they first had anal sex with another man. This variable was dichotomized and tabulated to assess the prevalence of anal sex under the age of 18.
Results: Across settings, 40.20% (1106/2751) of MSM had anal sex with a man before the age of 18. The highest percentage was in Lome, Togo (63.84%), while the smallest percentage was in Swaziland (14.46%). MSM under the age of 18 represented 12.14% of the study sample in The Gambia.

Country	Percentage (n/N) of MSM study participants who first had anal sex with a man when they were under the age of 18	Percentage of study participants under 18 years old
Bobo-Dioulasso, Burkina Faso	51.21% (169/330)	N/A
Ouagadougou, Burkina Faso	51.31% (176/343)	N/A
Kara, Togo	41.95% (138/329)	N/A
Lome, Togo	63.84% (226/354)	N/A
Gambia	43.69% (90/206)	12.14% (25/206)
Maputsoe, Lesotho	40.95% (129/315)	N/A
Maseru, Lesotho	35.85% (76/212)	N/A
Malawi	16.32% (55/337)	N/A
Swaziland	14.46% (47/325)	N/A

[Proportion of MSM sampled who had anal sex <18 y.o]

Conclusions: A substantial proportion of MSM participants had anal sex with a man under the age of 18. Further research on this group, including a waiver of requirements for parental consent for participation, is warranted. Given the relatively small proportion of study participants under the age of 18 in a setting where this was feasible, additional outreach strategies such as web-based recruitment may be necessary.

TUAC0305

Nuanced seroadaptive behaviors among Seattle men who have sex with men (MSM): sexual decision-making based on ART use/viral load and recency of partner HIV testing

C.M. Khosropour[1], D.A. Katz[2,3], J.C. Dombrowski[2,3], M.R. Golden[2,3]
[1]University of Washington, Epidemiology, Seattle, United States, [2]University of Washington, Medicine, Seattle, United States, [3]Public Health - Seattle & King County, HIV/STD Program, Seattle, United States
Presenting author email: ckhosro@uw.edu

Background: Seroadaptive behaviors among men who have sex with men (MSM) may protect against HIV. Anecdotally, some MSM incorporate partners' antiretroviral therapy (ART)/viral load (VL) or HIV testing frequency into sexual decision-making. The frequency and effect of these strategies is unknown.
Methods: HIV-negative MSM attending an STD clinic in Seattle, WA from March-December 2014 were enrolled in a study of seroadaptive behaviors. Men completed a computer-based survey on behaviors in the past 12 months. HIV testing was performed per clinic protocol. Among HIV-negative men with HIV-negative partners, we examined if the timing of the partner's last HIV test was associated with condomless anal intercourse (CAI). Of those with HIV-positive partners, we asked (in aggregate) if respondents' decision to have sex or use condoms was based on partner ART use or VL (i.e., ART/VL serosorting). We compared proportions with chi-square tests.
Results: We enrolled 988 (58%) of 1,718 eligible HIV-negative MSM. The mean age was 33 and 62% were white, non-Hispanic. Most (69%) had CAI with HIV-negative partners, 18% had CAI with HIV-positive partners, and 22% reported no CAI. The majority (86%) asked HIV-negative partners when the partner last tested negative. CAI was more common among men whose most recent partner tested ≤3 months ago compared to men whose partner tested >3 months ago or the partner did not know when he last tested (48% vs. 40%, P=.02). Of 222 men with HIV-positive partners, 60% and 64% decided whether to have sex/use condoms based on their partners' ART use or VL, respectively. CAI with an HIV-positive partner was more common among men who reported ART/VL serosorting compared to those who did not (79% vs. 57%, P=0.03), but testing newly positive for HIV was less common among men who reported ART/VL serosorting compared to men who did not (1/120 [1%] vs. 2/23 [9%]).
Conclusions: Among Seattle MSM, nuanced seroadapative behaviors such as ART/VL serosorting and using the recency of a partner's HIV test to inform sexual decision-making are common. The high prevalence of these behaviors suggests they could impact HIV incidence rates, but the individual- and population-level effects of these behaviors are uncertain.

TUAC0306

Viral load awareness and risk behaviour in male serodiscordant couples in Australia, Brazil and Thailand

B.R. Bavinton[1], F. Jin[1], G. Prestage[1,2], I. Zablotska[1], B. Grinsztejn[3], N. Phanuphak[4], R.K. Friedman[3], A.E. Grulich[1], Opposites Attract Study Group
[1]The University of New South Wales, The Kirby Institute, Kensington, Australia, [2]La Trobe University, Australian Research Centre in Sex, Health and Society, Melbourne, Australia, [3]Instituto de Pesquisa Clínica Evandro Chagas, Fundação Oswaldo Cruz, Rio de Janeiro, Brazil, [4]Thai Red Cross AIDS Research Centre, Bangkok, Thailand
Presenting author email: bbavinton@kirby.unsw.edu.au

Background: There are very limited data from homosexual male serodiscordant couples (HM-SDC) on the impact of antiretroviral therapy (ART) and viral load (VL) on HIV transmission risk, and on risk behaviours within such couples. To date, no studies have investigated the issue in middle income countries.
Methods: *Opposites Attract* is an ongoing multisite cohort study of HM-SDC in Australia, Brazil and Thailand. HIV-positive partners (HPP) had VL tested; HIV-negative partners (HNP) had HIV antibody tests and reported sexual behaviour and perception of the HPP's most recent VL test. Undetectable VL (UVL) was defined as < 200 copies/mL.
We compared couples from the three countries; baseline differences were examined with bivariate logistic regression.
Results: By January 2015, 242 couples were enrolled (Australia=137, Brazil=53, Thailand=52). The majority of HPP were taking ART (80.2%); this was lower in Thailand than in Australia and Brazil (p<0.001), accompanied by higher proportions with UVL in Australia (88.2%) and Brazil (85.0%) than in Thailand (69.2%, p=0.008). Overall, 61.2% of HNP perceived their HPP's last VL test result to be undetectable.
Brazilian and Thai HNP were more likely not to know the result (17.0% and 38.5%) compared to Australians (5.1%, p<0.001). Australian HNP reported more sex with other partners than Brazilian (p=0.013) but not Thai HNP (p=0.183).
Australian HNP reported more condomless anal intercourse (CLAI) with outside partners compared to both Brazilians (p=0.002) and Thais (p=0.012). 54.6% of HNP reported CLAI with study partner in the last 3 months. Compared to Australia (67.9%), this was lower in Brazil (45.3%, p=0.005) and Thailand (28.9%, p<0.001).

Overall, 63.5% of HNP who perceived the HPP's VL to be undetectable reported CLAI in the last 3 months, compared to only 40.4% of HNP in which the HPP's VL was perceived to be detectable/unknown (OR=0.39, 95%CI=0.23-0.66, p=0.001). While this was strongly associated amongst Australian couples (p=0.002), there was no such association in Brazil or Thailand.

	Total (n=242)	Australia (n=137)	Brazil (n=53)	Thailand (n=52)
HPP: Taking ART	194 (80.2)	124 (90.5)	45 (84.9)	25 (48.1)
HPP: Viral load <200 copies/mL (available for 227 HPP)	189 (83.3)	119 (88.2)	34 (85.0)	36 (69.2)
HPP: Adherence to ART >90% (of those taking ART)	170 (91.9)	107 (92.2)	40 (88.9)	23 (95.8)
HNP: Perceived VL of HPP				
Undetectable VL	148 (61.2)	107 (78.1)	34 (64.2)	7 (13.5)
Detectable VL	58 (24.0)	23 (16.8)	10 (18.9)	25 (48.1)
Don't Know VL	36 (14.9)	7 (5.1)	9 (17.0)	20 (38.5)
HNP: Any CLAI with outside partners, last 3 months	45 (18.6)	38 (27.7)	2 (3.8)	5 (9.6)
HNP: Any CLAI with study partner, last 3 months	132 (54.6)	93 (67.9)	24 (45.3)	15 (28.9)

[Baseline characteristics of HIV-positive and HIV-n]

Conclusions: Australian HNP were more aware of their partner's VL results. Australian HM-SDC with perceived UVL practiced more CLAI, suggesting they may be acting upon beliefs that treatment-as-prevention is effective. This pattern was not seen in Brazil and Thailand.

TUAC04 People Who Inject Drugs: Prevention and Care Cascade

TUAC0401

Estimating the number of people who inject drugs (PWID) in two urban areas in Mozambique using four different methods, 2014

I. Sathane[1], R. Horth[2], M. Boothe[2], C. Sema Baltazar[3], P. Young[4], H. Fisher[2], E. Teodoro[5], M.L. Gouveia[5], T. Lane[2], W. Mcfarland[2]
[1]I-TECH Mozambique, MARPS, Maputo, Mozambique, [2]University of California, San Francisco, United States, [3]National Institute of Health, Ministry of Health, Maputo, Mozambique, [4]Centers for Disease Control and Prevention, Maputo, Mozambique, [5]Ministry of Health, Department of Mental Health, Maputo, Mozambique
Presenting author email: isabels@itech-mozambique.org

Background: There are few data on HIV prevalence and the number of people who inject drugs (PWID) in Mozambique. As part of the Integrated Biological and Behavioral Surveillance (IBBS) Survey implemented in 2014, we conducted the first population size estimation among PWID in two urban areas, Maputo (n=353) and Nampula (n=139).
Methods: Given the lack of a gold standard, we synthesized four independent methods to estimate the number of PWID: unique object multiplier, wisdom of the crowd, sequential sampling, and literature review. The unique object estimate is calculated as the number of objects distributed to PWID pre-survey, divided by the proportion of survey participants who reported receiving the objects. The wisdom of the crowd method polls the participants on how many people they believe inject drugs in each city (responses equal to the personal network size were excluded). The sequential sampling method applies a Bayesian approach to the self-reported PWID network size of each participant to infer the size of the hidden population. In the literature review, estimates were based on proportions of adults who are PWID from other African locations applied to the 2014 census projections for Maputo and Nampula. A consensus meeting among stakeholders agreed that the median of all four methods was the best estimate of population size of PWID in each city and also agreed to the lowest and highest estimates as "acceptable bounds."
Results: HIV prevalence was 50.3% (95% confidence interval [CI]: 40.7-58.9) and 36.8% (CI: 24.3-49.3) in Maputo and Nampula, respectively. The numbers of PWID were estimated at 1445 (0.19% of adults) [acceptable bounds: 1281 (0.17%) - 3524 (0.46%)] and 465 (0.14%) [acceptable bounds: 354 (0.10%) - 3921 (1.16%)]. Using these population size estimates, there are 727 and 171 PWID infected with HIV and in need of care and/or treatment services in Maputo and Nampula, respectively.

Figure 1.A – Population Size Estimation using Four Independent Methods, Maputo City

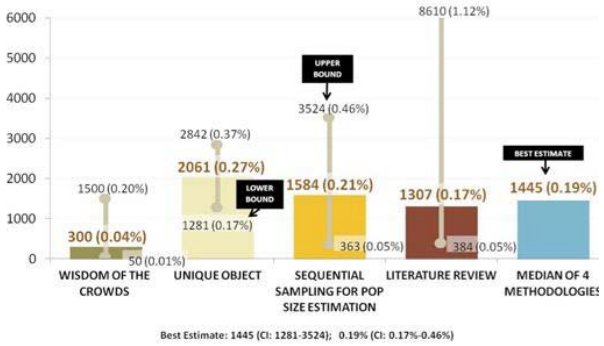
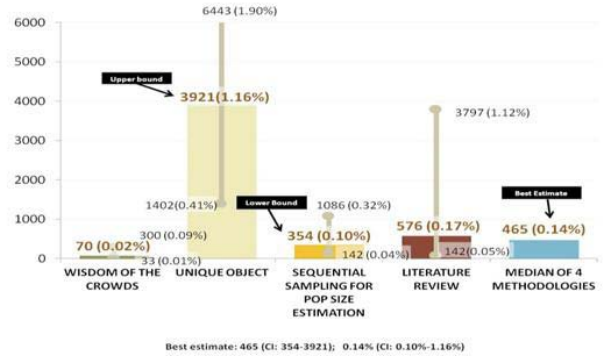


Figure 1.B – Population Size Estimation using Four Indpendent Methods, Nampula



[Population Size Estimation of PWID in Mozambique]

Conclusions: Our results highlight the feasibility of using the median of multiple methods to estimate the size of PWID in two urban areas in Mozambique. Given the limited population size and high rates of infection, harm-reduction, prevention interventions and HIV care and treatment services should be practical and affordable in this population.

TUAC0402

Efficacy of a network intervention in reducing HIV incidence among people who inject drugs in Ukraine: preliminary results from a clustered randomized trial

R. Booth[1], J. Davis[2], S. Dvoryak[3], J. Brewster[1], S. Strathdee[4], C. Latkin[5]
[1]University of Colorado Denver, Psychiatry, Denver, United States, [2]University of Colorado Denver, Denver, United States, [3]Ukrainian Institute on Public Policy, Kiev, Ukraine, [4]University of Californa San Diego, San Diego, United States, [5]Johns Hopkins University, Baltimore, United States
Presenting author email: robert.booth@ucdenver.edu

Background: HIV incidence among people who inject drugs (PWID) in Ukraine is among the highest in the world. We assessed the efficacy of two interventions, a network-based peer intervention combined with HIV testing and counseling (T/C combined; experimental condition, N=614) versus HIV testing and counseling alone (T/C alone; control condition, N=592), in reducing HIV incidence among PWID.
Methods: Between 2010-2014, 1205 HIV-seronegative PWID were recruited from street settings in Odessa, Donetsk and Nikolayev. We used a clustered randomized design that consisted of 611 networks and included: peer-leaders; first wave network members; and, second wave network members. Participants were randomly assigned to interventions in groups of 16 and interviewed at baseline, 6 and 12 months. Interviewers and HIV tester/counselors were not blinded to intervention. Cox regression was used to compare HIV incidence between groups, incorporating GEE to account for clustering.
Results: Preliminary results suggest that mean age and duration of injection was 31.8 and 11.7 years, respectively; 75% were male. In the past 30 days, 43% injected daily, 46% always injected with others, 78% had ≥1 sex partner. HIV incidence was 19.0 per 100 person-years (py) in the experimental condition compared to 31.8 per 100 py in the control condition (p<0.001). PWID in the experimental condition had a 39% reduced hazard for HIV seroconversion vs the control group (*p*<0.001).

With each year increase in age, the hazard increased by 5% (*p<0.001)* and, with each injection episode in the past 30 days, the hazard increased by 0.6% (*p*=0.02). Those who were sexually active in the last 30 days had a 26% reduced hazard (p=0.03).

Conclusions: The combined network-based peer intervention and was more efficacious in reducing HIV incidence among PWID in Ukraine than T/C alone.

TUAC0403

Factors associated with initiation of antiretroviral therapy among HIV-infected people who use illicit drugs

B. Joseph[1], M.-J. Milloy[1,2]
[1]British Columbia Centre for Excellence in HIV/AIDS, Vancouver, Canada, [2]University of British Columbia, Faculty of Medicine, Vancouver, Canada
Presenting author email: bjoseph@ualberta.ca

Background: Treatment-as-Prevention-based efforts to reduce HIV/AIDS-associated morbidity, mortality and HIV viral transmission among people who use illicit drugs (PWUD) rely on prompt engagement in antiretroviral therapy (ART). However, the longitudinal factors that promote or block initiation of ART among PWUD are not well described. Thus, we sought to identify factors associated with time from seroconversion to ART initiation among PWUD.

Methods: Using data from two observational prospective cohorts of illicit drug users linked to comprehensive ART dispensation records, we included HIV-seronegative individuals at baseline who seroconverted during follow-up. We fit multivariable Cox proportional hazards models adjusted for a time-updated measure of clinical eligibility for ART to identify factors independently associated with time to treatment initiation following seroconversion.

Results: We included 133 individuals of whom 98 (73.7%) initiated ART during follow-up at a rate of 17.6 per 100 person-years. In a multivariable model adjusted for clinical eligibility, living in the HIV epicenter (Adjusted Hazard Ratio [AHR] = 1.62, 95% Confidence Interval [95% CI] = 1.01 - 2.58), methadone maintenance therapy (MMT) (AHR = 2.37, 95% CI = 1.56 - 3.60) and a later year of interview (AHR = 1.07, 95% CI = 1.02 - 1.13) were associated with shorter time to ART initiation. Barriers to ART initiation were illicit income generation (AHR = 0.51, 95% CI = 0.32 - 0.79) and incarceration (AHR = 0.52, 95% CI = 0.28 - 0.97).

Conclusions: In this sample of community-recruited HIV-positive PWUD with well-defined dates of seroconversion, we found that illicit income generation and incarceration were barriers to ART initiation while MMT and living in the HIV epicenter promoted ART initiation independent of clinical eligibility. Current efforts to scale-up HIV treatment among PWUD should consider these factors in order to reduce HIV/AIDS-associated morbidity, mortality and HIV viral transmission.

TUAC0404

Periodic HIV testing and immediate antiretroviral therapy among people who inject drugs in Vietnam

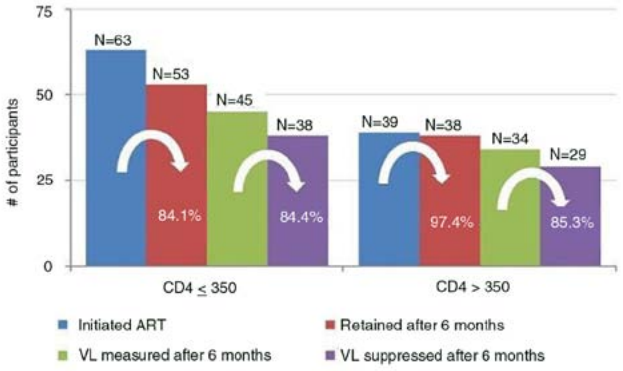
H.H. Nguyen[1], D.D. Bui[1], T.T.T. Dinh[2], M.S. Nguyen[2], H.T. Tran[3], L.H. Nguyen[3], T.T.V. Nguyen[4], Q.D. Vu[2], T.N. Do[1], A.K.A. Le[5], B.C. Nguyen[6], A. Suthar[4], Y.-R. Lo[4], H.T. Pham[3], M.G. Le[2], H.L. Nguyen[1], M. Kato[4]
[1]Viet Nam Authority for HIV/AIDS Control, Hanoi, Vietnam, [2]Ha Noi Medical University, Hanoi, Vietnam, [3]National Institute of Hygiene and Epidemiology, Hanoi, Vietnam, [4]World Health Organization, Hanoi, Vietnam, [5]Thai Nguyen Province AIDS Center, Thai Nguyen, Vietnam, [6]Thanh Hoa Province AIDS Center, Hanoi, Vietnam
Presenting author email: dothinhan@gmail.com

Background: In Vietnam, injecting drug use is the leading cause of HIV transmission. Multiple local transmission models suggest periodic HIV testing and counselling (HTC) and initiating antiretroviral therapy (ART) irrespective of CD4 count in people who inject drugs (PWID) can markedly reduce HIV-related mortality and transmission. Programme experience with this approach in Vietnam is limited.

Therefore, the acceptability and feasibility of this approach was assessed in two high-burden provinces. We present preliminary ART outcomes.

Methods: Village health workers, PWID peer educators, and health staff were educated on the new approach and the benefits and risks of immediate ART initiation. Since April 2014, HTC has been recommended to PWID every six months, and immediate ART, i.e. initiation irrespective of CD4 count, has been offered to PWID living with HIV in Thai Nguyen and Thanh Hoa provinces. Following consent, PWID were followed for 12 months. HIV viral load (VL) was assessed before ART start (baseline) and at months six and 12.

Results: Of 232 identified HIV-positive PWID, 218 (94%) agreed to participate and initiate immediate ART, among which 102 initiated ART before 30 June 2014. Of this cohort, 97.1% were males, median age was 36 years, 47.1% reported methadone use in the past three months, 38.2% had baseline CD4 counts greater than 350 cells/mm^3 and median baseline VL was 4.1 (IQR 2.3-5.2) log10 copies/ml. 91 of the 102 participants (89.2%) were retained after six months (eight died and three lost-to-follow-up). Retention was 84.1% and 97.4% among PWID with baseline CD4 counts below and above 350 cells/mm3, respectively (Figure). Excluding five patients who transferred to other care sites and seven patients whose samples were not available due to logistical issues, 67 of the 79 participants (84.8%) achieved viral suppression (i.e. VL < 1000 copies/ml) at month six. Viral suppression was 84.4% and 85.3% among PWID with CD4 counts below and above 350 cells/mm3, respectively (Figure)



[Figure]

Conclusions: The preliminary results suggest high uptake and adherence to ART irrespective of CD4 count among PWID; however, late presentation to care remains a critical problem. The results are informing the revision of the national guidelines to include immediate ART in key populations.

TUAC0405

Social and socio-economic benefits of antiretroviral therapy adherence among HIV-infected people who use illicit drugs in Vancouver, Canada

L. Richardson[1,2], T. Kerr[1,3], B. Hogg[1,4], S. Guillemi[1], J. Montaner[1,3], E. Wood[1,3], M.-J. Milloy[1,3]
[1]B.C. Centre for Excellence in HIV/AIDS, Vancouver, Canada, [2]University of British Columbia, Sociology, Vancouver, Canada, [3]University of British Columbia, Faculty of Medicine, Division of AIDS, Vancouver, Canada, [4]Simon Fraser University, Faculty of Health Sciences, Burnaby, Canada
Presenting author email: lrichardson@cfenet.ubc.ca

Background: There is extensive documentation of the direct clinical benefits of antiretroviral therapy (ART) adherence leading to plasma HIV RNA-1 viral load suppression. However, very little is known about the social, socio-economic and ancillary clinical benefits of ART adherence, particularly among people who use illicit drugs (PWUD).

Methods: We used longitudinal data from a prospective cohort of community-recruited HIV-positive PWUD in Vancouver, Canada, a setting of free and universal access to HIV care. Participant data were linked to comprehensive HIV clinical monitoring and ART dispensation records. We developed a series of generalized linear mixed effects models, adjusting for potential confounders. Models examine whether, among ART-exposed individuals, becoming optimally adherent to ART medication (i.e., ≥95% using a validated measure of pharmacy dispensation) resulted in associated social, socio-economic and ancillary clinical benefits, such as relationship initiation, transitioning out of homelessness, entering employment, ceasing involvement in illegal or prohibited income generation activity (e.g., street-based income generation, sex work, drug dealing or other illegal activities), and enrolling in addiction treatment.

Results: Between December 2005 and November 2013, of the 724 eligible study participants, 241 (33.3%) self-reported as women and 404 (55.8%) as Caucasian, with 463 (64.0%) individuals becoming ≥95% adherent to ART at least once during the study period. In final multivariate models, becoming adherent to ART was positively and significantly associated with ceasing prohibited or illegal income generation activities (adjusted odds ratio [AOR]: 1.52; 95% confidence interval [CI]: 1.20 - 1.94) and transitioning out of homelessness (AOR: 1.38; 95% CI: 1.12 - 1.71), while ART adherence was marginally associated with initiating a romantic relationship (AOR: 1.31, 95% CI: 0.96 - 1.81).

Conclusions: These findings suggest that becoming adherent to ART results not only in virologic suppression among HIV infected PWUD, but also increases the likelihood of reducing key drivers of social and socio-economic vulnerability. These secondary benefits of ART adherence hold the potential to reinforce ongoing engagement in HIV care and support significant improvements in quality of life and individual health among this marginalized population. Findings reinforce the clinical and non-clinical importance of promoting access and adherence to ART among HIV-positive individuals who use illicit drugs.

TUAC0406LB

Modelling the impact of improvements in the cascade of care for chronic hepatitis C among people who inject drugs (PWID) in Montréal, Canada

A. Cousien[1,2,3], P. Leclerc[3], C. Morissette[3], J. Bruneau[4], É. Roy[5], Y. Yazdanpanah[1,2,6], J. Cox[3,7]
[1]INSERM, IAME, UMR 1137, Paris, France, [2]IAME, UMR 1137, Univ Paris Diderot, Sorbonne Paris Cité, Paris, France, [3]Direction de santé publique du Centre intégré universitaire de santé et de services sociaux du Centre-Est-de-l'Ile-de-Montréal, Montréal, Canada, [4]Centre de recherche, Centre hospitalier de l'Université de Montréal (CRCHUM), Montréal, Canada, [5]Faculté de médecine et des sciences de la santé, Université de Sherbrooke, Campus Longueuil, Longueuil, Canada, [6]Service des Maladies Infectieuses et Tropicales, Hôpital Bichat Claude Bernard, Paris, France, [7]Chronic Viral Illness Service, McGill University Health Centre, Department of Epidemiology, Biostatistics and Occupational Health, McGill University, Montréal, Canada

Background: Since 2010, HCV incidence among active (i.e. injection past six months) PWID in Montréal remains greater than 15/100 person-years (p-y). The arrival of new direct-acting antivirals (DAA) with high sustained virological response rates and improved tolerability raises the question of whether treatment could be used to prevent HCV transmission. Our objective was to assess how improvements in the cascade of care can impact future HCV incidence, prevalence and complications among PWID in Montréal.
Methods: We used a dynamic model to simulate HCV transmission and natural history among active PWID in Montréal from 2015. The reference scenario (scenario 1) was the current cascade of care including new DAA as standard treatment (see Table). HCV prevalence and incidence after 10 years and the number of liver complications avoided after 40 years were estimated under different conditions: decreased time from chronic infection to diagnosis (scenario 2), greater adherence to treatment (scenario 3), improved treatment rate (scenarios 4 and 5) and a combination of these interventions (scenario 6). Due to a lack of data on time to linkage to care (time between diagnosis and first consultation related to hepatitis C), simulations considered three such intervals: 1, 3 and 5 years. A thousand simulations were performed per scenario.
Results: Scenarios 2 and 3 showed similar results for HCV prevalence (53.3% to 59.5%) and incidence (9.1 to 10.3/100 p-y) after 10 years, and less than a 3.4% difference in the number of liver complications after 40 years relative to the reference scenario. Improving access to treatment (scenarios 4 and 5) demonstrated a great decrease in all outcomes. When combining all interventions (scenario 6), prevalence and incidence decreased until 26.9% and 4.9/100 p-y, respectively, and the number of liver complications until 39.3%, depending on the time to linkage to care.
Conclusions: Our results suggest that decreasing time to diagnosis or improving treatment adherence is not sufficient to impact HCV prevalence, incidence and complications among PWID in Montréal. The current level of treatment access in the cascade of care is limiting a massive decrease in disease burden and transmission. A substantial treatment scale-up is necessary in this population.

Scenario	Average time before linkage to care (years)	Prevalence after 10 years (%) mean (95% CI)	Incidence after 10 years (/100 persons-years) mean (95% CI)	% of complications avoided compared to Scenario 1 over 40 years mean (95% CI)
Scenario 1 (Reference) **New DAAs under the current cascade of care:** average time from chronic infection to diagnosis δ=2.0 years annual lost to follow-up probability ψ=14%; initiation of treatment if linked to care α=5%/year; SVR rate with current adherence to treatment (SVR) = 81.3%	1 3 5	54.6 (54.4; 54.8) 57.7 (57.5; 57.8) 59.5 (59.4; 59.7)	9.4 (9.1; 9.6) 10.1 (9.8; 10.4) 10.3 (10; 10.6)	/ / /
Scenario 2 **Decrease time from chronic infection to diagnostic** δ=0.5 years	1 3 5	53.5 (53.3; 53.7) 56.8 (56.7; 57) 58.7 (58.5; 58.9)	9.1 (8.9; 9.4) 9.9 (9.6; 10.1) 10.1 (9.9; 10.4)	0.9 (-0.2; 2.0) 1.7 (0.8; 2.6) 1.7 (0.7; 2.7)
Scenario 3 **Improve adherence to treatment:** SVR rate likewise in clinical trials (SVR=90%)	1 3 5	53.3 (53.1; 53.5) 56.6 (56.5; 56.8) 58.5 (58.3; 58.7)	9.1 (8.8; 9.4) 9.6 (9.4; 9.9) 9.8 (9.5; 10.1)	2.7 (1.6; 3.8) 3.2 (2.2; 4.2) 3.4 (2.6; 4.3)
Scenario 4 **Improve treatment rate:** α=10%/year	1 3 5	45.6 (45.4; 45.8) 50.5 (50.3; 50.7) 53.5 (53.4; 53.7)	7.8 (7.6; 8.0) 8.4 (8.2; 8.7) 9.1 (8.9; 9.4)	15.5 (14.7; 16.3) 14.6 (13.7; 15.4) 12.4 (11.5; 13.2)
Scenario 5 **Improve treatment rate:** α=20%/year	1 3 5	34.1 (33.9; 34.3) 41.4 (41.2; 41.6) 45.7 (45.5; 45.9)	6.1 (5.9; 6.3) 7.3 (7.1; 7.5) 7.8 (7.6; 8.1)	29.6 (28.9; 30.2) 27.2 (26.3; 28.0) 24.3 (23.6; 25.1)
Scenario 6 **Combined scenario** combine scenarios 2,3 and 5	1 3 5	26.9 (26.7; 27.0) 35.7 (35.5; 35.8) 41.2 (41; 41.4)	4.9 (4.8; 5.1) 6.4 (6.2; 6.6) 7.2 (7.1; 7.4)	39.3 (38.8; 39.8) 34.8 (34.2; 35.4) 31.6 (30.8; 32.4)

CI: confidence interval
SVR: Sustained virological response

[TUAC0406LB Table]

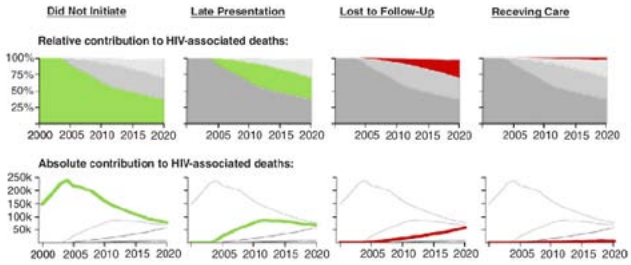
TUAD01 Innovations in Methods of Implementation Science

TUAD0101

Where to strengthen care: model-based triangulation of trends in the HIV care cascade

A. Bershteyn, D. Klein, K. Oishi, P. Eckhoff
Institute for Disease Modeling, Bellevue, United States
Presenting author email: abershteyn@intven.com

Background: The HIV "cascade of care" provides a framework for identifying priority areas for improvement of HIV services. In sub-Saharan Africa, the cascade has yet to be characterized nationally due to challenges such as distinguishing first initiation of care from re-initiation absent unique patient identifiers. Lacking direct data characterizing the cascade, we hypothesize that national-level temporal trends in care can be triangulated based on epidemiological, actuarial, and programmatic information fed into a quantitative model.
Methods: We simulated the HIV care cascade in South Africa using an epidemiological model calibrated to age- and gender-specific HIV prevalence and mortality, national population dynamics, and monitoring data from the public-sector HIV treatment program. Data were available up to 2012, beyond which we assumed continuation of current trends in scale-up. HIV-associated mortality in the model was classified into those dying without initiating care, having initiated late (CD4< 200), lost to follow-up (LTFU) after previous initiation, or currently in care.
Results: Failure to initiate care constituted the largest but most rapidly declining category of HIV mortality, predicted to decline from 47% of HIV-associated deaths in 2015 to 37% in 2020. Late initiation was the second-largest and declined more slowly because increasing CD4 counts at initiation were partially offset by growing numbers of patients initiating care. LTFU was the third-largest but the most rapidly-growing category of HIV mortality. Programmatic data about re-initiation of care is lacking, but under the assumption that half of patients LTFU will re-initiate care, deaths LTFU were not expected to surpass deaths due to late initiation by 2020. Those receiving care constituted 3% of HIV-associated deaths, mostly among those receiving treatment rather than in pre-ART care. This proportion remained constant over time because the growing population on treatment was offset by improvements in treatment quality, such as expansion of virological monitoring and availability of second-line regimens.



[Figure: HIV mortality along the care cascade]

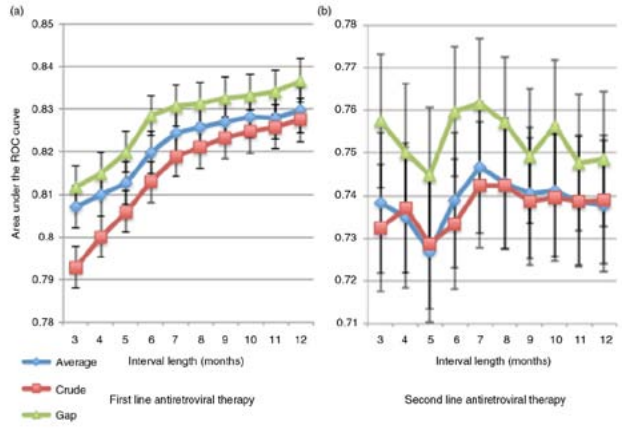
Conclusions: More data are required to fully characterize the spatial heterogeneities and dynamics of the care cascade. Nevertheless, trends revealed by model-based triangulation were consistent with findings in well-studied populations such as demographic surveillance sites. Failure to access care remains the largest but most rapidly declining category of HIV mortality.

TUAD0102

Optimizing tools for measuring short-term antiretroviral adherence from pharmacy refill data to predict virologic outcomes in resource-limited settings

R. Leisegang[1], J. Mcmahon[2], M. Hislop[3], K. Stinson[4], A. Boulle[4], J. Elliott[2,5], G. Maartens[1]
[1]University of Cape Town, Division of Clinical Pharmacology, Department of Medicine, Cape Town, South Africa, [2]Alfred Hospital, Department of Infectious Diseases, Melbourne, Australia, [3]Afrocentric Health Pty Ltd, Aid for AIDS, Cape Town, South Africa, [4]University of Cape Town, Department of Public Health, Cape Town, South Africa, [5]Burnet Institute, Centre for Population Health, Melbourne, Australia
Presenting author email: rory.leisegang@uct.ac.za

Background: Estimates of adherence to antiretroviral therapy (ART) using pharmacy refill data have outperformed self-report and can identify patients at risk for virologic failure, especially in settings where viral load testing is limited. Uncertainty exists about the best method to estimate adherence using pharmacy refill data and the optimal duration of data to predict virologic outcomes.
Methods: We identified individuals over 18 on first and second line ART from a national private sector (Aid for AIDS) and regional public sector (Khayelitsha) program. The area under (AUC) the receiver operating characteristic (ROC) curves for virologic suppression (VS) (viral load <400 copies/mL) was used to compare three short-term adherence estimate methods:
1) 'crude' - refills divided by months,
2) 'average' - days ART dispensed plus unused ART from prior dispensing divided by interval duration, and
3) 'gap' - interval duration less the number of days without ART coverage, divided by interval duration.
The 'gap' method is different to the 'average' method as it does not allow the adherence estimate to be artificially increased by additional ART dispensed after a possible 'gap' in ART coverage. The interval for pharmacy refill varied from 3 to 12 months.
Results: We included 56,472 individuals from the private program (median 1.7 years, 65 % female) and 24,466 from the public program (median 2.1 years, 65 % female). The 'gap' method consistently outperformed the other 2 methods (see figure 1). In the public program, the 'gap' method was 12% less potent due to significant data capture errors. Longer pharmacy refill intervals outperformed shorter intervals ('gap' ROC 0.837 [12 months], 0.812 [3 months]) in the more powered private dataset. When further separated by regimen line, the 'gap' method for second line was superior but the ROC AUCs estimates did not vary by the pharmacy refill interval. We identified possible cut-points for virological failure (VL>1000 copies/ml) in the private program: 80% and 72% for first and second line therapy. respectively.



[Area under ROC curve with 95% CI (private program)]

Conclusions: Adherence measures that identify gaps in pharmacy data were superior and consistent across programs and regimen lines and could be used to identify people at risk of poor ART outcomes.

TUAD0103

Estimating national coverage of antiretroviral therapy among HIV-infected persons using multiple methods, Kenya 2012

A. Kim[1], L. Nganga[1], I. Mukui[2], J. Wamicwe[2], S. Mwanyumba[3], N. Bowen[3], L. Wiesner[4], K. De Cock[1], KAIS Study Group
[1]US Centers for Disease Control and Prevention, Division of Global HIV/AIDS, Nairobi, Kenya, [2]Ministry of Heatlh, National AIDS and STI Control Programme, Nairobi, Kenya, [3]Ministry of Heatlh, National Public Health Laboratory Services, Nairobi, Kenya, [4]University of Cape Town, Division of Pharmacology, Cape Town, South Africa
Presenting author email: aakim@cdc.gov

Background: Accurate estimates of antiretroviral therapy (ART) coverage are needed to track progress towards global targets from the Joint United Nations Programme on HIV/AIDS (UNAIDS) which aim for 90% of HIV+ persons on ART by 2020. ART coverage is reported annually to UNAIDS using mathematically-modeled estimates of the number of HIV+ persons eligible for ART based on an assumed distribution of CD4 counts in the HIV+ population and the number of persons receiving ART in health facilities. We compared ART coverage reported to UNAIDS with coverage estimated from a nationally representative survey in Kenya using two independent methods.
Methods: The 2012 Kenya AIDS Indicator Survey was a population-based household survey of persons aged 18 months-64 years conducted from 10/2012-2/2013. Interviews collected data on ART use for persons reporting HIV+ status. Blood samples were tested for HIV, and HIV+ samples tested for ART by High Performance Liquid Chromatography coupled to Tandem Mass Spectrometry. We estimated and compared ART coverage among HIV+ persons aged 15-64 years based on: 1) routine program monitoring data; 2) self-report; and 3) biological confirmation of ART. ART eligibility in the survey was defined as: CD4 count≤ 350 cells/mm^3 or having active tuberculosis. Estimates were weighted to adjust for survey design and non-response.
Results: According to ART program monitoring data, 549,000 adults were receiving ART in 2012, covering 39.6% (confidence interval [CI] 36.8-43.0) of HIV+ persons and 78.3% (CI 74.8-82.8) of those ART-eligible. Of 11,626 survey respondents, 648 (5.6%) were HIV+ and 559 (86.3%) had samples available for ART testing. Among those, 42.5% (CI.4-47.7) tested positive for ART while 34.2% (CI 29.1-39.3) reported receiving ART. Based on biological confirmation of ART, coverage among ART-eligible persons was 71.0% (CI 63.2-78.9) or 444,000 persons while coverage based on self-report was 63.4% (CI 53.2-73.6) or 374,000 persons.
Conclusions: Self-report underestimated ART coverage by 70,000 persons while program data may overestimate coverage by up to 105,000 persons. Until monitoring systems for the national ART program are strengthened and mathematical models are updated to reflect actual need for ART, surveys that provide biological confirmation of ART may be required to accurately track national estimates of ART coverage.

TUAD0104

Crowdsourcing to spur first-time HIV testing among men who have sex with men and transgender individuals in China: a non-inferiority pragmatic randomized controlled trial

L. Han[1], W. Tang[2], J. Best[3], Y. Zhang[2], J. Kim[2], F. Liu[2], K. Mollan[1], M. Hudgens[1], B. Bayus[4], F. Terris-Prestholt[5], S. Galler[6], L. Yang[2], R. Peeling[5], P. Volberding[3], B. Ma[7], B. Yang[2], S. Huang[2], K. Fenton[8], C. Wei[9], J. Tucker[10]
[1]University of North Carolina at Chapel Hill, Biostatistics, Chapel Hill, United States, [2]Guangdong Provincial STD Control Center, Guangzhou, China, [3]University of California - San Francisco, Medicine, San Francisco, United States, [4]University of North Carolina at Chapel Hill, Kenan-Flagler Business School, Chapel Hill, United States, [5]London School of Hygiene & Tropical Medicine, London, United Kingdom, [6]Oxford University, Oxford, United Kingdom, [7]Blue City, Beijing, China, [8]Public Health England, London, United Kingdom, [9]University of California - San Francisco, Epidemiology and Biostatistics, San Francisco, United States, [10]University of North Carolina Project - China, Guangzhou, China
Presenting author email: jdtucker@med.unc.edu

Background: Improving first-time HIV testing among key populations, especially young MSM and transgender (TG) individuals, is a global health priority. However, most HIV testing campaigns do not reach untested populations and have minimal input from key populations. Crowdsourcing, the process of taking a task performed by an individual and opening it to a large group in the form of a contest, may enhance HIV testing interventions. We organized a non-inferiority, pragmatic randomized controlled trial to compare first-time HIV testing rates among MSM and TG individuals who received either a crowdsourced HIV test promotion intervention or a health marketing intervention.
Methods: Participants were recruited through three large MSM web portals in China. We randomly assigned 721 MSM and TG individuals (≥16 years old, never before tested for HIV) to one of two video interventions. The crowdsourced video was developed using an open contest and formal transparent judging while the evidence-based health marketing video was designed by experts. We followed up four weeks post-intervention via text message to assess HIV test uptake. Descriptive statistics and sensitivity analyses for missing data were carried out to as-

sess test uptake. Cost-minimization analysis was used to evaluate economic and financial costs of the two interventions. The trial was registered (NCT02248558).

Results: Overall, 624/721 (86.5%) MSM and TG individuals responded to the text message. HIV test uptake was similar between the crowdsourced arm (37.1%, 114/307) and the health marketing arm (35.0%, 111/317). Sensitivity analysis using imputation supported the similarity of the two approaches. Within the crowdsourced arm, individuals who previously viewed the video were more likely to receive HIV testing compared to first-time viewers (52.4% vs. 26.5%, p <0.001). Among those tested, 30.7% (69/225) reported a new HIV diagnosis. The crowdsourced intervention cost substantially less than the health marketing intervention in eliciting first-time testing ($131/person vs. $238) and detecting new HIV diagnoses ($415/person vs. $799).

	Crowdsourced				Health Marketing			
	Tested / Total (%)	RR	95% CI	p	Tested / Total (%)	RR	95% CI	p
Multi-time Video Watching	66/126 (52.4%)	1.97	1.47-2.65	< 0.001	67/151 (44.4%)	1.67	1.23-2.28	0.001
First-time Video Watching	48/181 (26.5%)	Ref			44/166 (26.5%)	Ref		
Northern Web Portal	106/316 (33.5%)	1.27	0.70-2.33	0.42	90/266 (26.6%)	0.82	0.57-1.88	0.30
Other Web Portals	8/36 (22.2%)	Ref			21/51 (41.2%)	Ref		
Yes - Condomless Sex	28/71 (39.4%)	1.21	0.84-1.74	0.62	26/62 (41.9%)	1.30	0.90-1.88	0.16
No - Condomless Sex	50/153 (32.7%)	Ref			52/161 (32.3%)	Ref		
Overall	114/307 (37.1%)				111/317 (35.0%)			

[Pre-specified sub-analyses among MSM in China]

Conclusions: We provide proof of principle for using crowdsourcing as a tool to enhance community engagement and improve HIV testing services. Crowdsourcing may be a cost-effective method to optimize HIV interventions, especially interventions targeting young key populations.

TUAD0105LB

The Effect of a Population-Based Health Department Data-to-Care Intervention to Increase HIV Care Engagement and Antiretroviral Use: A Controlled Evaluation

J.C. Dombrowski[1,2], J.P. Hughes[3], S.E. Buskin[2,4], J.M. Simoni[5], D. Katz[1,2], M. Fleming[2], A. Nunez[2], M.R. Golden[1,2,4]

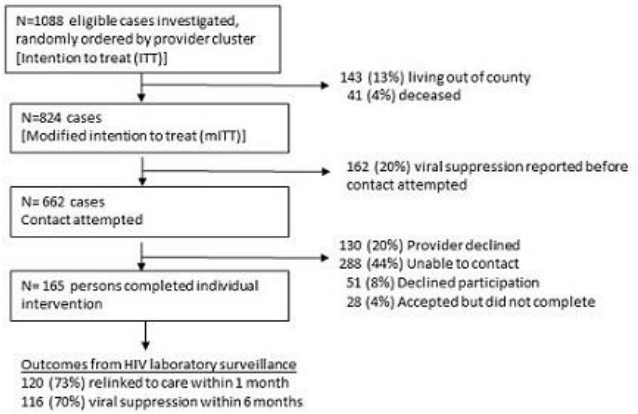
[1]University of Washington, Medicine, Seattle, United States, [2]Public Health - Seattle & King County, HIV/STD Program, Seattle, United States, [3]University of Washington, Biostatistics, Seattle, United States, [4]University of Washington, Epidemiology, Seattle, United States, [5]University of Washington, Psychology, Seattle, United States

Background: The US CDC promotes the use of HIV surveillance data to identify out-of-care persons and return them to care ("Data-to-Care")

Methods: We used stepped wedge cluster randomization to institute a Data-to-Care program in Seattle-King County, Washington, USA. We attempted to provide the intervention to all eligible persons in the county, initiated in a randomly assigned order based on cases' medical provider (the cluster). Eligible persons had 1) no CD4 or viral load (VL) reported for ≥12 months or 2) VL >500 and CD4 < 350 at last report. Program staff contacted patients to offer assistance relinking to HIV care and treatment. The primary study outcome was time to viral suppression (first VL< 200 reported to surveillance), starting from the program implementation date. The secondary outcome was care relinkage (first VL or CD4 reported). We used Cox Proportional Hazards to compare outcomes during control periods (before initiation of each case's provider cluster) to intervention periods (after initiation of the cluster). We censored cases at the time of ascertainment of relocation or death, or end of the observation period. The intention-to-treat (ITT) analysis included all eligible cases; the modified ITT (mITT) analysis excluded cases found to have died or moved.

Results: The ITT and mITT analyses included 1008 and 824 persons, respectively (Figure). Study staff provided the individual intervention to 165 persons, of whom 73% relinked to care within 1 month and 70% achieved viral suppression within 6 months. The incidence rate (IR) of viral suppression was higher during the intervention vs. control periods, but the difference was not statistically significant (Table). The HR associated with the intervention was higher among persons with last VL>500 in the past year than persons with no labs in the past year.

Conclusions: Data-to-Care programs can relink some persons to HIV care, but the effect of these programs may be limited by the large numbers of persons who have moved, died or cannot be reached, and the rate of relinkage to care in the absence of the intervention. Focusing on persons with recently reported unsuppressed viral loads rather than a gap in lab reports may be more effective and efficient.



[Flowchart of Program Implementation]

Population, Outcome	% Achieved by End of Observation Period	Hazard Ratio (95% CI) of Incidence Rates in Intervention vs. Control Period
Total Population, Viral Suppression		
ITT Analysis (N=1008)	30%	1.27 (0.89 - 1.80)
mITT Analysis (N=824)	37%	1.18 (0.83 - 1.68)
No labs for 12 months, Relinkage		
mITT Analysis (N=276)	47%	0.99 (0.74 - 1.34)
No labs for 12 months, Viral Suppression		
mITT Analysis (N=276)	28%	0.79 (0.40 - 1.55)
Last VL>500 in past year, Viral Suppression		
mITT Analysis (N=548)	41%	1.4 (0.96 - 2.19)

[Summary of Intention-to-Treat (ITT) and modified I]

TUAD02 Optimizing PMTCT Programme Implementation

TUAD0201

Retaining mother-baby-pairs in care and treatment: the mothers2mothers Mentor Mother Model

K. Schmitz[1], E. Scheepers[2], E. Okonji[2], V. Kawooya[3]

[1]mothers2mothers, Department of Programmes and Technical Support, Cape Town, South Africa, [2]mothers2mothers, Research and Strategic Information, Cape Town, South Africa, [3]mothers2mothers Uganda, Jinja, Uganda

Background: Retaining HIV-positive mothers and their babies in PMTCT care is critical for the elimination of mother-to-child-transmission. mothers2mothers is a peer education and psychosocial support programme operating in six Option B+ countries in Africa. m2m Mentor Mothers are women living with HIV who have recently experienced PMTCT. They are trained and employed to support other mothers and their families through the same process. In 2014 the m2m Mentor Mother Model implemented under the STAR-EC Programme in Uganda was evaluated externally in order to investigate whether maternal and infant PMTCT outcomes and maternal psychosocial well-being outcomes were associated with exposure to m2m Mentor Mothers.

Methods: A quasi-experimental matched area comparison design was used. PMTCT outcomes were measured retrospectively among 2,282 mother-baby-pairs who accessed PMTCT services between January 2011 and March 2014 in 31 intervention facilities (where m2m Mentor Mothers provided peer education and psychosocial support) and 31 matched control facilities (where no peer education and psychosocial support were provided). Furthermore, 796 pregnant women and new mothers accessing PMTCT between June 2012 and March 2014 across both study arms participated in facility based Psychosocial Wellbeing surveys. Bivariate and multivariate inferential statistical analysis was done using STATA 12. Propensity Score Matching was used to investigate the net effect attributable to the m2m standard-of-care.

Results: Comparison of the intervention and control sites indicated that clients in m2m-supported health facilities showed improved uptake of PMTCT services (see Table 1).

Outcome Indicator	Average effects among matched exposed subjects in m2m sites	Average effects among matched unexposed subjects in control sites	PSM Net Effect (Percentage points)	p-Value
Receipt of ARVs /ART for PMTCT among HIV-positive pregnant women	91.8%	95.1%	-3.3	<0.001
ANC attendance at least 4 times during pregnancy among HIV-positive women	49.30%	39.70%	9.6	<0.001
Delivery by skilled health personnel in past 12 months among HIV-positive women	87.10%	75.80%	11.3	<0.001
Retention in care among HIV-positive women 12 months after ART initiation	90.90%	63.60%	27.3	<0.001
Receipt of Nevirapine suspension at birth by HIV-exposed babies (ART prophylaxis for PMTCT)	86.00%	59.00%	27	<0.001
Percentage of HIV-exposed children who were given a PCR test at 6 weeks after birth	71.50%	45.80%	25.8	<0.001
Percentage of HIV-exposed children who were given an HIV test 6 weeks after cessation of breast feeding	60.50%	31.40%	29.4	<0.001
Percentage of HIV-exposed children who were given an HIV test 18 months after delivery	60.20%	18.10%	42.1	<0.001
Linkage of HIV-positive babies to pediatric ART	60.90%	27.80%	33	<0.001

[Table 1: Comparison of PMTCT outcomes]

The m2m model was further associated with increased coping self-efficacy (86.6% vs 64.5%, p< 0.001); coping behaviour (69.4% vs 56.9%, p<0.001); HIV disclosure and safer sex self-efficacy (71.7% vs 50.7%, p< 0.001); and reduction in the experience of depression (83.5% vs 78.1%, p=0.028).

Conclusions: m2m has developed and refined a simple, scalable, adaptable and sustainable model of peer education and psychosocial support that improves uptake of PMTCT services and addresses the challenges facing HIV-positive pregnant women and mothers. The evidence shows that m2m's psychosocial peer support helps HIV-positive pregnant women and new mothers and their families cope more effectively with HIV and enhances their psychosocial wellbeing. Integration of peer education and psychosocial support into clinical PMTCT standard-of-care is recommended.

TUAD0202

Effectiveness of conditional cash transfers to increase retention in care and adherence to PMTCT services: a randomized controlled trial

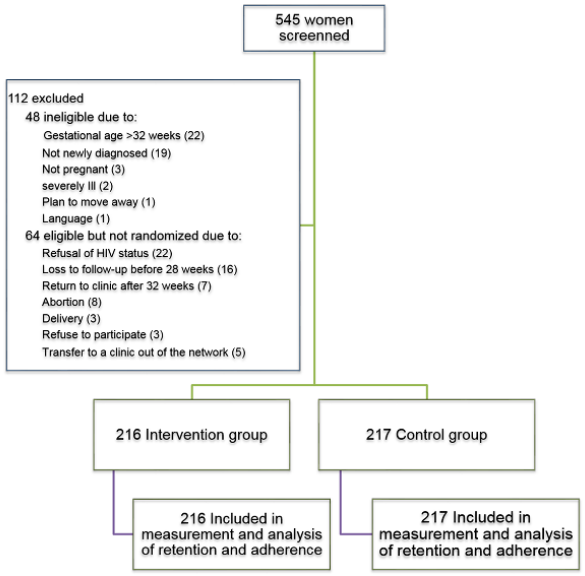
M. Yotebieng[1,2], H. Thirumurthy[3], K.E. Moracco[4], B. Kawende[5], J.L. Chalachala[5], L.K. Wenzi[5], N.L.R. Ravelomanana[2], A. Edmonds[2], D. Thompson[2], E. Okitolonda[5], F. Behets[2]
[1]Ohio State University, College of Public Health, Columbus, United States, [2]University of North Carolina at Chapel Hill, Department of Epidemiology, Chapel Hill, United States, [3]University of North Carolina at Chapel Hill, Department of Health Policy and Management, Chapel Hill, United States, [4]University of North Carolina at Chapel Hill, Department of Health Behavior, Chapel Hill, United States, [5]University of Kinshasa, School of Public Health, Kinshasa, Congo, Democratic Republic of the
Presenting author email: yotebieng.2@osu.edu

Background: Novel strategies are needed to increase retention in, and adherence to prevention of mother-to-child HIV transmission (PMTCT) services, and ultimately enhance PMTCT implementation effectiveness in sub-Saharan Africa.

Objective: To determine whether small, increasing cash payments conditioned on attending scheduled clinic visits and receiving proposed services can increase the proportion of HIV-infected pregnant women who attend PMTCT visits and adhere to available PMTCT services through six weeks postpartum.

Methods: Newly diagnosed HIV-infected women, ≤32 weeks pregnant, were recruited at antenatal care clinics in Kinshasa, Democratic Republic of Congo, and randomly assigned in a 1:1 ratio to an intervention group that received compensation on the condition they attend scheduled clinic visits and accept offered PMTCT services ($5 plus $1 increment at each subsequent visit) or to a control group that received usual care. Outcomes assessed included: retention in care measured by loss-to-follow-up (LTFU), and adherence to PMTCT services (attend all scheduled clinic visits and accept proposed services) through six weeks postpartum. Analysis was by intention to treat. The study is registered with clinicaltrials.gov: NCT01838005.

Results: Between April 2013 and August 2014, 612 potential participants were identified, 545 were screened, and 433 were enrolled and randomized (Figure 1). Participants in the two groups had similar characteristics at baseline. As of January 5, 2015, 407 had completed their six week postpartum visit or were no longer in care. Analysis of complete data showed that by six weeks postpartum, a lower proportion of participants in the intervention group (17.7%) than the control group (27.0%) were LTFU (unadjusted odds ratio (OR), 0.58; 95% confidence interval (CI), 0.36-0.94). Similarly, a higher proportion of participants in the intervention group (70.0%) than the control group (54.5%) attended all scheduled visits and accepted proposed services (OR=1.91; 95% CI, 1.21-2.87). Results were similar after adjusting for marital status, age, and education (Table 1).



[Figure 1. Participants Tree]

		Study Group		Odds Ratio (95% CI)			
	Overall n (%)	Intervention n (%)	Control n (%)	Unadjusted	P-value	Adjusted	P-value
Loss to follow-up							
Yes	91 (22.36)	36 (17.73)	55 (26.96)	0.58 (0.36, 0.94)	0.0255	0.58 (0.36, 0.93)	0.0235
No	316 (77.64)	167 (82.27)	149 (73.04)				
Attendance of each clinic visit and received services							
Yes	254 (63.41)	142 (69.95)	112 (54.90)	1.91 (1.27, 2.87)	0.0017	1.97 (1.30, 2.97)	0.0013
No	153 (37.59)	61 (30.05)	92 (45.10)				

[Table 1. Effect of conditional cash compensation]

Conclusions: Among newly diagnosed HIV-infected women, small, incremental cash incentives resulted in increased retention along the PMTCT cascade and adherence to available services. The overall effects of these incentives on HIV-free survival and cost-effectiveness warrant further investigation.

TUAD0203

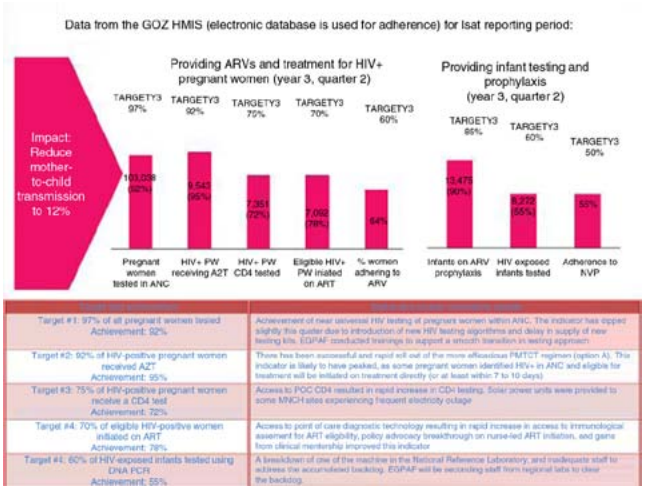
Using the critical path for rapid expansion and optimization of a PMTCT program towards elimination of new HIV infections in children

R. Musarandega[1], A. Mahomva[1], J. Robinson[2], E. Tumbare[1], P. Dave Sen[3], A. Hakobyan[4], A. Mushavi[5]
[1]Elizabeth Glaser Pediatric AIDS Foundation, Technical Department, Harare, Zimbabwe, [2]Elizabeth Glaser Pediatric AIDS Foundation, Global, Washington DC, United States, [3]Children's Investment Fund Foundation, Health Portfolio, London, United Kingdom, [4]Children's Investment Fund Foundation, Performance Measurement, London, United Kingdom, [5]Ministry of Health and Child Care, AIDS and TB Unit, Harare, Zimbabwe
Presenting author email: rmusarandega@pedaids.org

Background: Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) partnered with the Children's Investment Fund Foundation (CIFF) and Zimbabwe Ministry of Health and Child Care (MOHCC) to roll out the WHO 2010 and later 2013 PMTCT guidelines. EGPAF, MOHCC

and CIFF developed a "critical path" with a prioritised set of performance indicators, with population-based targets, that are the main drivers of impact. The indicators are reviewed quarterly, as they largely draw on routine monitoring data. If performance is lagging in a particular indicator, a diagnosis is undertaken to identify the reason, and corrective action explored. Critical path indicators and results for quarter 2, 2012 are in Figure 1. The EGPAF-CIFF goal was to reduce mother-to-child transmission (MTCT) of HIV from about 25% in 2009 to less ~9% by 2015.

Methods: Health facilities were supported to implement the guidelines through training and mentoring during site support visits, among other assistance. PMTCT data were collected quarterly from all supported health facilities, and performance of each indicator compared with established targets during data-driven program reviews held by EGPAF, partner program officers and MOHCC district staff. Reasons for under-performance and improvement strategies were identified and implemented in subsequent quarters through mentoring and coaching of health facility staff to improve service provision and patient follow-up.



[Fig. 1 PMTCT Critical Path]

Results: By October 2014, EGPAF was supporting 1,480 out of 1,560 sites to provide WHO 2013 PMTCT guidelines (Option B+). Service uptake in all critical path indicators increased significantly (p< 0.001) from 2009/10 to 2013/14 as follows: ANC bookings 68% - 100%, HIV testing 85% - 98%, AZT prophylaxis 32% - 91%, CD4 testing 41% - 67%, ART initiation for pregnant mothers 18% - 85%, EID 13% - 71%, mothers' adherence on ARV prophylaxis 34% - 77%. The national MTCT rate fell to ~9.0% in 2013.

Conclusions: Through use of the critical path cascade, EGPAF and CIFF supported the MOHCC to achieve a rapid scale-up of PMTCT services. There is a need to maintain coverage and quality PMTCT services and ensure that children needing ART are actively identified, started and maintained on treatment. EGPAF is intensifying support in these new areas.

TUAD0204

Attrition from antiretroviral treatment services among pregnant and non-pregnant patients following adoption of Option B+ in Haiti

J.W. Domercant[1], N. Puttkammer[2], L. Lu[3], K. Francois[4], D. Duncan[5], R. Grand'Pierre[4], D. Lowrance[1], M. Adler[5]
[1]Centers for Disease Control and Prevention, Port au Prince, Haiti, [2]International Training and Education Center for Health, Seattle, United States, [3]Eagle Applied Sciences, Atlanta, United States, [4]Ministry of Health of the Government of Haiti, Port au Prince, Haiti, [5]Centers for Disease Control and Prevention, Division of Global HIV/AIDS, Atlanta, United States
Presenting author email: viw5@cdc.gov

Background: Attrition from antiretroviral treatment (ART) services is an important determinant of HIV treatment outcomes. This study assessed factors associated with attrition among pregnant and non-pregnant patients initiating ART following adoption of Option B+ (universal ART eligibility for HIV-infected pregnant women) in October 2012 in Haiti.

Methods: Electronic medical records of adult patients initiated on ART from October 2012 to August 2014 at 73 health facilities (HF) from 8 of 10 Haitian administrative departments were analyzed. Within a survival analysis framework, attrition was defined as the first instance of failure to attend a HF visit for 90 days after a missed clinical or pharmacy-dispensing appointment, or an officially-recorded program discontinuation, whichever came first. Known transfers to alternative HF were treated as censored observations, not attrition cases. ART initiations during or within 12 weeks after pregnancy were deemed Option B+ cases. The Kaplan-Meier method and Cox proportional hazards regression, stratified by HF, were used to determine attrition and associated factors.

Results: Among 17,084 patients who initiated ART, 7,719 (45.2%) were non-pregnant women, 5,920 (34.7%) were men and 3,445 (20.2%) were pregnant women. At 6 months, attrition was 15.6% (95% confidence interval (CI): 14.8-16.4) for non-pregnant women, 17.0% (16.1-18.0) for men, and 30.1% (28.5-31.7) for pregnant women. At 12 months, attrition was 31.8% (95% CI: 30.6-33.0), 34.5% (33.2-35.9), and 50.8% (49.0-52.6) respectively. Adjusted for patient-level factors and HF, attrition risk was 63% higher among pregnant women and 16% higher among men, compared to non-pregnant women (p< 0.001). Significant protective factors included: receiving psychosocial counseling (hazard ratio (HR): 0.84, p< 0.001); cotrimoxazole prophylaxis (HR: 0.83, p< 0.001); tuberculosis treatment (HR: 0.88, p< 0.001) before ART initiation; having an HIV-positive household member (HR: 0.80, p< 0.05); living in the same commune as the HF (HR: 0.94, p< 0.05), and greater duration of pre-ART enrollment (HR: 0.99 for each 30-day increase, p< 0.001).

Conclusions: Following adoption of Option B+, ART attrition in Haiti was higher than that described in published reports from other resource-limited settings. Early, sustained, and tailored interventions are urgently needed to reduce ART attrition in Haiti, particularly among pregnant women.

TUAD0205

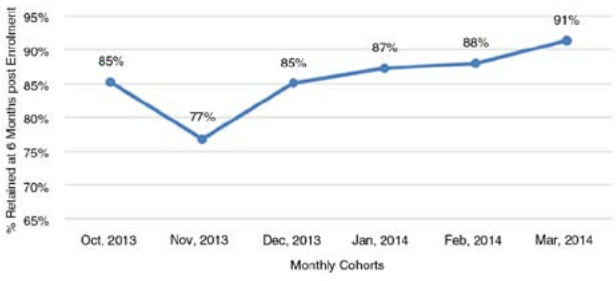
Evaluation of early experience implementing Option B+ in the northwest and southwest regions of Cameroon 2013-2014

P.M. Tih[1], E. Katayi[2], E. Mboh[2], E. Bonje[1], E. Lem[1], J.C. Awa[1], J.R. Lim[3,4], D. Duncan[5], L. Petit[6], F. Bianchi[6], T. Welty[1], M.N. Achu[7], G. Tayong[8], G. Tene[4,9], J.J. Mosoko[4], O. Bolu[4]
[1]Cameroon Baptist Convention Health Services, Bamenda, Cameroon, [2]Cameroon Baptist Convention Health Services, Mutengene, Cameroon, [3]Association of Schools and Programs of Public Health/U.S. Centers for Disease Control and Prevention Allan Rosenfield Global Health Fellowship, Washington, DC, United States, [4]U.S. Centers for Disease Control and Prevention, Yaounde, Cameroon, [5]U.S. Centers for Disease Control and Prevention, Atlanta, United States, [6]Elizabeth Glazer Pediatric AIDS Foundation, Washington, DC, United States, [7]Ministry of Public Health, Department of Disease Control, District Health Service, Kumba, Cameroon, [8]Ministry of Public Health, Department of Disease Control, District Health Service, Bamenda, Cameroon, [9]QED Group, LLC, Washington, DC, United States
Presenting author email: piustih@cbchealthservices.org

Background: The Cameroon Ministry of Public Health began implementation of life-long antiretroviral treatment (ART) for HIV-positive pregnant and breastfeeding women (Option B+) in 2013. This evaluation assesses early ART acceptability, retention, and Mother-to-child-transmission. Results will guide subsequent phases of the national rollout.

Methods: From October, 2013 - June, 2014, we recruited participants from 22 purposefully selected health facilities in the Northwest and Southwest Regions for an observational cohort evaluation. HIV-positive pregnant and breastfeeding women, not currently on antiretrovirals (prophylaxis or treatment), were eligible to participate in the assessment. Option B+ was offered to all eligible participants and a descriptive analysis was performed.

Results: Of 1,267 HIV-positive pregnant or breastfeeding women identified, 669 (53%) were eligible for the evaluation. Of those who were offered Option B+, 666 (99%) accepted life-long ART and 3 (< 1%) accepted ART only during pregnancy and breastfeeding. As of October 2014, 569 (85%) women remained alive and on treatment; 8 (1.2%) died, 17 (3%) discontinued ART and 34 (5%) were lost to follow-up. 56 (8%) did not return for their first refill after ART initiation; this percentage varied from 2% to 8% between facilities. The six month retention for monthly cohorts of women initiating Option B+ was 77%-91% (Figure 1). Of 409 infants born to the 669 women enrolled, 8 (2%) died, 3 (< 1%) were lost to follow-up. 403 (99%) received NVP prophylaxis within 72 hours of birth. By 8 weeks post-partum, 342 (89%) were tested for HIV deoxyribonucleic-acid, 9 (3%) received a positive result. The remaining infants are not yet old enough for HIV status determination. All HIV-infected infants initiated ART.



[Figure 1. Proportion of patients on ART Option B+ retained six months after treatment]

Conclusions: In Cameroon, Option B+ is highly accepted by HIV-positive pregnant and breastfeeding women and can achieve a high 6 month retention rate. Long term retention, mortality and final Mother-to-child-transmission after cessation of breastfeeding need further evaluation.

TUAD0206LB

Improving early ANC attendance through community engagement and dialogue: project ACCLAIM in three African countries

M.P. Kieffer[1], G. Woelk[1,2], D. Mpofu[3], R. Cathcart[1], ACCLAIM Study Group
[1]Elizabeth Glaser Pediatric AIDS Foundation, Washington, United States, [2]The University of North Carolina at Chapel Hill, Gillings School of Global Public Health, Dept of Health Behavior and Health Education, Chapel Hill, United States, [3]Elizabeth Glaser Pediatric AIDS Foundation, Mbabane, Swaziland

Background: Timing of first antenatal clinic (ANC) attendance in sub-Saharan Africa averages 24-25 weeks; however, to effectively prevent HIV transmission to infants, earlier ANC attendance and initiation of antiretroviral therapy are necessary.
Advancing Community Level Action for Improving Maternal and Child Health (MCH)/Prevention of Mother-to-child HIV Transmission (PMTCT), known as ACCLAIM, a three-arm randomized trial in 45 clusters across Swaziland, Uganda and Zimbabwe, aims to improve access, uptake and retention in MCH/PMTCT services.
Methods: The study randomized clusters and evaluated three interventions:
1) Community Leader Engagement (participation in the *Community Leaders Institute*, mentoring to engage in community action);
2) Community Days and dialogues (community event with structured dialogues on MNCH/PMTCT, and provision of health services); and
3) Male and Female MCH Classes (set of four structured sessions led by peer facilitators).
This sub-study analyzed early ACCLAIM results on earlier access to ANC services. Baseline gestational age (GA) data at first ANC visit were collected from health facilities before implementation and quarterly after implementation. We compared proportions of women attending ANC during first half of pregnancy (≤20 weeks gestation) at baseline and 6-12 months after interventions.
Results: 277 trained community leaders held >7,000 community meetings and engaged >27,000 individuals in dialogues at Community Days, identifying and addressing barriers, misperceptions and harmful gender norms. The proportion of women attending ANC ≤20 weeks gestation across the three countries increased by 36% from baseline; this trend was significant across the quarters observed (p< 0.0001).
Attendance during the first trimester (≤12 weeks) also increased, from 11.7% (84/719) to 14.1% (102/721) in Swaziland (p=0.163), and from 3.4% (24/705) to 12.0% (97/809) (p<0.0001) in Zimbabwe (Uganda data not available). Community dialogues actively focused on the benefits of early ANC and addressed norms of waiting until the woman "shows" before seeking ANC.

Gestational age at first ANC	Baseline July-September 2013 (January-March 2014, Uganda) n= 5071	6-12 months of implementation October-December, 2014 n= 4799	p-value
<=20 weeks	1532 (30.2%)	1975 (41.2%)	p <0.0001
21+ weeks	3539 (69.8%)	2824 (58.8%)	

[Change in Gestational Age at First Antenatal Care]

Conclusions: In our study, community based interventions have resulted in significant greater than one-third increase in ANC ≤20 weeks gestation in three African countries. Ongoing data analysis will provide data on the full potential of open community dialogues by trained community leaders to change community norms and health-seeking behaviors such as early access to ANC and MCH/PMTCT services.

Tuesday 21 July

Oral Poster Discussions

TUPDA01 Restricting the Virus inside and out

TUPDA0101

Association between CSF and peripheral markers of immune-activation/inflammation and elevated intrathecal HIV-RNA levels in a cohort of HIV-infected antiretroviral naïve individuals

E. Merlini[1], F. Iannuzzi[1], F. Bai[1], M. Trunfio[1], S. Bonora[2], A. Calcagno[2], E.S. Cannizzo[1], M. Basilissi[1], T. Bini[1], A. d'Arminio Monforte[1], G. Marchetti[1]
[1]*University of Milan, Health Sciences, Milan, Italy,* [2]*University of Turin, Turin, Italy*
Presenting author email: esther.merlini@unimi.it

Background: Since the association between high HIV-RNA replication in central nervous system and immune activation/inflammation has not yet been established, we aimed to investigate the inflammatory *milieu* in CSF and peripheral blood of HIV+ antiretroviral-naïve subjects with high CSF viremia compared to those with low CSF viremia, in the attempt to identify biomarkers that might be used as diagnostic tools.
Methods: 150 HIV+ cART-naïve pts underwent to lumbar puncture for CSF HIV-RNA quantification and were tested for peripheral T-cell immune-phenotypes (CD38/CD45RA/CD45R0/CD127 on CD4/CD8; flow cytometry). In a subgroup of 64 patients CSF/plasma TNF-a, IL-6, sCD14, IFNg, MCP-1, IP-10, neopterin, S100beta (ELISA, Luminex) were measured. We defined: high CSF HIV-RNA ≥10.000cp/ml (H-CSF), low CSF HIV-RNA < 10.000cp/ml (L-CSF), viral escape (VE) CSF/plasma HIV-RNA >1 $\log_{10}$ cp/mL. Statistical analyses: Chi-square, Mann Whitney test and univariate/multivariate logistic regression.
Results: 48/150 pts (32%) resulted H-CSF. VE was found in 5/150 pts (3%). No differences in gender, risk exposure categories, viral hepatitis co-infections, HIV duration, age and CD4+ nadir were found between L-CSF and H-CSF. H-CSF pts displayed higher plasma HIV-RNA (p=0.002) and VE (p=0.019). The univariate logistic regression showed that H-CSF are characterized by lower central memory CD127+CD4% (p=.026) and naïve CD8+CD45RA% (p=.017) and higher activated CD8+CD38%(p=.08) and memory activated CD8+CD38+CD45R0% (p=.021). In multivariate analysis, lower proportion of CD8+CD45RA% was the only parameter independently associated with H-CSF (AOR 0.934, IC95% 0.877-0.995, p=0.035), adjusting for plasma VL, CD4/CD8 ratio, CD127/CD4%,CD8/CD38%. Within the CSF, we found that H-CSF displayed significantly higher sCD14 (p< .0001), neopterin (p=.006), IL-6 (p=.002) and IP-10 (.035) and no differences in TNFa, MCP-1 and S100beta. Similarly, H-CSF showed higher circulating sCD14 (p< .0001), but not TNFa, IL-6 and IFNg.
Conclusions: The low percentage of naïve CD8+ T-cells, independently associated with higher CSF Viral Load, might be included in a panel of biomarkers useful to identify patients at major risk of high CSF replication, if confirmed by larger studies.
Besides, the finding of higher peripheral and CSF activation/inflammation in H-CSF group indicate a more complex scenario, where both districts cooperate in maintaining the inflammation within CNS, possibly affecting neuronal function, and therefore deserves further investigations.

TUPDA0102

Receptor mediated endocytosis directs subcellular trafficking and TLR signaling of HIV-1 in plasmacytoid dendritic cells

M. O'Brien[1], O. Manches[2], C. Wilen[3], V. Wu[2], N. Sunseri[4], N. Bhardwaj[2]
[1]*Icahn School of Medicine at Mount Sinai, Medicine, New York, United States,* [2]*Icahn School of Medicine at Mount Sinai, New York, United States,* [3]*Washington University School of Medicine, St. Louis, United States,* [4]*University of Chicago, Chicago, United States*
Presenting author email: mpowersobrien@yahoo.com

Background: Dysregulated type I interferon (IFN) responses contribute to immunopathology in chronic HIV infection, therefore it is critical to dissect the molecular mechanisms underlying HIV-stimulated IFN production. We examined the spatiotemporal regulation of IFN secretion by plasmacytoid dendritic cells (pDC), specialized cells that secrete high levels of IFN upon HIV recognition by Toll-like receptor (TLR) 7. We showed previously that intracellular trafficking of HIV to early endosomes is associated with potent IFN secretion but minimal NF-kB signaling, resulting in suboptimal pDC maturation; however, how HIV trafficking is determined and the causal link between HIV subcellular localization and differential TLR signaling are currently unknown.
Methods: Human pDC were purified from peripheral blood and were stimulated with GFP labeled: HIV, HIV pseudotyped with influenza hemagglutinin envelope (HA-HIV), and PR8 influenza. TLR7 expressing HEK NF-kB reporter cells, stably transfected with CD4 mutants with cytoplasmic tails directing trafficking to early endosomes (EE) or lysosomes, were activated with HIV and controls. Analysis included ELISA, flow cytometry and florescent microscopy. Cells were imaged using the Advanced Precision imaging system and images were analyzed using ImageJ.
Results: We compared the effects and spatiotemporal trafficking in pDC of HIV, influenza, and HA-HIV. We demonstrate that HA-HIV strongly activates maturation pathways (NF-kB) in pDC and traffics rapidly to lysosomes, similarly to influenza but unlike HIV, suggesting that viral envelope directs trafficking and resultant phenotype of ssRNA virions in pDC. We studied HIV-CD4 interactions in a HEK reporter cell system expressingTLR7 with functional NF-kB signaling, which we co-transfected with CD4 mutants whose cytoplasmic tails either directed CD4 trafficking to EE or lysosomes. We show that wild type (WT) CD4 localizes to EE, whereas CD4 mutated with either DEC-205 or LAMP1 tail localizes to lysosomes. HIV traffics to EE in WT CD4 expressing TLR7 HEK cells and fails to stimulate NF-kB signaling, whereas HIV traffics to lysosomes in DEC-205/LAMP1 expressing TLR7 HEK cells and stimulates NF-kB signaling, suggesting that rerouting of HIV (via CD4) to lysosomal compartments triggers NF-kB rather than IFN pathways.
Conclusions: CD4 receptor mediated endocytosis targeting early endosomes determines HIV intracellular localization and observed interferon-producing phenotype of HIV-activated pDCs.

TUPDA0103

HIV-1 Vpu exploits the crosstalk between BST2 and the ILT7 receptor to inhibit innate sensing of infected T cells by plasmacytoid dendritic cells

M.G. Bego[1], É.A. Côté[1], N. Aschman[2], J. Mercier[1], W. Weissenhorn[2], É.A. Cohen[1,3]
[1]*Institut de Recherches Cliniques de Montréal, Montréal, Canada,* [2]*Université Grenoble Alpes, Unit of Virus Host Cell Interactions, Grenoble, France,* [3]*Université de Montréal, Microbiology, Infectiology and Immunology, Montreal, Canada*
Presenting author email: eric.cohen@ircm.qc.ca

Background: Plasmacytoid dendritic cells (pDCs) constitute a major source of type-I interferon (IFN-I) production during acute HIV infection. Their activation results primarily from TLR7-mediated sensing of HIV-infected cells. BST2/Tetherin is a restriction factor that suppresses HIV release by cross-linking virions at the cell-surface. HIV-1 overcomes BST2 antiviral activity through Vpu, which partially downregulates BST2 cell-surface expression. Apart from its direct antiviral activity, BST2 was shown to bind the ILT7 pDC-specific inhibitory receptor and repress IFN-I production by activated pDCs. Here, we examined whether Vpu-mediated BST2 antagonism could modulate innate sensing of HIV-infected cells by pDCs.
Methods: PBMCs or isolated pDCs were co-cultured with T cells infected with wild type or Vpu-defective HIV-1 and innate sensing was evaluated by monitoring IFN-I production. BST2-mediated activation of ILT7 signaling was analyzed using an ILT7-reporter cell system.
Results: We show that Vpu attenuates the production of IFN-I during sensing of HIV-1 infected cells by pDCs. This control of innate sensing by Vpu could be prevented by: 1) depletion of BST2 from infected donor cells; 2) depletion of ILT7 in pDCs; or 3) blocking BST2-ILT7 interaction using anti-BST2 antibodies or soluble ILT7. Using a BST2 mutant that cannot cross-link budding virions but yet retains the capacity to repress IFN-I production by pDCs, we show that virion trapping on infected donor cells prevents BST2 from eliciting an inhibition of IFN-I production by pDCs. Interestingly, confocal microscopy analysis of virus producing cells reveals that in presence of Vpu there is a residual pool of surface BST2, which is excluded from viral budding sites and thus potentially accessible for interaction with ILT7 on pDCs. Lastly, using an ILT7 reporter cell system, we provide evidence that Vpu-mediated BST2 antagonism modulates the levels of available surface BST2 capable of engaging and activating ILT7 upon cell-to-cell contact.
Conclusions: Overall, this study sheds light on a novel Vpu-BST2 interaction that allows HIV to control innate sensing of infected cells by pDCs via the negative signaling exerted by the ILT7-BST2 pair. This mechanism of innate immune evasion is likely to be critical for efficient viral dissemination and establishment of viral reservoirs during acute infection.

TUPDA0104

HIV-1 transcriptional silencing caused by TRIM22 inhibition of Sp1 binding to the promoter

F. Turrini[1,2], A. Kajaste-Rudnitski[1], S.S. Marelli[1], C. Van Lint[3], A.T. Das[4], B. Berkout[4], E. Vicenzi[1]
[1]San Raffaele Scientific Institute, Milan, Italy, [2]Vita-Salute San Raffaele University, Molecular Medicine PhD Program, Milan, Italy, [3]University of Bruxelles, Gosselies, Belgium, [4]Center for Infection and Immunity Amsterdam, Academic Medical Center, University of Amsterdam, Amsterdam, Netherlands
Presenting author email: turrini.filippo@hsr.it

Background: HIV-1 latency is a multifactorial process resulting by the interplay between cellular transcription factors and the viral regulatory protein Tat. We have previously described the interferon-inducible restriction factor TRIM22 as a suppressor of basal and phorbol ester-dependent LTR-mediated transcription independently of NF-kB and of Tat/TAR interaction. As basal HIV-1 transcription is mainly driven by the binding of the cellular transcription factor Sp1, we have investigated whether TRIM22 could interfere with such Sp1-driven transcriptional activation of HIV-1 LTR.
Methods: 293T cells, lacking of endogenous TRIM22, were co-transfected with a TRIM22-expressing plasmid together with reporters vectors driven by the HIV-1 promoter containing either wild-type or mutated Sp1 binding sites or lacking of either one or two sites; reporter expression was assessed 48 hours post-transfection. Endogenous TRIM22 was knocked-down (KD) in SupT1 cells that were subsequently infected with HIV-1 molecular clones engineered to be dependent on an incorporated Tet-On gene expression system for activation of transcription while being independent of Tat/TAR interaction. Virus replication was monitored up to 32 days post-infection. Cell extracts from TRIM22-transfected 293T was subjected to:
i) immunoprecipitation,
ii) Western blotting,
iii) DNA pull-down and;
iv) Chromatin Immunoprecipitation (ChIP).
Results: TRIM22 overexpression suppressed Sp1-driven transcription of HIV-1, as its inhibitory activity was lost in the absence of Sp1 binding sites. In contrast, TRIM22 KD increased the replication of infectious clones that were exclusively dependent upon Sp1 binding to the promoter. Furthermore, immunoprecipitation experiments showed that TRIM22 and Sp1 can interact physically although this interaction does not affect the level of expression of endogenous Sp1 or its phosphorylation state. TRIM22 did not directly bind to the HIV-1 LTR by either *in vitro* pull-down experiments or in ChIP experiments, however TRIM22 expression drastically prevented the binding of Sp1 to the HIV-1 LTR.
Conclusions: TRIM22 inhibits Sp1-dependent transcription by interacting with Sp1 and preventing its binding to the HIV-1 LTR. Our findings bear relevance for the discovery of new pharmacological approaches aimed at targeting the reservoir of cells latently infected with replication-competent proviruses.

TUPDA0105

Polymorphisms in TRIM22 are associated with HIV-2 acquisition and disease progression

S. Simpson[1], T. deSilva[1], L.-M. Yindom[1], A. Leligdowicz[1], T. Vincent[2], S. Rowland-Jones[1]
[1]University of Oxford, Nuffield Department of Medicine, Oxford, United Kingdom, [2]Medical Research Council Unit, The Gambia, Fajara, Gambia
Presenting author email: shmona.simpson@trinity.ox.ac.uk

Background: Tripartite motif-containing protein 22 (TRIM22) is an E3 ubiquitin ligase with activity against HIV-1: high levels of TRIM22 expression are associated with reduced viral set-point following acute HIV-1 infection. The TRIM22 gene has been greatly shaped by positive selection, and its expression is sensitive to retroviral infection, Type I and Type 2 interferon. The mechanism by which TRIM22 exerts its antiviral effect is poorly understood. Further, the impact of TRIM22 genetic variation in the context of HIV-2 disease is unknown.
Methods: To test the hypotheses that TRIM22 expression antagonises HIV-2 infection and that polymorphisms in TRIM22 significantly modulate this effect, we conducted three studies. Firstly, TRIM22 was genotyped in sixty HIV-2 patients, comparing viral controllers and rapid progressors, and a similar number of age and sex matched controls from the same community in rural Guinea-Bissau. Using regression modelling, polymorphisms were analysed alongside immunological and virological data. Secondly, a model of TRIM22 was constructed using computational methods and the polymorphisms observed *in vivo* were mapped and analysed. Finally, baseline cDNA and protein levels of TRIM22 from C8166 cells were measured using quantitative RT-PCR and flow cytometry respectively. The cells were subsequently infected with HIV-2, and measurements repeated to determine whether TRIM22 gene expression is sensitive to HIV-2 infection.
Results: The data show that TRIM22 polymorphisms rs1063303 and rs7935564 are significantly associated with HIV-2 acquisition and disease progression. Further, polymorphisms observed *in vivo* cluster in functional regions that our modelling studies suggest may interact with the HIV-2 capsid. Finally, we show that TRIM22 gene expression is upregulated in the presence of HIV-2, in a lymphocyte cell line.
Conclusions: Taken together, our data show that TRIM22 expression is sensitive to HIV-2 infection and that polymorphisms in TRIM22 genes are significantly associated with HIV-2 acquisition and disease progression. Further the study has computationally characterised positively selected polymorphisms observed in vivo and the data show that these polymorphisms have the potential to significantly alter protein structure and function. These data provide the first analysis of TRIM genetic variation in the context of HIV-2 infection.

TUPDA0106LB

The negative checkpoint receptor TIGIT marks exhausted T cells during SIV infection and correlates with SIV disease progression

G.M. Webb[1], G.M. Chew[2], T. Fujita[3], B.J. Burwitz[1], H.L. Wu[1], J.S. Reed[1], K.B. Hammond[1], S.G. Hansen[1], M. Maurer[4], A.J. Korman[4], L.C. Ndhlovu[2], J.B. Sacha[1]
[1]Oregon Health & Science University, Vaccine & Gene Therapy Institute and Oregon National Primate Research Center, Beaverton, United States, [2]John A. Burns School of Medicine, University of Hawaii, Hawaii Center for HIV/AIDS, Department of Tropical Medicine, Honolulu, United States, [3]Tohoku University Graduate School of Medicine, Department of Microbiology and Immunology, Sendai, Japan, [4]Biologics Discovery California, Bristol-Myers Squibb, Redwood City, United States

Background: During chronic viral infections, high antigenic load continually stimulates T cells resulting in T cell exhaustion. Exhausted T cells increase expression of negative checkpoint inhibitors such as PD-1, which raise the threshold for activation and contribute to suppressed immune responses. Another recently discovered immune checkpoint receptor, TIGIT, is up-regulated on T cells in neoplasms and chronic LCMV infection.
We hypothesize that TIGIT functions as a negative checkpoint receptor marking dysfunctional T cells during SIV infection, and that modulation of TIGIT would restore anti-SIV-specific T cell responses.
Methods: Spleen, lymph node (LN) and PBMCs from SIV-naïve and SIV-infected rhesus macaques (RMs) were examined for surface expression of TIGIT. In vitro cytokine production was assessed via intracellular cytokine staining. Proliferative capacity was determined through CFSE dilution assays in the presence of antibodies blocking TIGIT and PD-1 pathways (anti-TIGIT mAb and anti-PD-L1 mAb).
Results: TIGIT expression was significantly up-regulated on $CD8^+$ T cells derived from the spleen and LN, but not PBMC in SIV-infected animals. The frequency of $TIGIT^+$ $CD8^+$ T cells in the LN significantly correlated with SIV viral load, and TIGIT expression was driven primarily by g-chain cytokines such as IL-2. TIGIT was expressed on ~40% of SIV-specific $CD8^+$ T cells, even in animals with full cART suppression of viral replication. While Ki-67 expression did not differ between $TIGIT^+$ and $TIGIT^-$ $CD8^+$ T cells, $TIGIT^-$ $CD8^+$ T cells produced significantly more IFN-g compared to $TIGIT^+$ $CD8^+$ T cells. Single and dual blockade of TIGIT and/or PD-1 signaling pathways restored proliferative capacity of SIV-specific T cells in vitro.
Conclusions: TIGIT is a negative checkpoint receptor that marks a novel population of functionally exhausted SIV-specific $CD8^+$ T cells and is associated with SIV disease progression. The enhancement of virus-specific T cell proliferative responses in the presence of single or dual blockade of TIGIT and/or PD-1 suggests that targeting the TIGIT pathway is a viable therapeutic approach to reverse T cell dysfunction. Given the high sequence homology of rhesus and human TIGIT, this provides a platform to further investigate TIGIT, along with other checkpoint inhibitors, as potential targets for mediating a functional cure for HIV.

TUPDB01 Complications: ART at Work

TUPDB0101

Prolongation of QTc interval in HIV-infected individuals compared to the general population is not caused by antiretroviral therapy

S. Esser[1], M.H.M. Geisel[2], M. Arendt[2], C. Schulze[3], V. Holzendorf[4], A. Warnke[1], N.H. Brockmeyer[5], M. Hower[6], D. Schadendorf[1], T. Neumann[3], L. Eisele[2], R. Erbel[3], S. Moebus[2], K.-H. Jöckel[2], N. Reinsch[3], HIV HEART Study Group and Heinz Nixdorf Recall Investigative Group
[1]University of Duisburg Essen, Department of Dermatology and Venerology, Essen, Germany, [2]University of Duisburg Essen, Institute for Medical Informatics, Biometry and Epidemiology (IMIBE), Essen, Germany, [3]University of Diusburg Essen, West German Heart Centre, Department of Cardiology, Essen, Germany, [4]Clinical Trial Centre Leipzig, University Leipzig, Coordination Centre for Clinical Trials (ZKS Leipzig - KKS), Leipzig, Germany, [5]Ruhruniversity Bochum, Clinic of Dermatology, Venerology and Allergology, Department of Sexual Health and Medicine, Bochum, Germany, [6]City Hospital Dortmund, Internal Medicine, Dortmund, Germany
Presenting author email: stefan.esser@uk-essen.de

Background: Prolongation of the QTc interval (QTc) increases the risk of cardiovascular events (CVE). The incidence of CVE is higher in HIV-infected (HIV+) patients compared with the general population. The impact of different antiretroviral therapies (ART), co-medication and HIV-infection on the electrical activity of the heart is rarely investigated in large HIV+ cohorts.
Methods: We compare QTc of HIV+ outpatients of the HIV HEART study (HIVH) and of controls of the population-based Heinz Nixdorf Recall study (HNR), both recruited from the German Ruhr area since 2000. HIVH cases were age- and sex-matched with HNR controls in a 1:2 ratio. QTc was measured and corrected using the Bazett's formula. We used crude and adjusted linear mixed models to account for the matched design and adjusted for QTc interval prolonging medication (QTc-PM, no ART). Differences in QTc between HIV specific factors and ART were evaluated using ANOVA in the HIVH subpopulation. All analyses were stratified by sex.
Results: 496 HIVH participants (83.3% male, aged 54.5±6.7) were matched with 992 HNR controls. We observed a longer QTc in HIVH subjects compared with HNR controls: 424±23 ms vs 411±15 ms for male and 435±20 ms vs 416±17 ms for female subjects (p< 0.0001 for both sexes). HIVH males used QTc-PM more often (22.3% vs 17.6% for HNR) than HIVH females (13.3% vs 24.7% for HNR). However, adjusting for QTc-PM the mean differences in QTc remained significant with 13 (95%CI: 11;15) ms for male and 19 (95%CI: 14;24) ms for female subjects. Prolongation of QTc (male >440 ms, female >460 ms) was pathologic in 22.8% vs 3.9% of HIVH and HNR males and in 12.1% vs 1.8% of the females. No differences in the QTc were observed within the HIVH population for different ART medications, for the clinical and immunological HIV status and for the route of HIV infection in both sexes.
Conclusions: HIV+ patients have longer mean QTc and more often pathological prolonged QTc compared with age- and sex-matched controls from the general population even after adjustment for intake of non-antiretroviral QTc-PM. ART, HIV stage and HIV transmission route are not associated with QTc prolongation.

TUPDB0102

Favourable effect on vitamin D and bone after switching from Atripla to darunavir/ritonavir: a randomised controlled clinical trial

L. Hamzah[1], J.M. Tiraboschi[2], M. Toby[2], H. Iveson[2], C. Mant[1], C. John[1], K. Burling[3], R. Kulasegaram[2], A. Teague[2], F.A. Post[4], J. Fox[2], MIDAS Study Group
[1]King's College London, London, United Kingdom, [2]Guys and St Thomas' NHS Foundation Trust, London, United Kingdom, [3]Cambridge University NHS Foundation Trust, Cambridge, United Kingdom, [4]King's College Hospital NHS Foundation Trust, London, United Kingdom
Presenting author email: lisa.hamzah@kcl.ac.uk

Background: Efavirenz has been associated with reductions in vitamin D (25[OH]D) and Tenofovir with increased bone turnover, reductions in bone mineral density (BMD), and renal tubular dysfunction (RTD).
We hypothesized that switching from Atripla to Darunavir/Ritonavir monotherapy (DRV/r) might increase 25[OH]D, and improve BMD and RTD.
Methods: Patients with HIV RNA < 50 copies/mL on Atripla for ≥ 6 months were randomized 1:1 to receive ongoing Atripla or DRV/r (800/100 mg once daily) for 48 weeks. Primary endpoint was change from baseline in 25[OH]D at week 48. Secondary endpoints included changes in BMD, bone turnover markers and RTD. Linear regression estimated the mean difference in 25[OH]D in patients on Atripla vs. DRV/r. Secondary endpoints were expressed as the mean (95% CI) observed between-arm difference from baseline.
Results: 70 subjects (86% male, 66% white, mean (SD) CD4 cell count 537.3 (191.5) per mm^3) were randomized, of whom 26 (DRV/r) and 31 (Atripla) completed the 48 week study on the allocated treatment. The mean (SD) difference between baseline and week 48 25[OH]D was 5.0 (5.9) ng/mmol for DRV/r and 1.2 (6.0) for Atripla.
After adjustment for baseline 25[OH]D and demographics, at week 48 DRV/r monotherapy was associated with a +3.5 (95% CI 0.5, 6.4) ng/mmol increase in 25[OH]D compared to Atripla (p=0.02). Subjects in the DRV/r arm experienced increases in BMD (mean between-arm difference (0.02 [0.003, 0.04] g/cm^2 at the lumbar spine, p=0.03, and 0.03 [0.006, 0.06] g/cm^2 at the neck of femur, p=0.02), and reductions in parathyroid hormone (PTH) (-20.4 [-38.8, -2.0] ng/l, p=0.03), bone-specific alkaline phosphatase (-7.1 [-9.7, -4.5]) IU/L, p< 0.0001) and serum type 1 pro-collagen (-16.9 [-26.5, -7.4] ug/L, p=0.0008), as compared with subjects on Atripla.
No significant difference in RTD (urine retinol-binding protein/creatinine ratio and phosphate reabsorption) was observed. Reasons for discontinuation in the DRV/r arm included side effects (n=4) and virus load rebound (n=2), all of which resolved with DRV/r discontinuation or regimen intensification.
Conclusions: A switch from Atripla to DRV/r resulted in significant improvements in 25[OH]D and PTH, and a 2-3% increase in BMD. DRV/r monotherapy provides a bone-friendly treatment option to patients with osteoporosis or increased fracture risk.

TUPDB0103

Long-term bone mineral density changes in antiretroviral-treated HIV-infected individuals

P. Grant[1], D. Kitch[2], G. McComsey[3], A. Collier[4], S. Koletar[5], K. Erlandson[6], M. Yin[7], B. Bartali[8], B. Ha[9], K. Melbourne[10], T. Brown[11]
[1]Stanford University, Infectious Diseases, Stanford, United States, [2]Harvard School of Public Health, Boston, United States, [3]Case Western Reserve University, Cleveland, United States, [4]University of Washington, Seattle, United States, [5]Ohio State University, Colombus, United States, [6]University of Colorado, Denver, United States, [7]Columbia University, New York, United States, [8]New England Research Institute, Watertown, United States, [9]Viiv, Research Triangle Park, United States, [10]Gilead Sciences, Foster City, United States, [11]Johns Hopkins University, Baltimore, United States
Presenting author email: pmgrant72@gmail.com

Background: Accelerated bone mineral density (BMD) loss occurs during the first two years of ART. Few studies have evaluated subsequent BMD changes, especially compared to uninfected controls.
Methods: ACTG A5318 performed one follow-up site-specific dual-energy x-ray absorptiometry (DXA) in HIV-infected individuals who had received baseline and follow-up DXAs during the randomized treatment trial A5202/A5224s. As controls, we obtained DXA results from uninfected participants enrolled in BACH/Bone and WIHS cohorts. Repeated measures analyses compared BMD change rate between HIV-infected and uninfected, adjusting for age, sex, race, and body mass index (BMI). In the HIV-infected group, we performed multivariable analyses evaluating association of HIV-specific (baseline and time-updated CD4 and viral load), HIV treatment-related (randomized ART regimen, cumulative tenofovir [TDF] exposure) and non-HIV related factors (age, sex, race, relevant concomitant medication use, BMI, total lean body mass) on BMD change rate.
Results: Baseline characteristics between HIV infected (n=97) and HIV-uninfected (n=630) participants were generally similar: median age, 40 vs. 46; % female, 14 vs. 14; % black, 34 vs. 35; median BMI, 24 vs. 29; and median years between first and last DXA, 7.5 vs. 6.9. Seventy-one percent of HIV-infected participants were on TDF at last DXA. Compared to controls, HIV-infected individuals had significantly greater adjusted BMD decline rate at lumbar spine (LS) and total hip (TH) during the first 96 weeks of ART (both p<0.001). Subsequently, on follow-up DXA, HIV infection remained significantly associated with greater adjusted BMD decline rate at LS (-0.29%/year; 95% CI: -0.49, -0.09; p=0.005) but not at TH (p=0.63). In the HIV group, the rate of BMD decline slowed after the first 96 weeks of ART (0-96 weeks vs. Late Change: LS: -0.75%/year vs. -0.19%/year, p=0.04; TH: -1.29%/year vs. -0.30%/year, p<0.001). During the late period, no HIV-related characteristic was associated with BMD loss, but lower total lean body mass (and not BMI) was associated with greater BMD loss at LS and TH (both p<0.001).
Conclusions: Although the rate of BMD decline slowed after the first 96 weeks after ART initiation in HIV-infected persons, the rate of bone loss at the lumbar spine was still significantly greater than HIV-uninfected controls.

TUPDB0104

Prevalence of nonalcoholic fatty liver disease and liver fibrosis among perinatally HIV-infected Asian adolescents with history of transaminitis

T. Sudjaritruk[1,2,3], T. Bunupuradah[3], L. Aurpibul[2], P. Kosalaraksa[4], N. Kurniati[5], T. Puthanakit[3,6]
[1]Faculty of Medicine, Chiang Mai University, Department of Pediatrics, Chiang Mai, Thailand, [2]Research Institute for Health Sciences, Chiang Mai University, Chiang Mai, Thailand, [3]HIV-NAT, Thai Red Cross - AIDS Research Centre, Bangkok, Thailand, [4]Srinagarind Hospital, Khon Kaen University, Khon Kaen, Thailand, [5]Cipto Mangunkusumo General Hospital, Department of Child Health, Jakarta, Indonesia, [6]Faculty of Medicine, Chulalongkorn University, Department of Pediatrics, Bangkok, Thailand
Presenting author email: tavitiya@gmail.com

Background: Liver disease is an important non-AIDS related morbidity in HIV-infected adults. Non-alcoholic fatty liver disease (NAFLD) is a clinical-pathological syndrome which may progress toward liver fibrosis and cirrhosis. The study objective was to determine the prevalence of NAFLD and liver fibrosis among perinatally HIV-infected adolescents with a history of transaminitis.

Methods: A cross-sectional study was conducted at 4 pediatric HIV centers in Thailand (Bangkok, Chiang Mai, Khon Kaen) and Indonesia (Jakarta). HIV-infected adolescents aged 10-25 years with virologic suppression and had transaminitis (ALT >30 U/L or AST >50 U/L) within past 12 months were enrolled. Adolescents with history of hepatitis B/C co-infection or significant alcohol consumption were excluded. The assessments included liver ultrasonography (USG-evaluation of fatty liver); transient elastography (TE-evaluation of liver stiffness), serum liver function test. Aspartate aminotransferase-to-platelet ratio index (APRI-biomarker of liver fibrosis) was calculated. Liver stiffness was defined as any liver fibrosis (TE ≥5.1 kPa) and significant liver fibrosis (TE ≥7.4 kPa). APRI >0.5 and >1.5 were defined as mild/moderate fibrosis and advanced fibrosis, respectively. Correlation of APRI and TE result was assessed.

Results: From August to December 2014, 39 adolescents were enrolled. Median (IQR) age was 17.2 (14.6-19.4) years; 47% were male. Median (IQR) duration of ART was 7.8 (4.4-11.2) years, of which 54% currently received non-nucleoside reverse transcriptase (NNRTI)-based regimen. Median (IQR) current CD4 cells count was 691 (535-979) cells/mm^3. Fatty liver was observed in 6 (15%) adolescents, of which 2 (5%) had severe fatty liver (Table1). Seventeen (46%) adolescents had any liver fibrosis and 6 (15%) had significant liver fibrosis (Table 1). Median (IQR) of ALT and AST were 30 (21-39) and 25 (20-31) U/L, respectively. Four (11%) had mild/moderate fibrosis by APRI. The APRI was moderately positively correlated with liver stiffness evaluated by TE (Pearson's correlation coefficient = 0.51; p-value = 0.001).

Sex	Age (yrs)	BMI (kg/m^2)	ALT (U/L)	AST (U/L)	Fatty Liver by USG	TE (kPa)	APRI
M	23	36.2	160	87	Severe	14.0	0.63
F	17	21.3	36	24	Severe	5.7	0.21
M	15	17.6	36	42	Mild	5.9	0.39
F	12	15.4	36	31	Mild	5.7	0.42
F	20	17.8	46	35	Mild	4.3	0.47
F	20	20.5	71	33	Mild	3.3	0.33
M	17	25.8	50	45	Normal	8.6	0.60
F	18	19.4	23	25	Normal	8.0	0.34
M	14	17.8	23	32	Normal	7.9	0.27
M	18	18.5	29	22	Normal	7.8	0.17
F	23	18.0	19	18	Normal	7.7	0.34

Abbreviation: M, male; F, female; BMI, body mass index; ALT, alanine aminotransferase; AST, aspartate aminotransferase; USG, ultrasonography; TE, transient elastography; APRI, aspartate aminotransferase-to-platelet ration index.

[Table1. Characteristics of perinatally HIV-infected adolescents with non-alcoholic fatty liver disease or liver fibrosis]

Conclusions: About one-third of perinatally HIV-infected adolescents with a history of transaminitis met criteria of fatty liver or liver fibrosis. Longitudinal follow-up to monitor for progression and provide appropriate interventions in a timely manner is needed.

Remark: This study is funded by CIPHER Grants (2014), International AIDS Society

TUPDB0105

Fixed dose combination EVG/COBI/TDF/FTC does not affect insulin resistance: the STRIBILD-IR study

C.D. Spinner[1], K.E. Kern[1], S. Noe[1], A. von Werder[1], C. Schwerdtfeger[1], R.M. Schmid[1], A. Zink[2], E. Wolf[3], R. Iakoubov[1]
[1]University Hospital Klinikum rechts der Isar, Department of Medicine II, Munich, Germany, [2]University Hospital Klinikum rechts der Isar, Department of Dermatology and Allergology, Munich, Germany, [3]Muc Research GmbH, Munich, Germany
Presenting author email: christoph.spinner@tum.de

Background: The incidence of insulin resistance (IR) and diabetes mellitus in HIV-patients, both contributing to cardiovascular morbidity and mortality, has been associated with antiretroviral therapy (ART). Only limited data exists on metabolic effects of regimens including newer drugs such as fixed dose combination drugs, particularly concerning IR.

Methods: In this prospective, open-label, randomized phase-I-study we investigated the effects of the recently available fixed dose combination of tenofovir disaproxil fumarate, emtricitabine, elvitegravir and cobicistat (TDF/FTC/EVG/cobi, group I) on IR, in comparison to established ART with TDF/FTC+Lopinavir/ritonavir (LPV/r, group II) and TDF/FTC+darunavir/ritonavir (DRV/r, group III). N=30 healthy, male volunteers were randomly assigned into one of the 3 study arms. IR was measured using golden standard method of hyperinsulinemic euglycemic clamp before and 14 days after initiation of study medication. Briefly, a constant insulin infusion (2 mIU/(kg*min)) was infused over 2h, glucose infusion was adjusted as necessary to achieve stable glucose levels (target 90±5 mg/dl). All volunteers took the study medication, as verified by pill counting. IR was evaluated using the mean glucose disposal rate normalized to body weight (M_{BW}, [mg glucose/min*kg]), as calculated during the clamp. To test for statistical significance of global and pairwise differences in IR analyses of variances and the Student's t-test was used To test for significant changes in IR within study arms, the paired t- test was used.

Results: The enrolled volunteers were young, non-obese, healthy males; no significant differences were detected concerning baseline characteristics (s. Table 1).

Group/ Parameter (Mean±SD)	I: TDF/FTC/EVG/cobi	II: TDF/FTC+LPV/r	III: TDF/FTC+DRV/r
Age (years)	26.3 (±4.8)	27.3 (±4.8)	27.2 (±2.3)
Weight (kg)	75.3 (±4.8)	70.2 (±8.3)	72.3 (±7.6)
Body height (cm)	183.5 (±4.2)	178.9 (±5.7)	180.0 (±5.5)
BMI (kg/m2)	22.4 (±1.1)	21.9 (±2.2)	22.3 (±1.5)
Fasting blood glucose (mg/dl)	82.0 (±5.1)	82.3 (±6.7)	83.3 (±6.0)

[Table 1: Baseline Characteristics]

Mean IR did not differ between the groups before treatment (I vs. II vs. III: 11.2±3.2 (SD, standard deviation); n=10 vs. 12.5±3.3; n=9 vs. 11.6±2.5; n=9). The medication was well tolerated; 2 patients were excluded from analysis due to medical (hypothyroidism) and technical (insulin pump error) reasons. TDF/FTC+LPV/r significantly affected IR after 14d of treatment as compared to baseline (9.2±1.8 vs. 12.5±3.3; p=0.037), but neither TDF/FTC/EVG/cobi (11.3±2.5 vs. 11.2±3.2; p=n.s.) nor TDF/FTC+DRV/r (11.3±2.4 vs. 11.6±2.5; p=n.s.) did.

Conclusions: Our study shows for the first time that neither treatment with the fixed dose combination TDF/FTC/EVG/cobi nor with TDF/FDC+DRV/r affects IR as compared to the established regimen TDF/FTC+LPV/r.

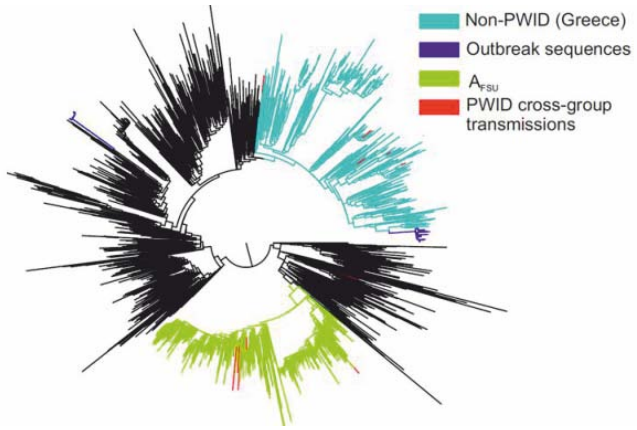
TUPDC01 Clusters, Clades and Cultures

TUPDC0101

Molecular investigation for HIV-1 cross-group transmissions during the outbreak period (2011-2014) in Athens metropolitan area: introduction of subtype A from Eastern Europe

D. Paraskevis[1], G. Nikolopoulos[2], V. Sypsa[1], M. Psichogiou[3], M. Malliori[4], S.R. Friedman[5], A. Hatzakis[1]
[1]Medical School, University of Athens, Department of Hygiene Epidemiology and Medical Statistics, Athens, Greece, [2]Hellenic Center for Diseases Control and Prevention, Athens, Greece, [3]Laikon General Hospital, Department of Propedeutic Medicine, Athens, Greece, [4]Medical School, University of Athens, Athens, Greece, [5]National Development and Research Institutes, (NDRI), New York, United States
Presenting author email: gknikolopoulos@gmail.com

Background: New diagnoses of HIV-1 infections among people who inject drugs (PWID) increased in Athens metropolitan area, Greece during 2011. Our aim was to identify potential cross-group transmissions between PWID and other risk groups using molecular methods.
Methods: HIV-1 subtypes were determined for 711 HIV-1(+) PWID sampled during 2011-2014. Cross-group transmissions among the PWID were those that originated from other groups as estimated by phylogenetic trees. Specifically cross-group transmissions corresponded to viral lineages from PWID that didn't fall into the outbreak transmission networks or the PWID recombinants. Further phylogenetic analyses were conducted for the sequences from cross-group transmissions.
Results: Among the 711 HIV-1(+) PWID, 630 (88.6%) sequences fell within 4 IDU transmission networks belonging to CRF14_BG (n=356, 50.1%), CRF35_AD (n=123, 17.3%), subtype B (n=106, 14.9%) and A (n=45, 6.3%); 48 (6.8%) were recombinants consisting of partial regions originating from the PWID-specific clades. On the other hand, sequences from 33 (4.6%) PWID didn't belong either to the PWID transmission networks or the recombinants, suggesting that they are evidence of potential cross-group transmissions. Phylogenetic analyses (n=28) for subtypes A and B detected most frequently among the cross-group transmissions suggested that most of these infections originated from non-PWID transmission networks in Greece and the former Soviet Union countries (A_{FSU}). Specifically we found that 9 (75.0%) of the subtype B infections originated from Greece, whereas 8 (50.0%) and 7 (43.8%) of subtype A strains were of A_{FSU} and Greek origin, respectively (Figure). The gender distribution didn't differ significantly between those infected within PWID networks (F: n=99; M: n=579) or the cross-group transmissions (F: n=7; M: n=26).



[Figure. Phylogenetic tree of subtype A sequences from PWIDs with evidence for cross-group transmissions plus sequences from the Greek epidemic sampled during 1999-2013 and a randomly selected global sample]

Conclusions: During the four year period of the HIV-1 outbreak among the PWID in Athens metropolitan area, we estimated that 33 (4.6%) of the infections in this group are due to cross-group infections. Notably, half of these cross-group infections due to subtype A originate from the large IDU epidemic in Eastern Europe (A_{FSU}). For subtype B however the majority of cross-group infections originated from Greece.

TUPDC0102

Clusters of HIV transmission among high-risk populations in Pakistan

L.H. Thompson[1], J.O. Wertheim[2], T. Reza[3], J.L. Wylie[4], F. Emmanuel[3], J. Brooks[5], J.F. Blanchard[6], P. Sandstrom[5]
[1]University of Manitoba, Community Health Sciences, Winnipeg, Canada, [2]University of California at San Diego, Department of Medicine, San Diego, United States, [3]Centre for Global Public Health - Pakistan, Islamabad, Pakistan, [4]University of Manitoba, Department of Medical Microbiology, Winnipeg, Canada, [5]Public Health Agency of Canada, National HIV and Retrovirology Laboratory, JC Wilt Infectious Disease Research Centre, Winnipeg, Canada, [6]University of Manitoba, Centre for Global Public Health, Winnipeg, Canada
Presenting author email: laura.thompson@alumni.utoronto.ca

Background: In Pakistan, people who inject drugs (PWID) have a high HIV prevalence (~27%) and the prevalence among sex workers (SW) has recently increased. There is considerable geographic heterogeneity of HIV prevalence, which may reflect multiple subepidemics with unique trajectories, characterized by specific risk contexts, behaviours, and sexual or syringe-sharing networks. This study uses genetic clustering to identify and characterize these HIV subepidemics of ongoing transmission.
Methods: Mapping and integrated behavioral and biological surveillance took place among 16,756 PWID and male (MSW), *hijra* (HSW) and female (FSW) SW across Pakistan in 2011. Of the 1,637 persons who tested HIV positive (9.8%), we were able to analyze gp41 sequences from 1,153. These sequences were aligned to a reference sequence: HXB2. We identified sequences that were highly similar (≤1% pairwise Tamura Nei 93 genetic distance) and deemed these persons potential transmission partners. Transmission clusters were constructed by connecting persons who share potential transmission partners. Clusters were characterized in terms of high risk population group membership and city. Logistic regression was used for tests of statistical significance.
Results: The prevalence of HIV was determined to be 27.3%, 5.2%, 1.6%, and 0.6% among PWID, HSW, MSW, and FSW respectively. Of the 1,153 sequences, 652 were clustered (56.5%) in 87 unique clusters ranging in size from 2 to 96 sequences. Average cluster size was 7.5 (s.d.=15), although clusters of 2 predominated. Compared with MSW, PWID were more likely to be clustered (Odds Ratio = 1.6, p = 0.01). Larger clusters were more likely to span multiple cities and include SW, with an average mixed PWID/SW cluster size of 23.6, compared with cluster sizes of 5 or 2 for clusters composed entirely of PWID or SW, respectively. Most PWID who were in clusters were in large clusters of nine or more individuals, whereas HSW and MSW tended to be in clusters of diverse sizes.
Conclusions: A comprehensive understanding of HIV transmission in Pakistan will be critical to design strategically targeted HIV prevention programs. Clusters may be indicators of ongoing transmission and thus an effective strategy for prevention programs could be to target the cities and population groups with high clustering.

TUPDC0103

Transmission networks of HIV-1 among men who have sex with men in East and Southeast Asia

K.K. Tee[1], R. Kantor[2], S. Sungkanuparph[3], Y. Takebe[4], P. Li[5], R. Ditangco[6], P. Phanuphak[7], T. Sirisanthana[8], B. Sim[9], W. Ratanasuwan[10], P. Kantipong[11], M. Mustafa[12], T.P. Merati[13], A. Jiamsakul[14], T. Singtoroj[15], A. Kamarulzaman[1],
TREAT Asia Studies to Evaluate Resistance - Monitoring (TASER-M)
[1]University of Malaya, Department of Medicine, Kuala Lumpur, Malaysia, [2]Alpert Medical School of Brown University, Department of Medicine, Providence, United States, [3]Mahidol University, Department of Medicine, Faculty of Medicine, Ramathibodi Hospital, Bangkok, Thailand, [4]National Institute of Infectious Diseases, AIDS Research Center, Tokyo, Japan, [5]Queen Elizabeth Hospital, Hong Kong, China, [6]Research Institute for Tropical Medicine, Manila, Philippines, [7]HIV-NAT/Thai Red Cross AIDS Research Centre, Bangkok, Thailand, [8]Chiang Mai University, Research Institute for Health Sciences, Chiang Mai, Thailand, [9]Hospital Sungai Buloh, Kuala Lumpur, Malaysia, [10]Mahidol University, Faculty of Medicine Siriraj Hospital, Bangkok, Thailand, [11]Chiangrai Prachanukroh Hospital, Chiang Rai, Thailand, [12]Hospital Raja Perempuan Zainab II, Kota Bharu, Malaysia, [13]Udayana University and Sanglah Hospital, Faculty of Medicine, Bali, Indonesia, [14]UNSW Australia, The Kirby Institute, Sydney, Australia, [15]TREAT Asia, amfAR, Bangkok, Thailand
Presenting author email: k2tee@um.edu.my

Background: The HIV epidemic among men who have sex with men (MSM) is expanding at an alarming rate in Asia. Understanding the dynamics of HIV-1 transmission among MSM through viral sequence analyses may provide essential information on the origin of viral lineages and the characteristics of disease spread.
Methods: We determined transmission networks of HIV-1 among MSM across countries in East and Southeast Asia. A total of 1,856 HIV-1 polymerase gene sequences were obtained from TREAT Asia Studies to Evaluate Resistance-Monitoring (TASER-M) sites in Hong Kong, Thailand, Malaysia, and the Philippines between 2006 and 2011. Time-stamped sequence datasets of HIV-1 subtype B (n=144) and CRF01_AE (n=186) from antiretroviral-naive MSM were identified and subjected to spatiotemporal analysis using Bayesian phylodynamic methods. A

transmission network was defined as a phylogenetic cluster (≥2 isolates) supported by >90% bootstrap values and Bayesian posterior probability value of 1 at the tree node.
Results: Phylogenetic reconstructions showed that 68% of HIV-1 subtype B and 46% of CRF01_AE sequences were grouped in 50 transmission networks of various sizes (mean size=5.6, range=2-32 sequences), with subtype B sequences having a higher tendency to form a network ($p< 0.0001$). With additional representative sequences from China, Mongolia and Myanmar from the Los Alamos National Laboratory HIV Sequence Database, 34 networks involving 154 subtype B-infected individuals and 16 networks involving 125 CRF01_AE-infected individuals were observed. Location mapping showed that the MSM networks in East and Southeast Asia were mostly localized (78%) in their respective countries, with 22% spanned beyond a single country. Genealogy-based analysis to estimate the divergence time for each transmission network indicated the continued emergence of new networks over the past three decades. The uninterrupted growth of sub-epidemics of various cluster sizes suggests the role of transmission networks as a continuous driving force of the epidemic among MSM in Asia.
Conclusions: Despite expanded access to antiretroviral therapy in Asia, our analysis showed continued regional emergence of recent HIV-1 subtype B and CRF01_AE networks among MSM. Strategies such as early diagnosis and treatment as prevention to reduce transmission risks among sero-discordant partners need to be expanded across the region.

TUPDC0104

Estimating the size of men who have sex with men (MSM) using modified capture-recapture method based on network sampling in the capital city of Georgia in 2014

L. Sulaberidze[1], A. Mirzazadeh[2,3], I. Chikovani[1], N. Shengelia[1], N. Tsereteli[4], G. Gotsadze[1]
[1]Curatio International Foundation, Tbilisi, Georgia, [2]University of California San Francisco, Global Health Sciences, San Francisco, United States, [3]Regional Knowledge Hub and WHO Collaborating Centre for HIV Surveillance, Kerman, Iran, Islamic Republic of, [4]Center for Information and Counseling on Reproductive Health - Tanadgoma, Tbilisi, Georgia
Presenting author email: l.sulaberidze@curatio.com

Background: Estimates of the number of people at high risk for HIV infection are crucial for prevention, treatment and care planning. Taking into consideration that Georgia is the country, where HIV prevalence is concentrated among MSM and information on the size of this key population was lacking, we conducted the study using seven different population size estimation methods in Tbilisi, Georgia. We want to focus on a new method proposed by Dombrowski among methamphetamine users in 2012. This represents capture-recapture using network sampling technique. Among MSM we first time applied this method with few modifications.
Methods: Modified capture-recapture requires singe sample, which for our study was 210 MSM 18 years and older recruited through Respondent Driven Sampling. The study participants were asked about their personal characteristics (approximate height, weight, hair color and ethnicity) and so called "telefunken codes" derived from the last four digits of their own mobile number. In difference to the original method that used six personal identifiers we dropped eye color (based on piloting results) and gender. This represented the capture. Afterwards the study participants were asked to provide the similar characteristics appealing to their five MSM contacts randomly selected from mobile phone directories. This represented the recapture. Some respondents (2.38%) did not have mobile phones with them and some did not have five MSM contacts in their mobile phone directory. To get to the final estimates Lincoln-Peterson method was used.
Results: Using the four-identifier categorical variables and the "telefunken code", we identified 36 matches between the two captures (205 captured and 770 recaptured). This led to the population size of 1.2% (95%CI, 0.9% - 1.6%) of the adult male population. The results were comparable to those from other methods used in our study (see table 1).

PSE method	Point estimate (18-59y)	Lower Bound (18-59y)	Upper Bound (18-59y)
Modified Capture-Recapture	4385	3115	5654
MSM size - Median of all seven estimates*	5100	3243	9088
MSM Prevalence in adult population	1.42%	0.90%	2.53%

*Estimates derived from the following methods: Network Scale-up,Web- and mob- App Multipliers, Service Multiplier, Unique Object Multipliers, RDS-based Handcock, Wisdom of Crowd,Modified Capture-Recapture

[Different MSM population size estimates from various methods implemented in Tbilisi, 2014]

Conclusions: Despite the study limitations - difficulty to get the "telefunken codes" for the recapture phase - modified capture-recapture method provides reasonable population size estimates for MSM when compared to the median estimates and their boundaries of other more established methods. Estimating size of MSM through modified capture-recapture method appeared to be feasible, simple, cost-saving and effective method that is valuable for future application.

TUPDC0105

Network-level factors associated with IPV perpetration among young urban Tanzanian men

M. Mulawa[1], H.L.M. Reyes[1], V. Foshee[1], C.T. Halpern[2], L. Kajula[3], S. Maman[1]
[1]University of North Carolina at Chapel Hill, Health Behavior, Durham, United States, [2]University of North Carolina at Chapel Hill, Maternal and Child Health, Durham, United States, [3]Muhimbili University of Health and Allied Sciences, Psychiatry and Mental Health, Dar es Salaam, Tanzania, United Republic of
Presenting author email: mulawa@live.unc.edu

Background: Research suggests that characteristics of an individual's social network may influence intimate partner violence (IPV) perpetration among men in sub-Saharan Africa. For example, studies indicate that network-level measures of gender norms or IPV acceptance may be associated with IPV perpetration. However, to date, no studies have identified network-level factors associated with IPV among East African youth. We used data from our on-going HIV prevention trial in Dar es Salaam, Tanzania with 1268 men, ages 15-59 years (mean=26), nested within 60 networks of randomly selected social clubs called "camps." The purpose of this study was to assess the degree to which variance in men's IPV perpetration was attributed to camp membership and to determine the effect of camp-level norms (gender norms and IPV attitudes) on IPV perpetration.
Methods: We used 2-level hierarchical linear models to model the relationship between individual and camp-level characteristics and past-year physical IPV perpetration, assessed using an adapted version of the World Health Organization violence against women instrument. Camp-level gender norms were computed by averaging responses among all camp members to an adapted version of the Gender Equitable Men Scale. All individual-level variables were group-mean centered to facilitate decomposition of between and within-camp effects. We estimated an unconditional random effects model to determine the proportion of IPV variance attributable to camp membership. Subsequent models sequentially introduced individual-level demographic/control variables, camp-level norms, and individual-level norms.
Results: A significant proportion of variance in IPV perpetration (3.1%) was due to between-camp differences (τ_{00}= 0.0054, p= .01). Increasing levels of camp equitable gender norms were significantly associated with decreasing IPV perpetration (γ=-0.167, p= .04), and this association remained after controlling for individual-level gender norms. Camp-level norms regarding IPV acceptance were not associated with IPV perpetration.
Conclusions: Studies have found a strong association between IPV and HIV. We found that membership in social groups with equitable gender norms reduced men's risk of perpetrating IPV, even after adjusting for their own views about gender norms and the acceptability of violence. This finding highlights the importance of multilevel HIV and IPV interventions that simultaneously address individual risk factors while making gender norms more equitable within social networks.

TUPDD01 Gender Matters: When, Why, and How

TUPDD0101

Gender differences in HIV testing behaviors by community-level and individual-level stigma in rural South Africa

S. Treves-Kagan[1], A. El Ayadi[2], A. Pettifor[3,4,5], C. MacPhail[4,6], R. Twine[5], S. Maman[3], K. Kahn[5], S.A. Lippman[1]
[1]University of California, Center for AIDS Prevention Studies, San Francisco, United States, [2]University of California, Bixby Center for Global Reproductive Health, Department of Obstetrics, Gynecology and Reproductive Sciences, San Francisco, United States, [3]University of North Carolina at Chapel Hill, Gillings School of Global Public Health, Chapel Hill, United States, [4]University of the Witwatersrand, Wits Reproductive Health and HIV Institute (WRHI), School of Clinical Medicine, Faculty of Health Sciences, Johannesburg, South Africa, [5]University of the Witwatersrand, Medical Research Council/Wits Rural Public Health and Health Transitions Research Unit (Agincourt), School of Public Health, Faculty of Health Sciences, Johannesburg, South Africa, [6]University of New England, Collaborative Research Network, Armidale, Australia
Presenting author email: sarah.treves-kagan@ucsf.edu

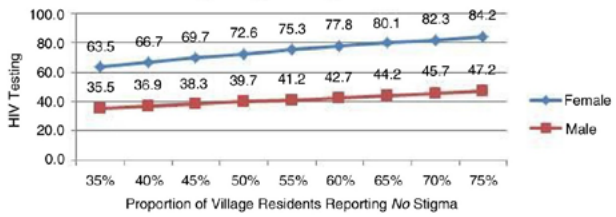
Background: Despite national testing campaigns and increased access to HIV treatment, stigma remains a significant barrier to testing in South Africa. A nuanced understanding of stigma and testing is instrumental in refining intervention programming. Stigma can be examined at either the individual or community level and may operate differentially by gender. Further, estimating HIV testing uptake achievable through stigma reduction interventions is critical for understanding potential impact.
Methods: We examined the relationship between anticipated HIV stigma at individual and community levels on recent HIV testing, stratified by gender, using data from a population-based sample of 1,126 adults aged 18-35 residing in 22 villages in Mpumalanga, South Africa.

Anticipated HIV stigma, or expectations of discrimination should one become HIV positive, was measured using a 9-item scale and dichotomized as *any* versus *no* stigma. Community-level stigma was defined as the proportion of individuals within each village reporting any anticipated stigma. We assessed associations of community and individual stigma and HIV testing for men and women. We then used multi-level regression models to estimate the potential effect of changing community-level stigma to improve testing uptake using the g-computation algorithm. Analyses were weighted to account for the survey design.

Results: Men tested less frequently (OR 0.22, 95%CI 0.14-0.33) and reported more individual anticipated stigma (OR 5.1, 95%CI 2.6-10.1) than women. Men reporting no individual-level stigma (vs some) were 48% more likely to have tested (p=0.08). For women, testing behavior was not associated with individual anticipated stigma but for each percentage point reduction in community-level stigma the likelihood of testing increased by 3% (p=0.03). We modeled gains in HIV testing at different levels of community stigma (Figure 1).

For example, results indicate a potential 15% intervention gain in HIV testing among women if community-level stigma decreased by 5%. Changing community-level stigma did not result in significant gains for men.

Conclusions: Our data indicates that HIV-related stigma influences HIV testing for men and women through different pathways. Stigma reduction programs may need to consider gender differences and tailor activities to the target population. Longitudinal research is needed to confirm projections and direction of effect.



[Figure 1: Proportion of Females and Males Testing for HIV under Various Community Anticipated Stigma Scenarios using G-Computation Algorithm, Mpumalanga Province, South Africa]

TUPDD0102

Men "missing" from population-based HIV testing: insights from qualitative research

C.S. Camlin[1], E. Ssemmondo[2], G. Chamie[3], D. Kwarisiima[2], N. Sang[4], E.A. Bukusi[4], C.R. Cohen[1], M.R. Kamya[2], D. Havlir[3]
[1]University of California - San Francisco (UCSF), Obstetrics, Gynecology & Reproductive Sciences, San Francisco, United States, [2]Infectious Disease Research Collaboration (IDRC), Kampala, Uganda, [3]University of California - San Francisco (UCSF), Medicine, San Francisco, United States, [4]Kenya Medical Research Institute (KEMRI), Kisumu, Kenya
Presenting author email: carol.camlin@ucsf.edu

Background: Men's uptake of HIV testing will be critical to the success of test and treat strategies in generalized epidemics. We used qualitative research methods to identify cultural factors and community level processes that influence HIV testing uptake in the context of an ongoing test and treat trial of 334,479 persons in East Africa (SEARCH, NCT# 01864603).

Methods: In-depth interviews, participant observation, and focus group discussions were used to evaluate contextual factors in communities that influenced uptake of baseline HIV testing. The study used a hybrid model of mobile HIV testing including community health campaigns (CHC) followed by home-based testing (HBT) for non-CHC attendees. Data were collected in 8 rural communities in Uganda and Kenya, and interpreted using Atlas.ti software. Analytical codes were defined and applied by an 8-person research team on the basis of theory and the empirical data, and iteratively refined during the analysis process.

Results: Structural barriers to male participation in community health campaigns led to reduced participation in CHCs and HBT: informal sector labor opportunities for men often require extended absences from rural households. Participants reported for example that during planting season, men needed to guard fields from monkeys from dawn until nightfall; in lakeshore communities, fishermen travel long distances and off-load fish at multiple beaches, using multiple residences and temporary lodgings. Community leaders were critical in outreach to promote CHC attendance, but power differentials between elder and younger men may have contributed to heterogeneous mobilization. Cultural factors including male gender norms counter to health-seeking behaviors, and valorizing risk-taking, also served as barriers to HIV testing. Men often tested "by proxy", inferring their HIV status from the test results of wives. Yet debates about HIV risks were vigorous, with many men questioning traditional masculine gender norms; moreover, the promise of antiretroviral therapy (ART) to prolong health appeared to motivate many men to participate in testing.

Conclusions: Mobile testing reduces but does not eliminate barriers to men's participation; however, the promise of ART may be enabling changes in male gender norms related to testing. Findings may be useful for developing novel strategies to improve male engagement in test and treat efforts.

Entrenched gender norms
• "Men are generally lazy… ,I am already infected and still want to show my male ego without considering my family'…many men as well are not ready to take up HIV test and would push their partners to go first and rely on their results." - Male youth Focus Group Discussion (FGD) participant, Sena
• "As men we have a lot of fear… Men also like giving excuses, that they are ever busy in the name of searching for the family, even if they have gotten this food that they are ever looking for [laughter]."- Male adult FGD participant, Sena
• "Many men believe that medical issues are women's affairs." -Male adult FGD participant, Ongo
• "Men are people with hardened hearts. They will hardly rush for any program. They can release their wives and children first to go, and for him, he assesses before going." - Female adult FGD participant, Kameke
Signs of changing gender norms
• "Interviewer: You have mentioned that most people do not test as couples; please tell me more about this?
• A good percentage of men are not faithful. It is men who would even end up enrolling for HIV care at a very far facility. Men should change and be free to test as couples so as to build trust. They should stop frustrating their women as well. [Female adult participant]
• Gender based violence is real and rampant in this community. This is so because there is no family dialogue to discuss family issues. I do dialogue in my house but when I introduced the HIV topics, many started avoiding the dialogue." - [Male adult participant], FGD Tom Mboya

[Illustrative Quotes]

TUPDD0103

Examining the relationship between pediatric PMTCT outcomes and knowledge of partner status

A. Schley, E. Skowronska, E. Okonji, E. Scheepers
mothers2mothers, Department of Programs and Technical Support, Cape Town, South Africa

Background: The mothers2mothers' Mentor Mother program empowers pregnant women and new mothers to make informed decisions about their maternal and reproductive health as well as their infants' health, through provision of peer education and psychosocial support. m2m's 2013 annual evaluation showed that discordancy was negatively associated with the uptake of pediatric PMTCT services. HIV-positive mothers who knew their male partners were HIV-negative were less likely to bring their infants for PCR testing at 6-8 weeks (OR=0.60, p= 0.005), or for a follow-up test at 18 months
(OR=0.75, p= 0.017), compared to mothers who knew their partners were HIV-positive. The aim of this study is to further investigate the role that knowledge of one's partner's HIV status plays in the uptake of pediatric PMTCT services.

Methods: Secondary analysis of m2m's 2013 internal program evaluation data was conducted. Data comprised of a representative random sample of 5,592 HIV-positive clients' longitudinal records
(routinely maintained by Mentor Mothers), enrolled from March through May 2012 in six African countries. The relationship between knowledge of partner status and uptake of pediatric PMTCT services was investigated through bivariate analysis (chi-square) and binary logistic regression analysis using STATA 12.

Results: Knowledge of partner HIV status was significantly associated with uptake of pediatric PMTCT services. Mothers who knew their partner's HIV status were more likely to take up pediatric PMTCT services compared to those who did not know their partner's status. The likelihood of improved uptake of PMTCT services was the highest among mothers who knew they were in a concordant relationship. There was no significant relationship between knowledge of partner status and uptake of infant ART.
(See Table 1)

	Unknown partner HIV status	Partner known HIV positive (known concordant relationship) OR (p-value)	Partner known HIV negative (known discordant relationship) OR (p-value)
Infant PCR test	1	1.96 (0.000)	1.20 (0.261)
Infant PCR test result	1	2.12 (0.000)	1.41 (0.022)
Infant 18 months test	1	1.89 (0.000)	1.41 (0.012)
Infant 18 months test result	1	1.91 (0.000)	1.44 (0.008)
Infant on ART	1	0.84 (0.505)	0.89 (0.751)

[Pediatric PMTCT & knowledge of partner status]

Conclusions: Additional primary research on the effects of concordancy and discordancy on PMTCT outcomes is recommended. Our secondary analysis suggests that uptake of pediatric PMTCT services is more likely to occur amongst clients who know that they are in a concordant relationship. This evidence supports m2m's inclusion of a tailored serodiscordant couples education and support intervention to facilitate mutual disclosure of HIV status in partners, especially in the context of Option B+, thus improving outcomes in the postnatal care cascade.

TUPDD0104

Who benefits from partner services in Mozambique? Results from a pilot program in a public, urban clinic

C. Feldacker[1], S. Myers[1], F. Cesar[2], Z. Parades[2], C. Ferrao[3], S.C. Citao[4], F. Mudender[2], M. Golden[5]
[1]International Training and Education Center for Health, Global Health, University of Washington, Seattle, United States, [2]International Training and Education Center for Health, Maputo, Mozambique, [3]Ariel Glaser Foundation, Maputo, Mozambique, [4]Provincial Department of Health, Maputo, Mozambique, [5]University of Washington Harborview Medical Center, Division of Allergy and Infectious Diseases, Seattle, United States
Presenting author email: golden@u.washington.edu

Background: Notifying partners of persons newly diagnosed with HIV can help identify undiagnosed infections and link people to care. Assisted partner services (APS) offers persons with newly diagnosed HIV infection help notifying and getting sex partners tested. APS is not widely available in sub-Saharan Africa, including Mozambique. We explore who benefits from APS as compared to passive services through a pilot program in an urban, public clinic in Maputo, Mozambique.
Methods: Between June-September 2014, four community health workers (CHWs) offered APS to 223 index patients (IPs) with recently diagnosed HIV: 220 accepted and 206 (94%) were retained at 8 weeks. CHWs used structured interviews to collect data at baseline, 4 and 8 weeks. At baseline, CHWs counseled IPs to notify partners and encourage their HIV testing, but did not offer to notify partners directly. At 4 weeks, with consent, CHWs notified partners to encourage testing. We used logistic regression , adjusted for clustering, to define the odds that APS increased HIV testing uptake and identified new HIV infections, setting significance at p< = 0.05.
Results: Of 206 IPs, 79% were female, 73% were married and 31% named > 1 sex partner. IPs named 283 partners, 278 had complete date: 59% are spouses. Of 192 people tested, 103 (53.6%) tested after APS at 4 weeks. Of 103 HIV positive diagnoses, 55 (53.4) were reported at 8, but not 4, weeks, suggesting APS-assisted identification of new HIV infections. APS appeared to increase both partner HIV testing and identification of HIV-infected partners across a range of subgroups (Table 1). The magnitude of impact varied. In multivariate analysis, APS appeared more effective among persons in ongoing sexual relationships and less effective among persons with multiple sex partners, a group in whom partner testing and HIV identification remained relatively low.

N=278	Tested Prior to APS # (%)	Total Tested at 8 weeks # (%)	OR testing Post v Pre APS* (Univariate)	OR testing Post v Pre APS ** (Multivariate)	HIV+ Prior to APS # (%)	Total HIV+ at 8 weeks # (%)	OR HIV+ Post v Pre APS * (Univariate)	OR HIV+ Post v Pre APS ** (Multivariate)
Male partner (ref: female)	59 (28.8)	142 (69.3)	1.61 (0.91-2.84)		33 (15.8)	78 (38.1)	1.51 (0.76-2.99)	
Live together	66 (43.4)	124 (81.6)	1.07 (0.67-1.70)		36 (23.7)	71 (46.7)	1.67 (0.92-3.03)	
IP has >1 sex partner	37 (27.4)	73 (54.1)	0.43 (0.26-0.72)	0.52 (0.31-0.89)	19 (13.6)	33 (24.4)	0.28 (0.15-0.52)	0.39 (0.20-0.77)
Has continuing sexual relations	78 (35.3)	172 (77.8)	2.78 (1.44-5.33)	2.09 (1.04-4.17)	43 (19.3)	94 (42.5)	3.36 (1.27-8.93)	1.92 (0.70-5.53)
IP reason for HIV testing: symptoms	20 (23.8)	52 (61.9)	0.99 (0.58-1.70)		9 (10.6)	24 (28.6)	0.74 (0.39-1.39)	
IP reason for HIV testing: prenatal	44 (37.0)	96 (80.7)	1.61 (0.97-2.67)		21 (17.2)	54 (45.4)	2.34 (1.30-4.21)	1.66 (0.91-3.03)
Total	89	192			48	103		

Results from logistic regression models using the (cluster) option in STATA. 95% CI presented in parentheses. * Results from univariate models. ** Results from multivariate models.

[Table 1: Factors associated with uptake of APS for]

Conclusions: APS significantly improves HIV testing uptake and case-finding among current sex partners: those in monogamous pairs benefit most. These findings suggest that the model of APS piloted in Mozambique might be most profitably focused on persons in ongoing partnerships and highlights the need for better interventions for persons with multiple sex partners.

TUPDD0105

Male partner acceptance of home-based syphilis and HIV testing offered to couples during pregnancy

J. Mark[1], J. Kinuthia[2], A. Osoti[3], M. Gone[2], V. Asila[2], S. Parikh[4], D. Krakowiak[4], B. Betz[4], B. Richardson[4], A. Roxby[4], C. Farquhar[4]
[1]University of Washington, Epidemiology, Seattle, United States, [2]Kenyatta National Hospital, Nairobi, Kenya, [3]University of Nairobi, Nairobi, Kenya, [4]University of Washington, Seattle, United States
Presenting author email: jmark55@uw.edu

Background: Testing partners for HIV in the antenatal period is an effective way to bring HIV services to couples. Leveraging antenatal HIV testing with point of care (POC) diagnostics for other sexually transmitted infections (STI) may improve male partner treatment services among couples.
Methods: We conducted a prospective study among male partners of pregnant women who received home-based couple HIV testing and education (HOPE) following a first antenatal visit in Kisumu, Kenya. From April to July 2014, rapid point of care (POC) syphilis testing (SD Bioline Syphilis 3.0) was added to the package of services for men and those with positive results were referred to the clinic for treatment. We assessed men's acceptance of testing and intention to seek clinic-based treatment and calculated an odds ratio to examine correlation between uptake of syphilis and HIV testing.
Results: Data were available for 73 (83%) couples receiving a HOPE visit. Men were on average 26 years of age (IQR:22, 29). At study entry, most men reported having previously tested for HIV (93%, n=68), of whom 7% reported being of known HIV positive status (n=5), and 80% reported knowing their female partner's HIV status (n=59). Of 73 men, 67 accepted syphilis testing (92%) among whom 64 intended to attend clinic STI treatment if they received a positive syphilis result (95%). HIV prevalence among the men was14.7% and one man (< 1%) was syphilis positive. In this group, 61 (83%) accepted both syphilis and HIV tests. Three men (4%) refused both tests and three men (4%) accepted HIV alone. Six men (8%) accepted syphilis alone, of whom 2 reported having been previously tested as HIV-positive. If a man accepted HIV testing, he was 10-fold as likely to accept syphilis testing, compared to a man who refused HIV testing (OR:10.2; 95% CI:1.05-89.3; p=0.02).
Conclusions: In a high HIV and low syphilis setting, home-based education and POC syphilis testing of male partners during pregnancy is highly acceptable when coupled with HIV testing and may encourage men to seek clinic-based STI services. Integration with HIV testing appears feasible, and syphilis test uptake is highly correlated with HIV test uptake.

TUPDD0106

Antiretroviral treatment uptake and correlates of adherence among men who have sex with men and transgender women in Mumbai, India

C. Pina[1], A. Dange[2], S. Neytra[2], H. Kambli[2], S. Karambe[2], R. Chhabra[1], V. Patel[1,3]
[1]Albert Einstein College of Medicine, Bronx, United States, [2]Humsafar Trust, Mumbai, India, [3]Montefiore Medical Center, Bronx, United States
Presenting author email: christopher.pina@med.einstein.yu.edu

Background: Understanding factors influencing ART adherence is needed to optimize treatment responses for HIV infected men who have sex with men (MSM) and Hijra/transgender women (TGW) in India. The objective of this formative study was to determine rates of ART uptake and adherence and explore potential factors associated with adherence in Indian MSM and TGW.
Methods: We conducted a cross-sectional survey in Hindi among all HIV positive MSM and TGW on ART accessing support services at a LGBT community based organization in Mumbai between July and September 2014. Non-adherence was measured by self-report and defined as missing any doses
(i.e. < 100% adherent) in the past 1 month and 3 months. Potential correlates of adherence assessed were sociodemographics, medication side-effects, depression (CESD-10), self-efficacy (GSE), internalized homophobia/stigma, and medication beliefs using chi-square or t-tests.
Results: Of the 300 individuals registered in the organization's HIV support program, 28.3% (85/300) were eligible for ART by current country standards (e.g. CD4 ≤350 or having an OI) with 22% (65/300) currently on ART. Of those on ART, 83% (54/65) were MSM and 17% (11/65) TGW; 40% (25/65) were married to women, and most (97%) received free ART through government clinics. Overall, 32% (21/65) were non-adherent in the past 1 month and 45% (29/65) in past 3 months. Correlates (p< .05) of non-adherence were similar for 1 month and 3 months and were associated with younger age, non-Kothi identity (MSM subgroup), alcohol use, having sex with women, feeling healthy, and negative medication beliefs but was not directly associated with depression, internalized homophobia, or medication self-efficacy.
Conclusions: In one of the first studies of adherence among MSM and TGW in India, ART treatment uptake and adherence were suboptimal. Modifiable factors associated with adherence may serve as targets for interventions to support adherence. Further work is however needed to verify self-report measures with biological outcomes and confirm findings in other samples of Indian MSM and TGW.

Tuesday 21 July

Poster Exhibition

Viral origins and evolution

TUPEA049

Phylogenetic estimation of the temporal spread of hepatitis C genotype 1a in North America

J. Joy[1], R. McCloskey[1], T. Nguyen[1], R. Liang[1], Y. Khudyakov[2], A. Olmstead[3], M. Krajden[3], J. Ward[2], P.R. Harrigan[1], J. Montaner[1], A. Poon[1]
[1]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada, [2]Centers for Disease Control and Prevention, Division of Viral Hepatitis, Atlanta, United States, [3]BC Centre for Disease Control, Vancouver, Canada
Presenting author email: jjoy@cfenet.ubc.ca

Background: Timing of the initial spread of hepatitis C genotype 1a (GT1a) in North America (NA) is controversial. 75 percent of NA HCV infected adults are within the cohort composed of individuals born between 1946 and 1964 ('baby boomers'). How HCV reached such high prevalence in this cohort remains unclear. Previous studies have largely implicated injection drug use during the 1960's and 1970's as well as infected blood products prior to adoption of blood donor screening in the early 1990s. We sought to test the concordance between timing of the spread in NA and previously hypothesized periods of high incidence.
Methods: We obtained all publicly available HCV genotype 1a sequence data from public databases for 5 HCV genes, and screened these data for sequences sampled in NA with known dates of collection. Repeated sequences from the same individuals were filtered by a phylogenetic pruning method. For each gene-specific data set, we reconstructed the dynamics of the effective number of infections using a smoothing method (Bayesian skyline) implemented in BEAST. This number is expected to be proportional to prevalence at the exponential phase of an epidemic.
Results: Bayesian skyline plots of all HCV gene regions indicated that the exponential phase of the GT1a epidemic in NA occurred between 1940 and 1965, and that prevalence plateaued between 1965 and 1989 before declining during the early 1990's. Our phylogenetic analyses suggest that the GT1a epidemic in NA had already attained the bulk of its current distribution before 1965.
Conclusions: Our results elucidate the early HCV epidemic dynamics in NA. The expansion of GT1a prior to 1965 suggests that, in addition to injection drug use and contaminated blood products, other nosocomial or iatrogenic factors may have contributed to the high rate of HCV infections in NA baby boomers. The decline in the rate of transmissions in the early 1990's corresponds with blood donor screening, the potential impact of harm reduction initiatives and changes in the patterns of injection drug use. Availability and molecular phylogenetic analysis of archived specimens from the 1940's and onward would improve our ability to time the evolution of the NA HCV GT1a epidemic.

TUPEA050

Origin and evolutionary history of HIV-2 in Cuba

L.Y. Machado[1], O. Martínez[2], H.M. Díaz[1], M. Blanco[1], E. Noa[1], D. Romay[1], M. Dubed[1]
[1]AIDS Research Laboratory, San José de las Lajas, Mayabeque, Cuba, [2]Universidad de las Ciencias Informáticas, Havana, Cuba
Presenting author email: liuberyans@infomed.sld.cu

Background: Infection with human HIV-2 is endemic in West Africa. The virus originated from West African sooty mangabeys during the first half of the 20th century and an epidemic initiation in Guinea Bissau that coincides with the independence war (1963-1974). The HIV-2 group A is categorized as epidemic group. The presence of HIV-2 group A in Cuba has been previously documented. However, is not known their origin and evolutionary history in Cuba. Here, we reconstructed the evolutionary history of HIV-2 group A to delineate the origin and epidemiology of this group in Cuba.
Methods: We used a Bayesian coalescent method to analyze the envelope gene of Cuban HIV-2 group A. The rate of nucleotide substitution was determined. And were used to date the phylogenies and reveal the evolutionary history of HIV-2 group A in Cuba.
Results: Multiple introductions of HIV-2 group A, mainly from Guinea Bissau and Portugal were detected. The most recent common ancestor of Cuban HIV-2 groups A was dated back to about 1972 (95 % HPD: 1966-1978). The rate of nucleotide substitutions was 5.02×10^{-3} substitutions per site per years (95 % HDP: $4.51\text{-}5.52 \times 10^{-3}$).
Conclusions: The results of this study allowed for the first time to estimated the evolutionary history of HIV-2 in Cuba and establish the basis for phylogeographic and phylodynamics studies.

Viral diversity, phylogenetics, phylodynamics

TUPEA051

Molecular epidemiology of clinical HIV-1 *pol* sequences isolated between January 2009 and July 2013 in Cuba

V. Kouri Cardella[1], L. Pérez[2], Y. Aleman[2], J. Perez[2], C. Fonseca[2], C. Correa[2], C. Aragonés[2], L.M. Ortega[2], J. Campos[2], Y. Schrooten[3], L. Vinken[3], Y. Soto[2], C.M. Limia[2], A.-M. Vandamme[3,4], K. Van Laethem[3]
[1]Institute of Tropical Medicine Pedro Kouri, STD Lab. Virology Department, Havana, Cuba, [2]Institute of Tropical Medicine Pedro Kouri, Havana, Cuba, [3]KU Leuven - University of Leuven, Leuven, Belgium, [4]Instituto de Higiene e Medicina Tropical, Universidade Nova de Lisboa, Lisboa, Portugal
Presenting author email: vkouri@ipk.sld.cu

Background: The HIV-1 epidemic in Cuba exhibits an extraordinarily high genetic diversity. The objectives of this study were to determine the HIV-1 subtype distribution and evolution and to investigate associated risk factors.
Methods: Samples were isolated from 838 unique HIV-1 patients (277 therapy-naïve and 561 therapy-experienced) attending the "Pedro Kouri" Institute in Cuba between January 2009 and July 2013. HIV-1 subtype was determined using Rega Subtyping Tool version 2, and confirmed by manual phylogenetic analysis, using CLUSTAL X and the neighbor-joining method in MEGA version 5. The assignment of recombinant forms was done using Simplot version 2.5. Time trends were investigated using 5 year intervals. The association among virological, epidemiological and demographic variables was investigated using Fisher test and logistic regression analysis (statistic package SPSS version 19).
Results: The most prevalent HIV-1 genetic forms in this dataset were subtype B (32.2%), BG recombinants (22.1%) and CRF19_cpx (17.2%). The distribution of subtypes and recombinants was not significantly different between therapy-experienced and therapy-naïve patients. Subtype B infection was associated with male (p=0.022 OR: 1.6; CI: 1.1-2.5) and MSM (p< 0.001 OR: 1.2; 95%CI: 1.4-2.9), while subtypes A, F, G and H were associated with heterosexuals (p< 0.005). Subtype H was more frequently detected among patients living in the east part of the country (p=0.003 OR: 1.7; CI: 1.2-2.3). The prevalence of subtypes A, C, F, G and H among individuals diagnosed with HIV-1 dropped significantly after 1990 (p< 0.05), while CRF BGs (20, 23, 24) significantly increased since 2001 (p≤0.0001 OR:2.9; IC:1.9-4.5). Interestingly, viral variant CRF19_cpx, recently associated with rapid progression to AIDS in Cuba, significantly increased in samples taken since 2011 (13.5% to 20.2%, p=0.0001, OR:4,33; IC:2,9-6,4). Conversely, subtype B showed a significant parabolic trend, increasing up to 2000, and decreasing again in subsequent years (p< 0.05).
Conclusions: This study indicates that the genetic diversity of the Cuban HIV-1 epidemic is still high. In recent years, the frequency of local recombinants is increasing while subtype B is decreasing.

TUPEA052

The *L*ocal *D*issemination *I*mpact of the HIV-1 *env* LDI tripeptide α4β7 binding motif

S. Helmold Hait[1], E. Stankiewicz Machado[2], E. Augusta Soares[3], E. Sprinz[4], M. Alves Soares[1,3]
[1]Universidade Federal do Rio de Janeiro, Pos Graduação em Genética, Rio de Janeiro, Brazil, [2]Universidade Federal do Rio de Janeiro, Instituto de Puericultura e Pediatria Martagão Gesteira, Rio de Janeiro, Brazil, [3]Instituto Nacional de Cancer, Divisão de Genética, Rio de Janeiro, Brazil, [4]Universidade Federal do Rio Grande do Sul, Departamento de Medicina Interna, Porto Alegre, Brazil
Presenting author email: sabrina.helmold@gmail.com

Background: α4β7, a gut homing receptor, plays a pivotal role on HIV pathogenesis during the acute phase of infection. HIV-1 uses a V2-loop LDI/V/X (AAs 179-181) tripeptide found in α4β7 natural ligands to target $CD4^+$T-cells to the GALT. We assessed the HIV-1 α4β7 binding tripeptide composition in different subtypes from major continents.
Methods: PCR amplification and sequencing of the HIV-1 Env V2 loop was performed in samples of HIV^+ adults (n=68) and infants from Brazil (n=27). We included V2 sequences retrieved from the Los Alamos HIV database from South America, Western Europe, South East Asia, China and North America. The α4β7 binding tripeptide composition and variability were compared regarding their respective origins using Chi-Square/Fisher's Exact test. AAs 179-181 conservation degree was verified using Shannon entropy.
Results: V2 sequences from South America presented high conservation of the D core (AA 180, 99.3%) and also a high prevalence of LDI over LDV in successfully disseminating subtypes C (78%), BF (58%), BC (58%) compared to subtype B (30%) (p-values< 0.05). Isoleucine at position 181 was prevalent in C, BC and BF variants (86.4%, 66.7%, 63.1%; Shannon indexes of 0.62, 0.64, 0.94). Global analysis revealed increased LDI frequency in HIV-1 forms going through expansion over previous dominant forms in West Europe (subtypes F, 87%; G, 59%; C, 62% and CRF01, 62%), Former Soviet Union (subtype A, 97%), China (CRF01, 69%; CRF07, 94%; CRF08, 84%) and South East Asia (CRF01, 77%) (p-values < 0.05). Although LDI was

not prevalent in increasing subtypes A (LDI, 41%; LDV, 48%) and CRF02 (LDI, 12%; LDV 38%) in East and Central Africa, LDV has been overgrown by LDI over time. The LDV-LDI shift over the years was observed for subtype B in South and North America, and in Western Europe.
Conclusions: Our results underpin the influence of the HIV-1 Env V2 α4β7 binding epitope composition and conservation on viral fitness transmission. Our data on the *l*ocal *d*issemination *i*mpact of the LDI tripeptide help to explain why certain HIV forms prevail and/or outgrow others in different areas of the world over the AIDS epidemic.

TUPEA053

Evolution of the HIV-1 envelope gene during suppressive cART

J. Bader[1], M. Däumer[2], A. Thielen[2], J. Böni[3], M. Gorgievski-Hrisoho[4], T. Klimkait[1], The Swiss HIV Cohort Study
[1]University of Basel, Biomedicine, Basel, Switzerland, [2]Institute of Immunogenetics, Kaiserslautern, Germany, [3]Institute of Medical Virology, Swiss National Center for Retrovirus, Zürich, Switzerland, [4]Institute of Infectious Diseases, University of Berne, Berne, Switzerland
Presenting author email: joelle.bader@unibas.ch

Background: The genetic diversity of HIV-1 presents currently a major obstacle for controlling and eventually curing infection. It has been claimed that sufficiently potent combination therapy (cART) blocks viral replication thus not allowing a molecular evolution of the targeted viral genes over years of therapy. In this context the viral cell tropism of HIV-1, affecting critical infection events, has only rarely been addressed. Aim of this study was to monitor the sequence evolution of the V3 loop under cART, particularly of cell-associated virus.
Methods: The Illumina Miseq platform was used to obtain deep sequencing results on provirus from chronically HIV-1 infected patients in the Swiss HIV Cohort Study during periods of virologic suppression. Virus remained fully suppressed throughout the study time, and all patients had experienced a good CD4 T cell recovery. Calculations were performed with MEGA 6.0.
Results: Distance relatedness calculations between the dominant variant at baseline and all variants at follow-up time points revealed evidence for sequence-based provirus evolution in five (62.5%) of eight cases during the pre-treatment period. During cART, of the total 17 patients seven (41.2%) continued to show evidence for evolution in their proviruses. In five (29.4%) patients the virus developed a greater diversity over time and therapy. Evidence for sequence evolution was observed in half of the cases with an increase in proviral loads despite suppressive therapy.
Conclusions: Prior to treatment initiation we confirmed a genetic evolution of HIV-1 genomes. Unexpectedly, and not reported so far, we found evidence for evolution in the V3 loop also in almost half of the observed cases with fully suppressed viral load. Our findings suggest an ongoing evolution of the envelope gene, associating with increasing proviral loads even during sufficient cART. As therapy should allow at best very restricted virus propagation in the circulation, we suggest that HIV persistence may be driven by proliferating infected cells. This may provide further evidence for ongoing active and cell-driven processes that permit viral "genetic modulation" and diversification, and thereby lends support to encouraging very early therapy initiation.

TUPEA054

Multiplexed highly-accurate next-generation sequencing of mixtures of full-length HIV genome variants

D. Dilernia[1], J. Ting-Chien[1], D. Monaco[1], M. Brown[2], Z. Ende[1], M. Deymier[1], L. Yue[1], E. Paxinos[2], S. Allen[3], A. Tirado-Ramos[4], E. Hunter[1]
[1]Emory University, Emory Vaccine Center, Atlanta, United States, [2]Pacific Biosciences Inc, Menlo Park, United States, [3]Emory University, Atlanta, United States, [4]University of Texas Helth Science Center, San Antonio, United States
Presenting author email: ddilern@emory.edu

Background: The third generation sequencing technology SMRT (Pacific Biosciences Inc.) provides the longest sequencing reads. However, the relatively high error rate in each read has precluded sequencing of genetic mixtures because true diversity is masked by high background noise. At the same time, this is the only NGS technology that could potentially provide full-length >9Kb HIV genome sequencing. Our objective was to develop a workflow of novel computer algorithms that would allow highly accurate PacBio sequencing of full HIV genome mixtures.
Methods: Samples were obtained from the Zambia Emory HIV Research Project (ZEHRP) discordant couples cohort (Lusaka, Zambia). Forty Single Genome Amplicons (SGAs) were obtained by limiting dilution RTPCR from two linkedtransmission pairs. Library preparations were performed following standard protocols. Sequencing reads were initially filtered (SMRT Analysis v2.2.0) and then subjected to the analytical algorithms presented here (MATLAB v2012a in UBUNTU 10.04). All the sequencing was performed in duplicate.
Results: Overall, the final algorithm involves
(i) statistical based differentiation of true diversity from background noise,
(ii) weighted classificatory analyses and
(iii) INDEL correction procedures.
Validation against Sanger sequencing of the same SGAs indicate that our algorithm is able to derive the sequence for each of the 40 full HIV genome variants in a mixture exhibiting various numbers of single nucleotide variations with an accuracy of >99.9%. This can be achieved using one single SMRT Cell. Results were identical between replicates. Neither in silico artificial sequences nor in silico recombination between different variants was observed. Importantly, our algorithm did not require the a priori definition of the number of sequences in order to get an accurate result and it was able instead to explore the entire data set and provide the real number of unique genetic variants present in the original sample. This was true even for variants differing by one single nucleotide. The methods described here did not require the barcoding of each SGA.
Conclusions: This novel approach can make full-length genome HIV sequencing more cost effective than Sanger sequencing of limited genomic segments and can facilitate the study of HIV quasispecies diversity at the whole-HIV genome level.

TUPEA055

HIV-1 circular recombinant CRF02-AG: rapid spread in Russia and neighboring countries

F. Moskaleychik[1], V. Laga[1], E. Delgado[2], Y. Vega[2], A. Fernandez-Garcia[2], L. Perez-Alvarez[2], G. Kornilaeva[1], A. Pronin[3], Y. Zhernov[1], A. Tatarintsev[1], A. Turgiev[1], M. Thomson[2], M. Bobkova[1], E. Karamov[1]
[1]Gamaleya Research Center for Epidemiology and Microbiology, Laboratory of Immunochemistry, Moscow, Russian Federation, [2]Centro Nacional de Microbiologia, Instituto de Salud Carlos III, Majadahonda, Madrid, Spain, [3]AIDS Center of Moscow Region, Moscow, Russian Federation
Presenting author email: karamov2004@yandex.ru

Background: Genetic analysis makes it possible to monitor the development of HIV/AIDS epidemic (i.e., to determine dominant strains and their spread and to identify new variants). The epidemic in Russia may be divided into several stages. In the late 1980s / early 1990s, individual cases of infection with diverse HIV-1 subtypes were observed. In the mid-1990s, subtype A1 gained dominance, which was spread by injecting drug users (IDUs); of note, its circulating variants in different regions were highly homogeneous. A new recombinant form, CRF03_AB, appeared and started propagating a while later. The introduction of CRF02_AG was first reported in 2006.
Methods: The viral RNA was isolated from serum samples of HIV-infected patients, using a bioMérieux (France) NucliSENS® miniMAG® platform. HIV-1 genome sequences were obtained by an in-house method involving direct sequencing of the amplified fragments of the full genome. The obtained amplicons were sequenced on an Applied Biosystems (U.S.A.) ABI Prism 3130 genetic analyzer. The sequences were processed using BioEdit v. 7.0.5.3 alignment editor. Phylogenetic analysis was performed using MEGA v. 5.1 software. Reference HIV-1 sequences were taken from the genetic database of the Los Alamos National Laboratory (U.S.A.).
Results: Near full-length genome sequence of the recombinant CRF02_AG, circulating in Russia (Moscow region), was obtained for the first time. A worldwide phylogenetic tree of near full-length genome sequences of CRF02_AG was constructed. Three clearly clustering geographic groups were found (CIS, South Korea, and France), suggesting a single-virus introduction in each of the regions above. The CIS cluster, exhibiting minimum genetic diversity, was, therefore, relatively young. The phylogenetic analysis of *env* sequences within this cluster made it possible to clearly discriminate three branches, two Russian and one Uzbek. The low genetic diversity in the two Russian clusters indicates that at least two independent introductions of the recombinant CRF02-AG took place in Russia recently.
Conclusions: The investigations we have carried out using partial and near full-length genome HIV-1 sequences led us to conclude that the spread of CRF02_AG in Russia is rapid and occurs across different regions. The new wave of the epidemic was caused by several introductions from Uzbekistan.

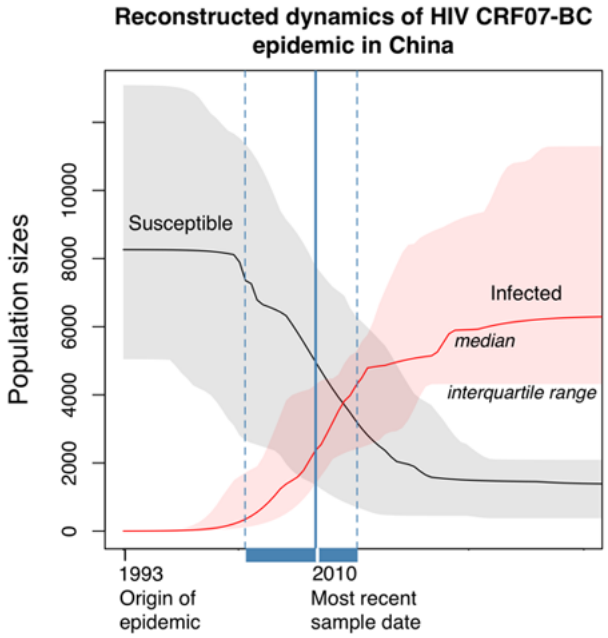
TUPEA056

A new framework for reconstructing epidemic dynamics from virus sequences: model validation and application to the HIV CRF07-BC epidemic in China

A. Poon[1,2]
[1]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada, [2]University of British Columbia, Medicine, Vancouver, Canada
Presenting author email: apoon@cfenet.ubc.ca

Background: Many RNA viruses, such as HIV, evolve so quickly that genetic differences can accumulate between different infections within weeks. Consequently, the epidemic spread of the virus leaves a distinct imprint on the genetic diversity of virus infections. I present a new framework (*kernel-ABC*) that enables investigators to fit a wide range of epidemic models to sequence data and compare its performance to leading phylodynamic software. This method is then used to analyze a recent HIV epidemic of CRF07-BC in China, the dominant variant among injection drug users in the northwestern region.

Methods: To validate the model, transmission trees were simulated under a birth-death susceptible-infected-removed (BDSIR) model using the MASTER program within BEAST2. Molecular evolution was simulated over these trees using INDELIBLE with a codon model trained on HIV data. Trees were reconstructed from these sequences by maximum likelihood (RAxML) and rooted under a molecular clock with a root-to-tip method. The model was fit by approximate Bayesian computation (ABC), where parameters were adjusted until the model yielded simulations resembling the "observed" trees given a customized kernel similarity measure. These same data were analyzed using the serial BDSIR method in BEAST2.
Results: The root-to-tip method was consistently more accurate than BEAST2 for estimating the age of simulated epidemics. BEAST2 overestimated the initial sizes of the susceptible population by a factor of ~5 and underestimated transmission rates by a factor of ~10. In contrast, ABC obtained accurate estimates of these epidemic growth parameters. However, BEAST2 was more successful at estimating lineage death parameters of the BDSIR model (mortality and sampling rates). Based on these results, the kernel-ABC method was used to reconstruct the growth of the HIV CRF07-BC epidemic in China from *n*=314 published sequences of gp120 from this region. The epidemic was estimated to have originated in 1993. Kernel-ABC reconstructed the mid-point of exponential growth around 2010 at approximately 2,200 cases, and predicted the epidemic would reach about 6,600 cases (interquartile range 4,301-10,982).



[Reconstructed dynamics of HIV CRF07-BC epidemic]

Conclusions: The simulation-based kernel-ABC method provides a highly versatile framework for fitting epidemic models to virus sequence variation. Model validation on simulated data demonstrated good performance relative to leading software for phylodynamics.

TUPEA057

Prevalence, evolutionary dynamics and transmission pattern of HCV, HIV-1 and HPgV among injecting drug users

K.T. Ng[1], Y. Takebe[2], Y.M. Lee[1], A. Wahab[1], W.Z. Chow[1], H.A. Abed Al-Darraji[1], L.Y. Ong[1], A. Kamarulzaman[1], K.K. Tee[1]
[1]University of Malaya, Centre of Excellence for Research in AIDS (CERiA), Kuala Lumpur, Malaysia, [2]AIDS Research Center, National Institute of Infectious Diseases, Tokyo, Japan
Presenting author email: k2tee@yahoo.com

Background: Co-circulation of HIV-1 and human pegivirus (HPgV) in HCV-infected individuals is common. Despite the epidemiological impact, co-analysis on the evolutionary dynamics and transmission network profiles of these bloodborne viruses remains scarce, especially among individuals with multiple infections.
Methods: A total of 228 subjects with a history of intravenous drug exposure were recruited in Kuala Lumpur, Malaysia between 2009 and 2010. Nested-PCR was performed to amplify the 5'-UTR region and NS5B gene of both HCV and HPgV, and the *gag-pol* gene of HIV-1. Phylodynamic profiles of each transmission networks were elucidated using maximum likelihood inference and Bayesian coalescence approach. A transmission network was defined as a phylogenetic cluster (≥2 isolates with genetic distance of ≤2.5%) supported by >90% bootstrap values and Bayesian posterior probability value of 1.0 at the tree node.
Results: HCV and HIV-1 seropositivity was estimated at 94% each. Based on the availability of sequence data, mono-infection was detected in 38.8% (64/165) of the subjects (HCV=36, HIV=27, HPgV=1). Cases of dual-infection and HCV/HIV/HPgV triple-infection were detected in 40.6% (67/165; HCV/HIV = 48, HCV/HPgV = 8, HIV/HPgV = 11) and 20.6% (34/165) of the subjects, respectively. Bayesian coalescent analysis indicated that the predominant HCV, HIV-1 and HPgV genotypes were introduced into the injecting drug user (IDU) population in Kuala Lumpur through multiple sub-epidemic lineages that arose as early as 1950s (HCV), 1980s (HIV-1) and 1990s (HPgV). Four HCV transmission networks involving subtypes 1a, 1b, 3a and 3b were later identified. In addition, five and six transmission networks were observed among HIV-1 (CRF33_01B) and HPgV (genotype 2), respectively. Most of the transmission networks (93%) emerged after the early 2000s with new transmission networks continue to emerge thereafter, despite increased access to antiretroviral therapy and other intervention measures. The lack of phylogenetic evidence and discrete temporal distributions among multiply infected individuals suggested that HCV/HIV, HCV/HPgV and HIV/HPgV co-transmissions were rare, and that these individuals probably acquired the infections from more than one transmission network.
Conclusions: Continuous emergence of new transmission networks and coexistence of multiple subepidemics from various common ancestors are likely to fuel the onward transmissions of HCV, HIV-1 and HPgV among IDUs.

TUPEA058

Identification and genetic characterisation of a novel HIV-1 circulating recombinant lineage (CRF74_01B) among people who inject drugs in Malaysia

H.T. Cheong[1], W.Z. Chow[1], Y. Takebe[2], J.B. Chook[1], K.G. Chan[3], H.A. Al-Darraji[1], C. Koh[1], A. Kamarulzaman[1], K.K. Tee[4]
[1]Centre of Excellence for Research in AIDS (CERiA), Department of Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia, [2]AIDS Research Centre, National Institute of Infectious Diseases, Toyama, Shinjuku-ku, Tokyo, Japan, [3]Division of Genetics and Molecular Biology, Institute of Biological Sciences, Faculty of Science, University of Malaya, Kuala Lumpur, Malaysia, [4]Centre of Excellence for Research in AIDS (CERiA), Department of Medicine, Faculty of Medicine, University of Malaya, Department of Medicine, Faculty of Medicine, Kuala Lumpur, Malaysia
Presenting author email: k2tee@um.edu.my

Background: In Malaysia, HIV-1 epidemics have largely been driven by sharing of needles among people who inject drugs (PWIDs) until recently. Due to the high tendencies to recombine, the diversity and complexity of HIV-1 epidemics have been increasing. This scenario was exemplified by the discoveries of numerous circulating recombinant forms (CRFs) in China, Thailand, Malaysia and Singapore.
Methods: In order to study the detailed recombinant structures for a monophyletic cluster of protease-reverse transcriptase (PRRT) sequences in neighbour joining (NJ) tree, near full-length genomes were amplified and subjected to bootscanning plot and informative sites analyses. Putative parental subtypes of each sub-genomic segment were then confirmed through NJ analyses. Next, phylogenetic relationship between amplified sequences and reported CRFs sharing similar breakpoints were studied using the maximum-likelihood and Bayesian Markov chain Monte Carlo (MCMC) sampling methods.
Results: From a genotype screening of HIV-1 strains circulating among PWIDs recruited between 2010 and 2011, we found that 6/207 (2.9%) PRRT sequences formed a monophyletic cluster with strong bootstrap support (>80%) in NJ analysis. Near full-length genome sequencing revealed that these strains had identical recombinant structure composed of CRF01_AE and subtype B', with eight breakpoints dispersed in the *gag-pol* and *nef* regions. This new recombinant lineage was designated as CRF74_01B. Remarkably, this CRF shared four and two recombination hotspots with the previously described CRF33_01B and the less frequent CRF53_01B, respectively. Maximum-likelihood and Bayesian MCMC analyses in multiple genomic regions showed that CRF74_01B is closely related to both CRF33_01B and CRF53_01B. This observation suggests that CRF74_01B was probably a direct descendent from specific lineages of CRF33_01B, CRF53_01B and subtype B'. Since CRF33_01B has been proven by studies elsewhere to have expanded within various risk populations in Malaysia, it is highly probable for CRF33_01B to become implicated in the emergence of CRFs and other unique recombinant forms in the future.
Conclusions: We report a novel HIV-1 genotype designated as CRF74_01B among six epidemiologically-unlinked PWIDs in Kuala Lumpur, Malaysia. The characterisation of the novel CRF74_01B is of considerable significance towards the design of disease diagnosis, treatment and prevention strategies.

TUPEA059

Kive: a framework for version control of bioinformatic pipelines and data, and its application to HIV resistance genotyping

R. Liang[1], E. Martin[1], R. McCloskey[1], D. Kirkby[1], J. Nakagawa[1], T. Nguyen[1], P.R. Harrigan[1,2], A. Poon[1,2]
[1]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada, [2]University of British Columbia, Medicine, Vancouver, Canada
Presenting author email: rliang@cfenet.ubc.ca

Background: Bioinformatic pipelines have become essential tools in modern biomedical and clinical laboratories. However, pipelines are usually under constant development and there is no convenient framework for tracking which data sets were produced by which version of a pipeline. As a result, bioinformatic analyses are seldom reproducible.
We present a new framework for the version control of pipelines and data, and its use in the development and validation of a pipeline for HIV resistance genotyping by next-generation sequencing.
Methods: *Kive* was developed in the *Python* scripting language within the *Django* web framework. It runs as a web server that interacts with a *PostgreSQL* relational database. *Kive* features an intuitive web interface, including a point-and-click toolkit for assembling and running pipelines. When pipelines are executed within *Kive*, it automatically records the digital fingerprints (checksums) and filesystem locations of all intermediate data sets and results. This enables the easy retrieval of complete version information for every pipeline step that generated a specific set of results from raw data. *Kive* includes user and group administration to control data access privileges, and a queuing system for distributing jobs for parallel execution in a clustered computing environment.
Results: *Kive* was used to track the development and testing of a pipeline for processing HIV short read data from an Illumina MiSeq platform at the BC Centre for Excellence in HIV/AIDS. This complex pipeline comprised scripts in a variety of languages (*Python*, *Ruby*, *R*, and *bash*) passing data between several different software packages. Using *Kive* for the automated processing of MiSeq data greatly facilitated the validation and documentation of the impact of each change in bioinformatics methods on clinically significant variables (prevalence of HIV resistance mutations).
Conclusions: Clinical laboratory accreditation programs, such as the program maintained by the College of American Pathologists, have begun to issue new requirements for the documentation and archival of bioinformatic pipelines. As an open-source and inherently customizable framework, *Kive* can enable laboratories to meet these requirements in a cost-effective manner with minimal disruption to existing computing infrastructure. The public release of *Kive* will be available at: https://github.com/cfe-lab/Kive.

TUPEA060

Newly diagnosed HIV-1 infections in Spain frequently group in clusters of subtype B and non-subtype B genetic forms

E. Delgado, J. Martínez, M.T. Cuevas, A. Fernández-García, Y. Vega, V. Montero, C. Carrera, M. Sánchez, E. García-Bodas, L. Pérez-Álvarez, M.M. Thomson,
Spanish Group for the Study of HIV-1 Antiretroviral Drug Resistance and Tropism
Instituto de Salud Carlos III, Centro Nacional de Microbiología, Majadahonda, Spain
Presenting author email: mthomson@isciii.es

Background: A recent increase in phylogenetic clustering among new HIV-1 infections has been observed in many countries, frequently associated with men who have sex with men (MSM). Here we analyze phylogenetic clustering among newly diagnosed HIV-1 infections of 6 regions of Spain.
Methods: Samples were collected from HIV-1-infected individuals newly diagnosed in 2013 and 2014, attended in 19 hospitals from 6 Spanish regions (Galicia, Basque Country, Navarre, Castilla y León, Madrid, and Extremadura). RNA extracted from plasma was used for RT-PCR amplification and sequencing of protease and reverse transcriptase (PR-RT), env V3 region, or both. Phylogenetic analyses were performed via maximum likelihood with RAxML and PhyML, applying the GTR+G+I evolutionary model. Clusters were defined as those supported by bootstrap values ≥90% with RAxML and by aLRT SH-like values ≥0.9 with PhyML, and comprising ≥4 individuals with a majority being native Spanish. In these analyses, sequences from samples collected in previous years in Spain and sequenced by us were also included.
Results: A total of 430 samples from new HIV-1 diagnoses of 2013-2014 were sequenced, either both in PR-RT and V3 (n=262), only in PR-RT (n=144), or only in V3 (n=24). Most were from Basque Country (n=212), Galicia (n=133), and Navarre (n=50). Non-subtype B infections were 132 (31%). Ninety four clusters of ≥4 individuals were identified, of which 32 comprised ≥10 individuals. Eighteen clusters were of non-subtype B genetic forms, including the largest one, of subtype F (n=131). Viruses grouping in clusters of ≥4 and of ≥10 individuals were 223 and 122 (52% and 28%), respectively. Clustering among MSM was more frequent than among heterosexuals (60% vs. 41% and 37% vs. 16%, grouping in clusters of ≥4 and ≥10 individuals, respectively).
Conclusions: A high proportion of newly diagnosed HIV-1 infections in Spain group in clusters of subtype B and non-subtype B genetic forms, most frequently among MSM. The recent expansion of HIV-1 clusters in many countries reflects an active dynamic of viral propagation via sexual transmission, requiring the reinforcement of public health measures aimed at the prevention of high risk sexual behavior.

TUPEA061

Prevalence of defective HIV-1 genome in HIV-infected patients on long-term cART and correlation with characteristics of patients

C. Psomas[1,2], B. Montès[3], S. Eymard-Duvernay[2], V. Le Moing[1,2], E. Delaporte[1,2], J. Reynes[1,2], A. Makinson[1,2]
[1]Academic Hospital of Montpellier, Infectious Diseases Department, Montpellier, France, [2]UMI 233, IRD Montpellier University, Montpellier, France, [3]Academic Hospital of Montpellier, Virology Department, Montpellier, France
Presenting author email: c-psomas@chu-montpellier.fr

Background: APOBEC3 protein family members restrict human immunodeficiency virus type 1 (HIV-1) replication through the induction of G-->A hypermutation inducing defective HIV-1 genomes; this phenomenon could be clinically relevant in long term non progressors or patients having an optimum virologic response under combination antiretroviral therapy (cART). The objective of our study was to estimate the prevalence of HIV-1 hypermutation in HIV-infected patients on successful cART, as well as to analyze the factors associated to a higher hypermutation score.
Methods: Peripheral blood mononuclear cells of HIV-infected patients on long term cART for at least 24 months were collected by Ficoll density gradient centrifugation. Bulk sequencing of the reverse transcriptase (RT) and the protease (PT) regions was used to detect the presence of G-->A hypermutation and to quantify hypermutation with the following published score: ratio of (number of G-->A substitutions/number of consensus G) to (number of mutations/number of nucleotides sequenced). Associations between age, sexe, HIV-infection and cART duration, HIV clade, CD4 T cell count, CD8 T cell activation and hypermutation score were analyzed using a linear regression model.
Results: Seventy patients under cART and 9 naive patients were included in the study; male sexe was predominant (81%), median age was 52 years (IQR 46-58) and median CD4 T cell count was 564/mm3 (378-723). Clade B was preponderant (58%). Median duration of HIV infection was 16 years (9-22), and median cART duration was 12 years (7-16). Prevalence of hypermutation was 20% in treated patients with variable levels of hypermutations per patient (median 1; range 1-3), comparatively to a prevalence of hypermutation of 11% in naive patients. The median value of hypermutation score was 1.3 (0.9-1.6) for PT region, and 1.2 (1.0-1.6) for RT region.
Factors associated with a higher hypermutation score of RT and PT in the multivariate analysis were age less than 45 years (p=0.018), shorter cART duration (p=0.066), higher CD8 T cell activation (p=0.094) and viral B clade (p=0.036).
Conclusions: Hypermutation is frequent in treated HIV-infected patients. Duration of cART may decrease the prevalence of hypermutation. Understanding of mechanisms related to defective virus is crucial in order to advance in terms of HIV virus eradication.

TUPEA062

Full-length ultra-deep sequencing of HIV-1 transmission partners reveals the impact of intra-host evolution on immune control

J. Brener[1], R. Batorsky[2], A. Gall[3], P. Kellam[3], T. Allen[2], P. Goulder[1], P.C. Matthews[1]
[1]University of Oxford, Oxford, United Kingdom, [2]Ragon Institute of MGH, MIT and Harvard, Cambridge, United States, [3]Wellcome Trust Sanger Institute, Cambridge, United Kingdom
Presenting author email: jacqui.brener@wolfson.ox.ac.uk

Background: The advent of next generation sequencing technology has provided a sensitive platform for producing extensive datasets that allow novel and detailed analyses of viral adaptation and immune control of HIV. In the context of expression of HLA alleles associated with superior viral control, such as HLA-B*27:05 and HLA-B*57:01, such data may provide critical insights into the determinants of immune control. This study set out to establish the mechanisms responsible for loss of viral control by focusing on individuals who express favourable alleles but still lose immune control. Performing such studies in transmission partners allows for HLA-mediated selection to be closely tracked, by providing an approximation of the transmitted founder sequence.
Methods: We performed full-length HIV high-throughput Illumina sequencing on longitudinal samples from three transmission pairs infected with B Clade, C Clade and CRF01_AE Clade HIV respectively. All three recipients were infected by HLA-B*27:05/HLA-B*57:01-negative donors and expressed HLA-B*27:05. Two of the recipients also expressed HLA-B*57:01. All three recipients progressed to AIDS despite expression of favourable HLA alleles.
Results: We analysed intra-host variability across the full genome and at CD8+ T Cell epitopes to identify polymorphisms both at the consensus and minor variant level that were associated with disease progression in the recipients. In an HLA-B*27:05/B*57:01 positive progressor we found that accumulation of escape mutations at low levels preceded fixation of these mutations within the population and predicted disease progression. We identified minor

variant transmissions and reversion of transmitted mutations as a marker of viral fitness cost, and demonstrated clade-specific differences in the transmitted virus that directly implicate the viral sequence as a determinant of HLA-mediated immune control of HIV. Overall, we observed a remarkable degree of intra-host sequence conservation except at a small number of key sites, implicating these specific sites in immune control of HIV.
Conclusions: The novel insights afforded by the use of next generation sequencing technology and transmission pair studies may be critical for furthering our understanding of intra-host viral evolution and immune control.

Viral fitness

TUPEA063

Consequences of HLA-B*13-associated escape mutations on HIV-1 replication and Nef protein function

A. Shahid[1], X.T. Kuang[2], G. Anmole[2], A. Olvera[3], L. Cotton[1], C. Brander[3,4], M.A. Brockman[1,2,5], Z.L. Brumme[1,5]
[1]Simon Fraser University, Faculty of Health Sciences, Burnaby, Canada, [2]Simon Fraser University, Department of Molecular Biology and Biochemistry, Burnaby, Canada, [3]Irsicaixa AIDS Research Institute, Barcelona, Spain, [4]ICREA, Barcelona, Spain, [5]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada
Presenting author email: ashahid@sfu.ca

Background: HLA-B*13, a protective HLA class I allele, selects CTL escape mutations across HIV-1, but their effects on viral replication and protein function remain incompletely understood. We assessed the impact of 10 published HLA-B*13 escape mutations in Gag, Pol and Nef on viral replication.
We also assessed the impact of Nef mutations on cell-surface CD4 and HLA class I downregulation, and the latter's consequence for recognition of virus-infected cells by epitope-specific T-cells.
Methods: HLA-B*13 escape mutations in Gag (A146S, I147L, K436R, I437L), Pol (Protease-L63S; RT-Q334N, T369A, K374R) and Nef (E24Q, Q107R) were engineered alone and in biologically relevant combinations (defined via analysis of longitudinal HIV-1 RNA sequences from 9 B*13+ seroconverters and cross-sectional sequences from 69 B*13+ chronic patients) into an HIV-1_{NL4-3} backbone. Viral replication was determined using a GFP-reporter T-cell assay. Nef-mediated CD4 and HLA-A*02 downregulation was assessed by flow cytometry. Recognition of infected target cells by HIV-1-specific effector cells was assessed via co-culture with an NFAT-driven luciferase reporter T-cell line specific for the A*02-restricted Gag-FK10 peptide.
Results: Of all mutations tested, only Gag I437L incurred a 14% replicative reduction, alone and in combination with A146S and/or I147L. This defect was rescued to wild-type (HIV-1_{NL4-3}) levels by K436R. A novel B*13 epitope was identified in $p24^{Gag}$ ($GQMVHQAI_{140-147}$). Single Nef mutations did not affect CD4 or HLA-A*02 downregulation; however, the Nef double mutant was nearly 70% impaired for the latter function (for context, the canonical Nef $M20A_{NL4-3}$ mutant defective for HLA downregulation was >90% functionally impaired). Correspondingly, luciferase signal emitted by HIV-1-specific effector cells upon co-culture with HIV-$1_{E24Q/Q107R}$-infected target cells was 2-fold higher than for cells infected with NL4-3 or single Nef mutants.
Conclusions: A minority of HLA-B*13-driven escape mutations modestly dampen HIV-1 replication or Nef function, which could contribute in part to B*13-associated protection from disease progression. The observation that a naturally-occurring (albeit rare; 4%) Nef double mutation impairs HLA downregulation and enhances recognition of infected cells by HIV-1-specific T-cells suggests a novel escape-associated defect that ironically dampens a key viral immune evasion strategy. Improved understanding of the mechanisms underlying HLA-associated protective effects may have implications for HIV-1 vaccine design.

TUPEA064

Drug susceptibility and viral fitness of integrase strand transfer inhibitor and nucleoside reverse transcriptase inhibitor resistance mutations in combination

K. Andreatta, M. Miller, K. White
Gilead Sciences, Inc, Clinical Virology, Foster City, United States
Presenting author email: kristen.andreatta@gilead.com

Background: Coformulated elvitegravir (EVG)/cobicistat (COBI)/emtricitabine (FTC)/tenofovir disoproxil fumarate (TDF) is the first single tablet regimen to combine an integrase (IN) strand transfer inhibitor (INSTI) with a nucleoside reverse transcriptase (RT) inhibitor (NRTI) backbone (FTC/TDF). In phase III clinical trials of EVG/COBI/FTC/TDF, the majority of HIV-1 isolates with emergent drug resistance contained the FTC resistance (-R) mutation M184V/I in RT accompanied by a primary INSTI-R mutation in IN. Here, the in vitro characteristics of mutant viruses containing M184V in RT and Q148R or N155H in IN were evaluated, alone and in combination, for potential cross-class interactions.
Methods: HIV-1 with the RT mutation M184V (RT-M184V) and the IN mutations Q148R (IN-Q148R) and N155H (IN-N155H) were constructed as single site-directed mutants and as RT+IN combinations. Phenotypic susceptibility assays and pairwise growth competitions evaluated drug resistance and viral fitness.
Results: Viruses with single IN-Q148R or IN-N155H mutations exhibited reduced susceptibility to EVG (35- and 111-fold, respectively) and cross-resistance to raltegravir (RAL). The addition of RT-M184V to either IN mutant did not affect the level of resistance to INSTIs. All viruses containing RT-M184V had greatly reduced susceptibility to FTC (>1000-fold). All viruses studied retained full sensitivity to tenofovir (TFV). In the absence of drug, the viral fitness of RT and/or IN mutants was diminished relative to wild-type in the following order: wild-type > RT-M184V ≥ IN-N155H ≥ RT-M184V+IN-N155H ≥ IN-Q148R
≥ RT-M184V+IN-Q148R. In the presence of drug concentrations approaching physiologic levels, drug resistance counteracted the replication defects, allowing single mutants to outcompete wild-type with one drug present and double mutants to out-compete single mutants with two drugs present.
Conclusions: The RT-M184V, IN-Q148R, and IN-N155H mutations altered susceptibility to their corresponding inhibitor classes with no cross-class resistance detected, consistent with the lack of cross-class resistance observed for RT-M184V, RT-K65R, and IN-E92Q mutations in previous studies. The deleterious effects of the mutations on viral fitness were additive in the absence of drug, but resistance compensated for fitness defects in the presence of drug. These results suggest that during antiretroviral treatment with multiple drugs, the development of viruses with combinations of mutations may be favored despite diminished viral fitness.

TUPEA065

SIV CTL escape mutations resulting in loss of viral fitness can be maintained after transmission into MHC-I-mismatched hosts

T. Nomura[1], S. Seki[1,2], M. Nishizawa[1], S. Harada[1], K. Yoshimura[1], T. Matano[1,2]
[1]National Institute of Infectious Diseases, AIDS Research Center, Tokyo, Japan, [2]University of Tokyo, Institute of Medical Science, Tokyo, Japan

Background: In HIV infections, cytotoxic T lymphocyte (CTL) responses exert strong suppressive pressure on viral replication and often select for mutations resulting in escape from CTL recognition with viral fitness costs. For our understanding of the mechanism of HIV evolution by transmission in population, it is important to investigate how the loss of viral fitness by these mutations affects in vivo viral replication and disease progression after viral transmission into MHC class I (MHC-I)-mismatched hosts. Here, we examined whether these mutations can be maintained and affect disease progression after transmission in a macaque AIDS model.
Methods: Four MHC-I haplotype 90-120-Ia-negative rhesus macaques (recipients) were inoculated with plasma that had been obtained from a 90-120-Ia-positive macaque (donor) one year after simian immunodeficiency virus mac239 (SIVmac239) challenge. Virological and immunological analyses were performed in these macaques.
Results: Multiple mutations including eight 90-120-Ia-associated CTL escape mutations were dominant in the 90-120-Ia-positive donor at one year after challenge. Three (Gag216S, Gag244E, and Gag375M) of the eight mutations were confirmed to result in loss of viral fitness in vitro. One 90-120-Ia-negative recipient controlled viral replication, but the remaining three showed persistent viremia and developed AIDS in 14-22 months after the plasma transmission. Most of the CTL escape mutations were maintained without reversion until AIDS onset in the latter three animals; two of them showed no reversion. In the remaining one, two mutations reverted, but Gag244E and Gag375M were maintained.
Conclusions: SIV CTL escape mutations resulting in loss of viral fitness can be maintained after viral transmission into MHC-I-mismatched hosts. Even those viruses carrying these mutations with decreased replicative ability can induce persistent viremia and develop AIDS without reversion. These results would contribute to our understanding of the mechanism for accumulation of CTL escape mutations in HIVs by transmission in humans.

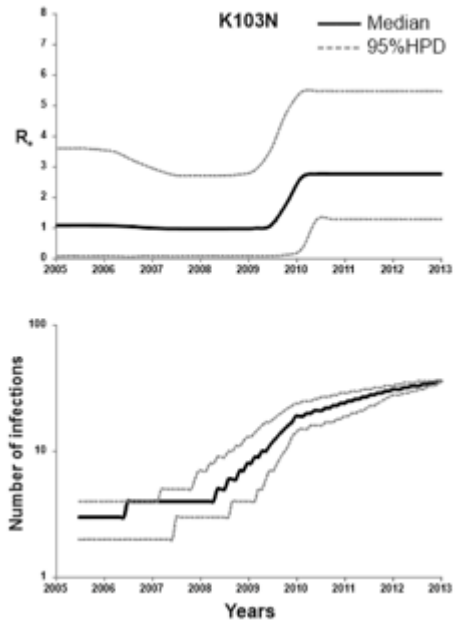
Antiretroviral resistance mechanisms

TUPEA066

Transmission dynamics of local networks of transmitted resistance to NNRTIs suggest an increasing incidence over time in Greece: the added value of molecular epidemiology to public health

D. Paraskevis[1], A. Zavitsanou[1], E. Magiorkinis[1], P. Gargalianos[2], G. Xylomenos[2], M. Lazanas[3], M. Chini[3], A. Skoutelis[4], V. Papastamopoulos[4], A. Antoniadou[5], A. Papadopoulos[5], M. Psichogiou[6], G. Daikos[6], G. Chrysos[7], V. Paparizos[8], S. Kourkounti[8], H. Sambatakou[9], N. Sipsas[10], G. Koratzanis[11], P. Panagopoulos[12], E. Maltezos[12], S. Drimis[7], A. Hatzakis[1]
[1]Medical School, University of Athens, Department of Hygiene Epidemiology and Medical Statistics, Athens, Greece, [2]G. Genimatas General Hospital, Athens, Greece, [3]Red Cross Hospital, General Hospital, Athens, Greece, [4]Evaggelismos General Hospital, Athens, Greece, [5]Attikon University, General Hospital, Athens, Greece, [6]Laikon General Hospital, Department of Propedeutic Medicine, Athens, Greece, [7]Tzaneio General Hospital, Athens, Greece, [8]A. Syngros Hospital, Athens, Greece, [9]Ippokrateion General Hospital, Athens, Greece, [10]Laikon General Hospital, Department of Pathophysiology, Athens, Greece, [11]Sismanogleio General Hospital, Athens, Greece, [12]Democritus University of Thrace, Alexandroupolis, Greece
Presenting author email: ppanago@med.duth.gr

Background: HIV-1 transmitted drug resistance (TDR) to NNRTIs has been shown to compromise first-line response to treatment. The prevalence of resistance to NNRTI was previously estimated to be 15.9% among drug naïve individuals sampled during 2003-2013 in Greece. Our aim was to estimate the effective reproductive number (*Re*) and the transmission dynamics of four major transmission networks of NNRTI resistance in Greece.
Methods: Phylogenetic analysis was conducted in sequences from 179 individuals with NNRTI resistance and 959 cases without resistance infected with subtype A in Greece, and 797 sequences sampled globally. Phylodynamic analysis was performed using newly developed birth-death models (BDM) allowing estimation of important epidemiological parameters such as the effective reproductive number (*Re*).
Results: Phylogenetic analyses revealed that the majority of individuals infected with resistant strains belonged to monophyletic clusters. Specifically, 49 out of 54 (90.7%) of sequences with 103N, and 98 out of 125 (78.4%) with 138A belonged to one and three phylogenetic clusters (transmission networks), respectively. The prevalence of 103N showed a significant increasing trend over time, whereas no trend was found for 138A. The time of the most recent common ancestor (tMRCA) was in 2001 (95%HPD:1996-2005) for the 103N cluster and in 1993 (95%HPD:1986-1999), 1994 (95%HPD:1987-1994) and 2005 (95%HPD:2000-2008) for the three 138A networks. Although the time of origin was estimated several years ago, the *Re* for all transmission networks was increasing (*Re*>1) the last few years (2009-2013). The highest *Re* was found for 103N (2.77) versus 2.1 for the most recent 138A cluster (figure). For the rest two networks, *Re* was 1.3 and 1.7 (maximum values).



[figure]

Conclusions: Our study suggests that the most prevalent mutations associated with resistance to NNRTIs were transmitted through local networks in Greece. Notably, phylodynamic analysis allows estimating that resistance the last few years has been actively propagated with an increasing incidence. Those belonging to the active TDR networks are the priority population for prevention. Our study highlights the added value of the latest advances in molecular epidemiology to public health regarding the identification of critical parameters which allows identifying those belonging to active transmission networks. This is of key importance to public health.

TUPEA067

HIV resistance pathways support the use of lamivudine (3TC) and dolutegravir (DTG) in combination

T. Mesplède, D. Singhroy, B. Spira, M. Wainberg
McGill University AIDS Centre, Lady Davis Institute for Medical Research - Jewish General Hospital, Montréal, Canada
Presenting author email: tibo_mes@hotmail.com

Background: A single daily pill regimen combining lamivudine (3TC), abacavir and dolutegravir was recently approved for treatment of HIV-positive individuals. Given that both the M184I/V emtricitabine/3TC-associated resistance mutations and the R263K DTG-associated resistance mutation negatively affect HIV replication capacity, we investigated the effects of combining M184I/V with R263K on HIV-1 susceptibility to 3TC and DTG and viral fitness. We hypothesized that combining these resistance mutations may lead to a decrease in viral fitness that may, in fact, benefit the rare individuals who may fail 3TC/DTG-based therapy.
Methods: TZM-bl cells were infected with WT, M184I, M184V, R263K, M184I/R263K and M184V/R263K viruses to measure infectiousness and resistance against 3TC and DTG. Viral fitness was measured in long-term infectivity assays with PM1 cells. Integration efficiency was assessed using Alu-mediated PCR.
Results: Our experiments revealed that DTG and 3TC synergize to inhibit HIV-1 replication. The M184I/V and R263K mutations conferred high-level resistance against 3TC (>100-fold) and low-level resistance against DTG (2.2-fold), respectively. Combining M184I/V with R263K did not significantly change levels of resistance conferred by single mutations against either drug. Single mutations decreased HIV-1 infectiousness by 1.5 to 2.1-fold whereas the M184I/R263K and M184V/R263K combinations reduced infectiousness by 2.9 and 2.4-fold, respectively. Long-term infectivity assays showed similar decreases in HIV-1 viral fitness for both combinations of mutations. Alu-mediated PCR results supported these observations.
Conclusions: Combining 3TC- and DTG-specific mutations resulted in a further decrease in HIV-1 infectiousness and replication capacity without conferring additional levels of resistance. This suggests that individuals failing 3TC/DTG-based therapy may exhibit lower viral loads than those observed with other combinations of drugs and supports the use 3TC or emtricitabine in combination with DTG.

TUPEA068

Evolution of HIV-1 integrase following selection of R263K with further dolutegravir treatment: a case report from the P1093 study

C. Vavro[1], P. Palumbo[2], A. Wiznia[3], C. Alvero[4], B. Graham[5], T. Fenton[4], R. Hazra[6], E. Townley[7], A. Buchanan[1], J. Horton[1], R. Viani[8], P1093 Study Group
[1]GlaxoSmithKline, Infectious Diseases R&D, Cary, United States, [2]Dartmouth Medical School, Lebanon, United States, [3]Jacobi Medical Center, Bronx, United States, [4]Harvard School of Public Health, Boston, United States, [5]Frontier Science Research Foundation, Inc., Amherst, United States, [6]NICHD, Bethesda, United States, [7]HJF-DAIDS, NIAID, Bethesda, United States, [8]University of California, San Diego, United States
Presenting author email: cindy.l.vavro@gsk.com

Background: Recent clinical and in vitro reports have identified R263K in HIV-1 integrase (IN) as a key treatment-emergent resistance-associated mutation (RAM) for dolutegravir (DTG). Given the low incidence of this mutation in the clinical setting, little is known of the impact this IN mutation has on further IN evolution under DTG treatment. Here we report on integrase resistance evolution over 3 years of DTG and Truvada treatment in a 12 yr adolescent from P1093 study.
Methods: P1093 is a phase I/II, multicenter, open-label pharmacokinetics (PK), safety, dose-finding study of DTG plus optimized background regimen in pediatrics. Longitudinal HIV-1 RNA (VL), clonal IN genotypes, DTG fold-change (FC) in IC_{50}, and IN replication capacity (RC) were investigated.
Results: The patient had a history of NRTI and PI use but the pretreatment genotype showed no primary RAM's to NRTI's or PI's. Intermittent adherence to both Truvada and DTG was reported throughout study. PK data collected through Week 24 showed adequate DTG exposure. Entry VL was 7739 copies/mL and fell below 400copies/mL during the first 24 weeks. However, the median VL over 3 years was 3940 copies/mL. Virologic failure was confirmed on Week 36 with an acquisition of R263R/K and the patient remains on study for an additional 2+ years. Integrase clonal analysis with corresponding DTG FC was conducted at Pretreatment, Week 36 and Week 136.

Timepoint	HIV-1 RNA	Total Clones Tested	IN Linked Substitutions / # Clones	Clonal Median DTG FC FC	Clonal Median IN RC %
Pretreatment	7739	8	L74V / 4 clones	0.97	95%
			L74I / 1 clone	0.97	29%
			L74L / 3 clones	1.16	81%
Week 36	9978	8	R263K / 4 clones	2.0	97%
			V201I / 3 clones	1.19	92%
			V201I, R263R / 1 clone	1.26	128%
Week 136	1367	16	A49G, M50V, V201I, R263K / 12 clones	4.17	49%
			A49G, M50V, E138T, S147G, V201I, R263K / 4 clones	6.33	28%

[IN Clonal Anaysis]

Phylogenetic analysis of all clonal data suggests the 4 clones from Week 136 harboring A49G, M50V, E138T, S147G, V201I, and R263K cluster together with a bootstrap of 99% and show more evolutionary distance consistent with continued drug pressure. At Week 136, additional linked IN mutations with R263K result in decreased DTG susceptibility. At Week 136 decreases in median IN RC were also noted, however, these measurements were performed on HIV-1 IN only and may not provide complete characterization of viral fitness. Therefore, the IN RC results should be taken with caution.

Conclusions: Continued DTG treatment in a single pediatric patient with uncontrolled viremia following selection of R263K resulted in additional linked drug RAMs in IN leading to a decrease in DTG susceptibility.

Host genetics of HIV susceptibility and disease progression

TUPEA069

Degradation of HIV-1 Nef by ubiquitin (Ub) specific protease 15 (USP15)

I.-W. Park[1], D. Pyeon[2]
[1]University of North Texas Health Science Center, Cell Biology and Immunology, Fort Worth, United States, [2]University of Colorada School of Medicine, Immunology and Microbiology, and Medicine, Aurora, United States
Presenting author email: inwoo.park@unthsc.edu

Background: Previous studies have demonstrated that HIV-1 Nef is essential and may be sufficient for HIV-1-associated AIDS pathogenicity; that is, genetic or physical knockout of Nef alone can protect HIV-infected patients from AIDS. However, molecular methods of incapacitating Nef in the infected hosts have not appeared to date.
Methods: Cellular proteins interacting with HIV-1 Nef were identified by the yeast two-hybrid followed by co-immunoprecipitation analyses. Protein degradation was determined by Western Blot analysis, and replicability of HIV-1 was measured by monitoring reverse transcriptase (RT) activity in the culture supernatants.
Results: Our yeast two-hybrid screening followed by co-immunoprecipitation analysis demonstrated that Nef interacted with ubiquitin specific protease 15 (USP15) which stabilizes proteins by deubiquitination and by preventing autoubiquitination of substrates. Association of Nef with USP15 suggests that Nef and USP15 must be a pivotal regulator in regulation of viral/cellular protein decay. In fact, Nef and USP15 were reciprocally degraded, although USP15-mediated degradation of Nef was more dramatic than Nef-mediated USP15 degradation. Further, USP15 degraded not only Nef but also HIV-1 structural proteins, Gag and Env, thereby significantly inhibiting HIV-1 replication. In contrast, Gag and Env did not degrade USP15, indicating that the Nef and USP15 complex, not any other viral protein, plays an integral role in coordinating viral protein degradation and hence HIV-1 replication. Moreover, Nef and USP15 globally suppressed ubiquitination of cellular proteins, indicating that these proteins are critical determinants for the stability of not only viral but also cellular proteins.
Conclusions: Taken together, these data indicated that one or more defined motifs of USP15 can be regulated to abrogation of Nef and that elucidation of the molecular mechanisms of Nef/USP15-mediated degradation of viral and cellular proteins will provide insights on the nature of pathobiologic and defense strategies of HIV-1 and HIV-infected host cells, respectively, and clues for development of therapeutic agents against AIDS.

TUPEA070

Independent association of host immunogenetic factors with vertical HIV transmission

J. Mania-Pramanik[1], S. Ahir-Bist[1], V. Chavan[1], S. Kerkar[1], P. Samant-Mavani[2], R. Nanavati[3], P. Mehta[4]
[1]National Institute for Research in Reproductive Health, Infectious Diseases Biology, Mumbai, India, [2]Seth G. S. Medical College & K.E.M Hospital, Department of Obstetrics and Gynecology, Mumbai, India, [3]Seth G. S. Medical College & K.E.M Hospital, Department of Neonatology, Mumbai, India, [4]Seth G. S. Medical College & K.E.M Hospital, Department of Microbiology, Mumbai, India
Presenting author email: jayantimania@rediffmail.com

Background: In India, various intervention programs are introduced to reduce mother to child HIV transmission. Despite this many children (5%) still acquire the infection, indicating possible association of genetic factors such as HLA and Cytokines genes. Present study aimed to evaluate if these factors are associated with vertical HIV transmission.
Methods: Infants of HIV positive women attending the PPTCT and ICTC of Seth G.S. Medical College and K.E.M. Hospital, Mumbai, India, between January 2010 and June 2014 were enrolled with their mothers' consent. Clinical history of mothers, blood samples within 24 hours of delivery for viral load analysis and blood from the infants was collected for HIV screening, analysis of HLA alleles and single nucleotide polymorphisms in 13 cytokine genes at 22 loci using PCR-SSP method. SPSS, Haploview and PyPop software were used for statistical analysis.
Results: Thirty HIV positive and 60 HIV negative children at the end of their 18th month follow up were considered for this study. The type of treatment given to the mothers and their viral load at the time of delivery had significant (p=0.001) influence on transmission. CT and CC genotype at IL1R (rs2234650), GG and GA at TNF-α (rs1800629) were significantly associated either with susceptibility/ protection. Haplotypes of IL-1 and TNF genes also showed an association with transmission or protection. HLA-A*01,-B*40,-B*37 and-DRB1*09 were associated either with transmission or protection. Logistic regression analysis further confirmed significance independent association of HLA-B*40 (p = 0.022) with protection and HLA-DRB1*09 (p = 0.019) with susceptibility. Few HLA haplotypes were exclusively present in either of the groups.
Conclusions: This study possibly for the first time reports association of specific SNPs of IL-1R and TNF-α gene with risk of vertical HIV transmission. Specific HLA alleles and haplotypes were also associated either with susceptibility or with protection from HIV transmission. Besides confounding factors, these genetic factors are independently associated with HIV infection. Allelic polymorphisms of these genes could be associated with altered immune response leading to either transmission or protection. These findings update the knowledge of host immune genes association with perinatal HIV transmission. The identified factors can be further exploited as possible susceptible/protection markers.

TUPEA071

Expression analysis of α4 integrin and related genetic polymorphisms in HIV acquisition and disease progression of infected individuals

L.R. Goes[1], A.L. Moraes Giannini[2], S. Helmold Hait[2], E. Stankiewicz Machado[2], D. Alves Costa[3], E. Georges Kallás[3], L.C. Santos Thuler[1], A.F. Andrade dos Santos[2], J. Arthos[4], M. Alves Soares[1,2]
[1]Instituto Nacional de Câncer, Rio de Janeiro, Brazil, [2]Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil, [3]Universidade de São Paulo, São Paulo, Brazil, [4]National Institutes of Health, Bethesda, United States
Presenting author email: liviargoes@gmail.com

Background: HIV gp120 can interact with the α4β7 integrin, providing a favorable environment for virus transmission. α4β7 is important during the initial course of HIV infection, when intense viral replication and lymphocyte depletion occur in gut-associated lymphocyte tissue. A study with multiple sclerosis patients showed a higher prevalence of CC genotype in the SNP-rs1449263, located in the promoter region of the *itga4* gene (α4 integrin), possibly related to a higher expression of this gene. In this study we assessed the distribution of SNP-rs1449263 different genotypes and if they influence *itga4* gene expression.
Methods: Distribution of SNP-rs1449263 genotypes was assessed in three cohorts. Seroconversion cohort: 222 HIV$^+$ adults from USP; pediatric cohort: 89 children from IPPMG/UFRJ and HSE/RJ, where 61 were HIV+ and 28 were exposed-uninfected (EU) born to HIV-infected mothers; and a control group: 68 HIV- adults from Rio de Janeiro. A DNA fragment containing the SNP-rs1449263 was PCR-amplified and sequenced. Allelic and genotypic frequencies were calculated. *itga4* gene expression was assessed by real-time PCR. Surface protein expression was investigated by flow cytometry.
Results: A higher prevalence of CT (54%), followed by TT (29%) and CC (17%) was found in HIV+ adults. Patients carrying the C allele had less CD8$^+$ T-cells in the early phase of infection when compared to those who do not carry it. Among HIV- adults, we observed 41% CT, 33% TT and 26% CC. Among pediatric HIV+ patients, we found 54% CT, 30% CC and 16% TT, while among EU, we found 53% CT, 37% TT and 10% CC. Fifty-one samples submitted to *itga4* gene expression analysis showed a higher expression in the CC genotype group compared to the others. The same was observed for individuals carrying the C allele compared to non-carriers. Five samples were subject to flow cytometry analysis to assess the presence of α4 protein on the cell surface, and the results corroborated those obtained in the real-time PCR.

Conclusions: We show that the CC genotype increases *itga4* gene expression, and that may differ among HIV+ and HIV- subjects. Further analysis is required to assess the influence of α4 expression on progression to AIDS.

TUPEA072

Human leukocyte antigen (HLA) typing and novel allele description by next generation sequencing in HIV-1-infected individuals from Southern Brazil

I. Prellwitz[1], B. Alves[1], E. Sprinz[2], H.N. Seuanez[1,3], M. Soares[1,3], E. Soares[1]
[1]Instituto Nacional de Câncer, Programa de Genética, Rio de Janeiro, Brazil, [2]Hospital de Clínicas de Porto Alegre, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil, [3]Universidade Federal do Rio de Janeiro, Departamento de Genética, Rio de Janeiro, Brazil
Presenting author email: imprellwitz@gmail.com

Background: The human leukocyte antigen (HLA) system plays an important regulatory role in the immune response. The classical HLA genes A, B and C are involved in T-cell mediated cytotoxic immunity controlling HIV-1 viremia. Studies show that the B*35 and B*53 alleles lead to a rapid disease progression, whereas "protective" alleles of the host such as B*27 and B*57 are associated with immune control of infection and slower progression. Next-generation sequencing (NGS) enables resolving the ambiguity of genotypes caused by the large number of existing polymorphisms, and provides a high-resolution typing. Our project aims to determine the HLA-A, B and C alleles by NGS, evaluating different methodologies for assembly, reconstruction and identification of novel alleles of HIV+ patients from southern Brazil.
Methods: HIV+ patients have been followed at Hospital das Clínicas de Porto Alegre from 2002-2003 up to present. HLA-A, B and C genes were PCR-amplified, and libraries were sequenced in an Illumina HiSeq 2500. Generated reads were analyzed in FastQC and trimmed with Sickle. The Omixon-Target algorithm was used for allele typing based on the IMGT/HLA database. Reads were assembled with reference with BWA. Variants sites were detected with GATK using the UnifiedGenotyper tool. All alignments and variant determination results were visually inspected with IGV.
Results: Eighty-six patients have their HLA-A, B and C alleles PCR-amplified and sequenced. Eighty-one samples had their data analyzed and trimmed. Allele frequencies were similar to those reported in southern Brazil. Ten samples were homozygous for HLA-A (12%), 11 for HLA-B (13%) and 10 for HLA-C (12%). HLA-B*35 was found in 19 patients (11%). Until now, 162 (33%) alleles have been tested for reconstruction of new alleles, and six (4%) are indicative of possible new alleles.
Conclusions: Different algorithms have been tested for HLA allele reconstruction and typing. HLA studies in HIV-infected patients with an ethnic background of the southern region of Brazil, are relevant to a better understanding of host genetic factors that respond to this viral infection.

TUPEA073

Absence of an association between mannose binding lectin deficiency and HIV-1 disease progression in an adult population in Zimbabwe

R.B.L. Zinyama-Gutsire[1], C. Chasela[2], P. Per Kallestrup[3], S. Rusakaniko[4], M. Christiansen[5], B. Ngara[6], E. Gomo[7], H. Ullum[8], C. Erikstrup[9], H.O. Madsen[9], B. Stray-Pedersen[10,11], P. Garred[8], T. Mduluza[12]
[1]University of the Witwatersrand, School of Public Health, Johannesburg, South Africa, [2]University of the Witwatersrand, Faculty of Health Sciences, School of Public Health, Johannesburg, South Africa, [3]Aarhus University, Centre for Global Health, Department of Public Health, Aarhus, Denmark, [4]University of Zimbabwe, College of Health Sciences, Harare, Zimbabwe, [5]Statens Serum Institute, Department of Clinical Biochemistry, Immunology and Genetics, Copenhagen, Denmark, [6]Letten Research Foundation, Harare, Zimbabwe, [7]University of Zimbabwe, Department of Medical Laboratory Sciences, College of Health Sciences, Harare, Zimbabwe, [8]Copenhagen University, Rigshospitalet, Department of Clinical Immunology, Copenhagen, Denmark, [9]Rigshospitalet, Tissue Typing Laboratory, Department of Clinical Immunology, Copenhagen, Denmark, [10]University of Oslo, Division of Women and Children, Rigshospitalet Oslo University Hospital, Oslo, Norway, [11]University of Zimbabwe, Harare, Zimbabwe, [12]University of Zimbabwe, Biochemistry Department, Harare, Zimbabwe
Presenting author email: gutsirerbl@yahoo.com

Background: Deficiency in plasma Mannose Binding Lectin (MBL) due to single nucleotide mutations at the MBL exon1 gene structural region and promoter regions is a common opsonic defect. HIV disease progression is influenced by host genetic factors. Relationship between MBL deficiency and HIV disease progression in Zimbabwean adults is not known. We assessed association between MBL deficiency and disease progression in Zimbabwean ART -naïve adult males and females enrolled in the Mupfure Schistosomiasis and HIV cohort (MUSH cohort), established between 2001 and 2007.
Methods: We analysed blood samples of the MUSH cohort for plasma MBL levels using ELISA assays, MBL2 genotypes and promoter region alleles were detected by allele-specific oligonucleotide PCR (ASO-PCR) where specific sequences were used for each allele, HIV-1 status, viral load and CD4$^+$ T cell counts. Generalised Estimating Equations (GEE) models were used to determine association between MBL deficiency and hiv-1 disease progression.
Results: We assessed 198 HIV positive adults, 83% (164) women, median age (IQR) of 31 (27 to 39) years old. Prevalence of HIV-1 in this population was 18% and plasma MBL deficiency was also 18%. Among these HIV infected individuals we found no association between plasma MBL deficiency (p=0.626), MBL2 structural genetic variants (p=0.633), MBL2 promoter region variants (p=0.602) and change in CD4$^+$ T cell count and viral load from baseline to 3 years follow up.
Conclusions: Plasma MBL deficiency and MBL2 genetic variants had no effect on disease progression in this population.

Systems biology approaches to HIV infection

TUPEA074

Global mapping of HIV-1 and host-cells molecular interactions

A. Deshiere[1], I. Martinez-Ferrando[2], C. Joly-Beauparlant[3], Y. Breton[1], M. Ouellet[1], C. Mohien[2], F. Raymond[3], L. Robitaille[3], J. Corbeil[3], D.R. Graham[2], M.J. Tremblay[1], Laboratory of Human Immuno-Retrovirology
[1]Laval University, Infectious Disease Research Centre, Quebec City, Canada, [2]The Johns Hopkins University School of Medicine, Department of Molecular and Comparative Pathobiology, Department of Pharmacology and Molecular Sciences, Baltimore, United States, [3]Laval University, Infectious Disease Research Centre, CHU de Quebec and Departement de Microbiologie, Infectiologie et Immunologie, Quebec City, Canada
Presenting author email: alexandre.deshiere@gmail.com

Background: HIV-1 *in vitro* models using human primary cells are strongly limited by the low rate of productive infection occurring even with large amounts of virus. Thus, only 2 to 20% of activated CD4 T-cells or macrophages appear to offer a favorable environment for successful replication of HIV-1 (productive cells). Among a large majority of "bystander" cells (uninfected and abortively infected cells not expressing HIV-1 proteins), a weak fraction of the total population integrates the virus and remains in a latent state by redirecting the cell chromatin machinery. To date, very little is known about cellular events leading to successful virus replication and latency in primary cells due to the difficulty of studying separately productively HIV-1-infected cells from the latent and "bystander" cells.
Methods: We developed a collection of replicative reporter viruses allowing the sorting of these different populations (productive, bystander and latent cells) through an immunomagnetic capture of small surface epitopes (HA, HSA) or flow-cytometry sorting of fluorescent proteins (ZsGreen, E2-Crimson) co-expressed with the viral genome in productive and latent cells. We used this method to isolate infected CD4 T-cells and MDMs and analysed their transcriptomic and proteomic profiles using a high throughput RNA sequencing analysis and 2D-gel separation combined with mass spectrometry.
Results: Integrated bioinformatics analysis of -omics data allowed us to detect with a high resolution the modulated transcripts and proteins controlling the successful replication of HIV-1 in CD4 T-cells and macrophages. We identified several new genes, miRNA, lncRNA and proteins, as well as extracellular markers specifically expressed at the surface of infected cells that could be keys for a specific eradication of infected and latent cells. The different targets are currently validated by RNA interference for their functions affecting HIV-1 transcription and latency.
Conclusions: The acquired data shed new light on HIV-1 replication mechanisms and will allow the emergence of new specific inhibitory strategies against the constitution of persisting virus reservoirs and AIDS propagation. Identification of surface proteins specifically expressed in infected cells are also interesting candidates for a vaccine targeting HIV-1 host cells instead of the virus itself that is known to be highly variable.

Preclinical drug development

TUPEA075

TLR7 agonist GS-9620 is a potent inhibitor of acute HIV-1 infection in human PBMCs

R.A. Bam, S.R. Yant, A. Irrinki, J. Hesselgesser, C.R. Frey, T. Cihlar
Gilead Sciences, HIV Biology, Foster City, United States
Presenting author email: rujuta.phadke@gilead.com

Background: GS-9620 is a potent and selective oral TLR7 agonist that activates plasmacytoid dendritic cells (pDCs) to produce various cytokines including interferon-α (IFN-α). GS-9620 induced prolonged suppression of hepatitis B virus (HBV) in animal models of chronic infection and is now being tested in patients with chronic HBV infection. GS-9620 has also been shown to activate HIV expression in peripheral blood mononuclear cells (PBMCs) from virally suppressed patients and is being evaluated clinically for HIV-1 latency reversal. To further support the clinical testing of GS-9620 we investigated its effect on acute HIV-1 infection *in vitro*.
Methods: Anti-HIV-1 activity was tested in PHA-activated PBMCs or purified total $CD4^+$ T cells using multi-cycle and single-cycle infection assays. Specific immune cell subsets (pDC, NK, B or $CD8^+$
T cell) were depleted from PBMCs by negative selection prior to antiviral testing. Conditioned supernatant from GS-9620-treated complete or pDC-depleted PBMCs were tested for antiviral effect on purified HIV-infected $CD4^+$ T cells. Cytokines were quantified by ELISA or Luminex assay. Blocking antibodies against IFN-α or IFN-α/β receptor were used to assess the role of IFN-α signaling in anti-HIV-1 activity.
Results: GS-9620 potently inhibited HIV-1 in multi-cycle infection of PBMCs (mean EC_{50}=0.536 ± 0.830 μM, n=27 donors). In a single-cycle PBMC infection assay, 48-hour pretreatment significantly improved the potency of GS-9620 (EC_{50}=0.027 ± 0.030 μM, n=21 donors), consistent with a block in virus entry or early-stage HIV-1 replication. Depletion of pDCs, but not other immune cell subsets, reduced GS-9620 activity (21 to 277-fold, n=4 donors). IFN-α was detected in GS-9620-treated total PBMC cultures, but not in pDC-depleted cultures. Although GS-9620 was inactive in purified
$CD4^+$ T cells, HIV-1 replication was potently inhibited by GS-9620-conditioned PBMC media or recombinant IFN-α. IFN-α blocking antibodies abolished GS-9620 antiviral activity.
Conclusions: GS-9620 is a potent inhibitor of HIV-1 replication in primary PBMCs. Its antiviral activity is dependent on interferon-α produced by activated pDCs. Immune modulatory effects of GS-9620 leading to simultaneous activation of HIV-1 expression and inhibition of acute HIV-1 infection are important considerations for its clinical evaluation since the antiviral effect may help restrict potential local spread of virus upon *in vivo* latency reversal.

TUPEA076

A novel acylguanidine-based inhibitor of HIV-1 egress

P. Mwimanzi[1], I. Tietjen[2], A. Shahid[1], S.C. Miller[2], D. Fedida[2], Z. Brumme[1,3], M. Brockman[1,3]
[1]Simon Fraser University, Burnaby, Canada, [2]University of British Columbia, Vancouver, Canada, [3]British Columbia Centre for Excellence, Vancouver, Canada
Presenting author email: pmwimanz@sfu.ca

Background: Discovery of new antiretroviral drugs is necessary to enhance treatment options and counter resistance. Here, we investigate the anti-HIV activity of a novel acylguanidine compound, SM111, and characterize its ability to block viral egress.
Methods: The ability of SM111 to alter replication of WT NL4.3, NL4.3ΔVpu, and recombinant NL4.3 strains encoding major protease (PI), Reverse Transcriptase (RT) and Integrase (INT) inhibitor resistance mutations was assessed using GFP-reporter CEM T-cells and primary PBMC. Passaging experiments in CEM cells were performed to select NL4.3 mutants with decreased susceptibility to SM111. To assess virion release in the presence or absence of SM111, intracellular and extracellular p24 was measured at 48 hours post-transfection using 293T cells.
Results: SM111 caused minimal cytotoxicity, but reduced replication of WT NL4.3 as well as PI-, RT- and INT-resistant strains in a dose-dependent manner (>95% reduction in CEM cells and 57% in PBMC). Passaging experiments led to outgrowth of three independent NL4.3 variants harboring gross mutations in Vpu's transmembrane domain, including a 5AA deletion spanning Vpu codons 13-17 (strain A), a stop codon at highly conserved W22 (strain C) and a substitution (I17R) (strain H). Notably, SM111 retained partial activity against NL4.3ΔVpu in CEM cells and PBMCs (52% and 30% reduction, respectively) as well as passaged strains A, C, and H (92% 54%, and 16% reductions in CEM T-cells versus 65%, 11%, and 10% in PBMC, respectively). Intracellular p24 expression in transfected 293T cells was comparable between SM111 and no-drug control; however, a dose-dependent reduction in supernatant p24 of up to 10-fold was observed in the presence of SM111.
Conclusions: SM111 inhibited WT HIV-1 as well as drug-resistant strains. It selected major mutations in Vpu's transmembrane domain, but these mutants and NL4.3ΔVpu remained partially sensitive to the drug in T cell lines and PBMCs. SM111 blocked virion release in 293T cells. Together, these results indicate that SM111 displays a unique mechanism of action, targeting a step in viral egress that may be modulated by Vpu and require interaction with an unknown host cell factor(s).
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TUPEA077

Novel CD4-mimetic small molecules show enhancement of the neutralization activity of anti-cryptic V3 neutralizing antibody, KD-247

S. Harada[1], Y. Irahara[2], H. Tamamura[2], T. Matano[1], S. Matsushita[3], K. Yoshimura[1]
[1]National Institute of Infectious Diseases, AIDS Research Center, Shinjuku, Japan, [2]Tokyo Medical and Dental University, Institute of Biomaterials and Bioengineering, Bunkyo, Japan, [3]Kumamoto University, Center for AIDS Research, Kumamoto, Japan
Presenting author email: shigeh@nih.go.jp

Background: CD4 mimetic small molecules, such as NBD-556, inhibit the gp120-CD4 interaction and can also induce conformational changes in gp120 by exposing masked epitopes of neutralizing antibodies on the Env protein.
Methods: Nineteen YIR compounds were designed and synthesized to interact with the conserved residues in the Phe43 cavity of gp120 using our previously reported method. A chimeric clone containing the primary KP-5P virus isolate (subtype B, R5) gp160 within a pNL4-3 backbone was constructed. The susceptibility of the infectious clone to entry inhibition and neutralization sensitivity to the anti-cryptic V3 neutralizing monoclonal antibody (nMAb) KD-247, in the presence of the YIR compounds, was determined using the TZM-bl assay. Results were compared to the parental NBD-556 compound.
Results: All 19 YIR compounds inhibited the KP-5P infectious clone with an IC_{50} in the range of 2.6-16 μM. YIR compounds showed an almost-5-fold improvement activity compared to NBD-556. Neutralizing activity of KD-247 against the KP-5P clone was also measured in the absence or presence of YIR compounds (range: 125-1,000 nM). KD-247 neutralizing activity was much less potent against the KP-5P clone (IC_{50} of >200 μg/ml). However, when pretreated with at least 125 nM of the YIR compounds the KP-5P clone became highly sensitive to KD-247, exhibiting an IC_{50} in the range of 3.3-23 μg/ml. These results suggest that YIR compounds render primary HIV-1 sensitive to neutralization by nMAbs directed against the V3 region involved in co-receptor binding, similar to the potent NBD-556.
Conclusions: The CD4-mimetic small molecules, YIR compounds, may be useful in inhibiting HIV-1 infection not only by directly obstructing the interaction between gp120 and CD4, but also enhancing sensitivity to neutralizing antibodies.

TUPEA078

BMS-955176: characterization of a 2nd-generation HIV-1 maturation inhibitor

B. Nowicka-Sans, T. Protack, Z. Lin, Z. Li, S. Zhang, N. Meanwell, M. Cockett, A. Regueiro-Ren, M. Krystal, I. Dicker
Bristol-Myers Squibb, Research and Development, Wallingford, United States
Presenting author email: ira.dicker@bms.com

Background: BMS-955176 is a 2nd-generation HIV-1 maturation inhibitor (MI). A 1st-generation MI, bevirimat, showed efficacy in early-phase studies, but ~50% of subjects had virus with reduced susceptibility associated with naturally occurring Gag polymorphisms. Assays designed to optimize target specificity, virologic potency, polymorphic coverage, and human serum binding were used to identify an improved maturation inhibitor clinical candidate.
Methods: BMS-955176 inhibition of Gag cleavage in HIV-1-infected cells and specific binding to Gag in virus-like particles (VLPs) was used to assess MI targeting. Potency was optimized using a panel of engineered reporter viruses containing polymorphic changes in Gag that reduce susceptibility to bevirimat (including V362I, Q369H, V370A/M/Δ and T371A/Δ). Candidates were then evaluated against a library of recombinant viruses containing *gag/Pr* genes from clinical isolates to assess their spectra of activity. Activity of BMS-955176 was also assessed against a series of clinical isolates in peripheral blood mononuclear cells (PBMCs) and a panel of antiretroviral-resistant viruses. Serum effect was assessed in 10% fetal bovine serum (FBS) *vs.* 40% human serum/10% FBS + 27 mg/mL human serum albumin (HuSA).
Results: BMS-955176 inhibits HIV-1 protease cleavage at the CA/SP1 junction within Gag in HIV-1-infected cells and binds tightly and reversibly to Gag in purified HIV-1 VLPs. The average antiviral EC50 was 3.9±3.4 nM toward a library of 87 *gag/Pr* recombinant subtype B viruses containing 96% of subtype B polymorphic Gag diversity near the CA/SP1 cleavage site. Clinical isolates of HIV-1 subtypes A, AE, C, D, F and G evaluated in PBMCs exhibited EC50s of 1.5-31 nM. Activity was maintained against a panel of reverse transcriptase-, protease- and integrase inhibitor-resistant viruses, with EC50s similar to wild-type. Average human serum binding was 86%; a ~6-fold reduction in EC50 occurred in the presence of 40% human serum/10% FBS + 27 mg/mL HuSA.
Conclusions: BMS-955176 is a 2nd-generation MI that inhibits HIV-1 protease cleavage at the CA/SP1 junction within Gag. BMS-955176 has potent *in vitro* anti-HIV-1 activity in the presence of a range of Gag polymorphisms associated with reduced susceptibility to a 1st-generation MI, broad coverage of HIV-1 subtypes, and low human serum binding. These data support further clinical development of BMS-955176.

TUPEA079

Small molecule activator of protein phosphatase 1 (SMAPP1) activates latent HIV-1 provirus

T. Ammosova[1], M. Tyagi[2], S. Iordanskiy[3], K. Smith[4], N. Kumari[4], A. Ilatovskiy[5], Y. Saygideger-Kont[6], A. Ivanov[4], A. Uren[6], D. Kovalskyy[7], M. Petukhov[5], F. Kashanchi[3], S. Nekhai[1]
[1]Howard University, Center for Sickle Cell Disease and Department of Medicine, Washington, United States, [2]George Washington University, Department of Medicine, Washington, United States, [3]George Mason University, National Center for Biodefense and Infectious Diseases, Manassas, United States, [4]Howard University, Center for Sickle Cell Disease, Washington, United States, [5]Petersburg Nuclear Physics Institute and St. Petersburg State Polytechnical University, St. Petersburg, Russian Federation, [6]Georgetown University, Lombardi Comprehensive Cancer Center, Washington, United States, [7]Enamine LLC, Monmouth Jct., United States

Background: Eradication of latent HIV-1 provirus requires reactivation of transcriptionally silent proviruses that are not affected by antiretroviral drugs. In latently infected T cells, the lack of host transcription factors and viral protein Tat lead to the reduction in viral gene expression. We previously showed that protein phosphatase-1 (PP1) activates HIV-1 transcription by controlling CDK9 phosphorylation. We developed a library of small molecular compounds targeted to a non-catalytic site of PP1 and found a molecule (SMAP1) that activated latent HIV-1.
Methods: Chronically infected with HIV-1 cell lines ACH2 and OM10.1 and latently infected Jurkat T-cells and THP-1 cells were treated with the compounds and HIV-1 transcription was monitored. SMAPP1 binding to PP1 was analyzed using Biacore, *in vitro* PP1 assay and in silico docking analysis. The effect of SMAPP1 on T cells was analyzed using proteomics approach.
Results: SMAPP1 activated one round HIV-1 infection and latent HIV-1 in chronically infected T-cells and monocytes. SMAPP1 induces PP1 activity in vitro and increased expression of PP1 regulatory subunit Sds22 in cultured cells. Docking of SMAPP1 to PP1 showed its binding to a pocket that overlaps with the predicted Sds22-binding site.
Conclusions: We developed a new compound, SMAPP1, which targets PP1 and may affect the PP1 binding to its regulatory subunit sds22 increasing HIV-1 Tat activated transcription. These compounds can be used for purpose of eradication of HIV-1 in combination with the anti-retroviral HIV-1 therapy.

TUPEA080

Discovery and anti-HIV-1 activity of a new class of diheteroarylamide-type anti-HIV-1 agents acting on HIV-1 alternative splicing

P. Cheung[1], D. Horant[2], L. Bandy[2], S. Karagiosov[2], P.R. Harrigan[1,3], B. Chabot[4], D. Grierson[2]
[1]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada, [2]University of British Columbia, Pharmaceutical Sciences, Vancouver, Canada, [3]University of British Columbia, Department of Medicine, Vancouver, Canada, [4]Université de Sherbrooke, Sherbrooke, Canada

Background: Our research, built upon an earlier observation that a tetracyclic indole compound (IDC16) inhibits HIV-1 pre-messenger RNA splicing, is aimed at identifying novel HIV-1 splicing inhibitors that are more readily accessible by synthesis than IDC16 and not cytotoxic (devoid of DNA interchelating properties). A diversity-driven library synthesis approach was used to design six different families of flexible di-heterocyclic compounds that mimic the essential features of the IDC16 structure. The most potent compound, C8, was selected for detailed analysis of its anti-HIV-1 activity against a comprehensive panel of HIV-1 mutant strains conferring resistance to all known anti-HIV-1 drugs. Further studies (Chabot et al) revealed that this molecule interferes with the activity of the splicing factor SRSF10.
Methods: Parallel synthesis strategies were used to prepare the library of 240 potential IDC16 mimics. The evaluation of the antiretroviral activity of this collection was determined by a T-cell reporter assay that expresses green fluorescent protein upon HIV-1 infection. The level of infection was monitored using flow cytometry. To investigate the adverse effect on cell viability, we employed Guava ViaCount Assay (Millipore) on the same reporter cells.
Results: Of the four structurally related diheteroarylamide compounds identified as active in the preliminary screen, the anti-HIV-1 profile of compound C8 was studied in detail. C8 was active against a broad range of wild-type and drug-resistant HIV-1 variants. C8 inhibits wild-type subtype A strain 97USSN54, and subtype B strain IIIB with IC50's of 0.9 µM and 0.6 µM, respectively. For multidrug-resistant viruses, C8 inhibits an HIV-1 variant resistant to both NRTI and NNRTI with IC50 of 1.3 µM. Compound C8 was also active against viruses resistant to protease inhibitors, integrase inhibitors, and CCR5 antagonist inhibitors with IC50's of 1.4 µM, 1.5 µM, and 0.9 µM respectively. In addition, at 16 µM concentration, C8 elicited a modest change only in cell viability (85.2 to 65.8%) after 24 h.
Conclusions: These results show that C8 remains active against the entire panel of HIV-1 mutants studied, and that it displays no cross-resistance to the above antiretroviral agents. Our findings also show that C8 most likely does not act on the traditional drug targets.

TUPEA081

Discovery of novel HIV-1 inhibitors from natural products

I. Tietjen[1,2], K. Andrae-Marobela[3], D. Williams[4], F. Ntie-Kang[5], P. Mwimanzi[2], P. Amoa Onguéné[6], B.M. Abegaz[7], R. Andersen[4], D. Fedida[1], Z.L. Brumme[2,8], M.A. Brockman[2,8,9]
[1]University of British Columbia, Anesthesiology, Pharmacology, and Therapeutics, Vancouver, Canada, [2]Simon Fraser University, Faculty of Health Sciences, Burnaby, Canada, [3]University of Botswana, Department of Biological Sciences, Gabarone, Botswana, [4]University of British Columbia, Department of Earth, Ocean, and Atmospheric Sciences, Vancouver, Canada, [5]University of Buea, Department of Chemistry, Buea, Cameroon, [6]University of Douala, Department of Chemistry, Douala, Cameroon, [7]African Academy of Sciences, Nairobi, Kenya, [8]University of British Columbia, British Columbia Centre for Excellence in HIV/AIDS, Vancouver, Canada, [9]Simon Fraser University, Department of Molecular Biology and Biochemistry, Burnaby, Canada
Presenting author email: itietjen@mail.ubc.ca

Background: Rapid scale-up of antiretroviral (ARV) treatment programs has significantly reduced morbidity and mortality due to HIV infection in resource-limited settings such as parts of sub-Saharan Africa. However, new HIV inhibitors are needed to minimize adverse effects and overcome potential resistance to existing drugs.
Natural products are a promising but undervalued resource for identifying new antiviral compounds that act via distinct mechanisms.
Methods: We used a GFP-reporter CEM T-cell assay to screen candidate natural products for anti-HIV activity. *In vitro* replication of WT NL4.3, NL4.3ΔVpu, and recombinant NL4.3 strains encoding major protease (PI), reverse transcriptase (RT) and integrase (INT) resistance mutations was assessed in the presence of each compound, and results compared to uninfected control cells. We then used this assay to examine potential inhibitors from three sources: 1) A panel of 8 pure natural products obtained from the pan-African Natural Product Library (p-ANAPL) with structural similarity to published inhibitors of HIV-1 Vpu, 2) A series of 9 plant extracts from sub-Saharan Africa supported by traditional medicinal knowledge; and 3) A library of 255 pure marine natural products from Southeast Asia.
Results: We identified two compounds from the p-ANAPL, ixoratannin A-2 and boldine, that inhibited WT NL4.3 and displayed weaker activity against NL4.3ΔVpu (ixoratannin A-2: EC50 = 34.4 and 52.0 µM; boldine: EC50 = 50.2 and >100 µM, for NL4.3 and NL4.3ΔVpu, respectively). Two crude plant extracts supported by traditional knowledge, KM1 and KM5, inhibited WT NL4.3 replication (KM1: EC50s = 0.5 and 23.3 µg/mL for KM1 and KM5, respectively) and demonstrated similar activity against ARV-resistant viruses. Three additional antiviral compounds from marine natural product sources displayed EC50s < 1 µM and CC50s > 1 µM, including p2b7 (EC50 = 8 nM, CC50 = 3.0 µM, selectivity index = 375). Notably, p2b7 also similarly inhibited NL4.3 strains encoding PR, RT, and INT-resistance mutations.
Conclusions: We have identified new sources of anti-HIV agents from pure natural products and crude extracts supported by traditional medicinal knowledge. Several compounds inhibited drug-resistant strains, suggesting mechanisms of action that are different from licensed ARVs.

TUPEA082

Development of efficient parallel synthesis strategies for the generation of compound libraries of anti-HIV agents that alter HIV alternative splicing

M. Zamiri[1], Z.S. Lin[1], A. Koperniku[1], B. Chabot[2], P. Cheung[3], D. Grierson[1]
[1]University of British Columbia, Faculty of Pharmaceutical Sciences, Vancouver, Canada, [2]Université de Sherbrooke, Microbiology and Infectious Diseases, Sherbrooke, Canada, [3]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada
Presenting author email: maryam1998@hotmail.com

Background: Our research is directed toward the discovery of new classes of anti-HIV drugs that:
i) act through unexploited mechanisms of action,
ii) bypass the problem of drug resistance,
iii) display minimal, or no, toxicity, and
iv) address the problem of activating the latent viral pool.
HIV produces over 40 distinct mRNAs by alternative splicing. In this context, targeting the expression or activity of splicing regulators using small molecules is being explored as a novel anti-HIV strategy, as the exquisite reliance of HIV on splicing may render it sensitive to even slight disturbances in splicing.
Methods: Based on the finding that a fused tetracyclic indole compound, IDC16 inhibits HIV replication by acting on HIV-1 pre-mRNA splicing, a diversity-driven library synthesis-screening program allowed the identification of four novel diheteroarylamide-compounds, **C8**, **E5**, **C2** and **D3**, as anti-HIV agents. Preliminary data showed that **C8** has the highest inhibitory effect in HIV-1 replication through interaction with SRSF10. In the subsequent SAR-driven phase of this program, highly efficient and environmentally clean strategies have been perfected for the synthesis of diheteroaryl amide-type structures. Molecular modeling plays an important role in the study of the conformational properties of these library molecules.

Results: Two green and efficient strategies for amide synthesis have been developed: the reaction of a stable acid fluoride with N-silylated heteroaromatic amines and the reaction of a lipophilic thioester and non-silylated heteroaromatic amines. In both cases, the desired product precipitates out from the reaction in pure form. Furthermore, based on molecular modeling, a variety of new compounds, including inverse amides and amide bioisosteres and alternative structures (4,6-diheteroaryl substituted pyrimidine, and pyrazolopyridinones) are being prepared to examine their activity.
Conclusions: The acid fluoride and thioester approach to the construction of the amide bond is particularly well adapted to the construction of libraries of anti-HIV agents targeting HIV alternative splicing. In addition, molecular modeling provides insight into the active conformation of **C8** analogues, providing insight as to the nature of the interactions between **C8** and SRSF10.

Preclinical microbicide development

TUPEA083

Antiviral activity of 5-Hydroxytyrosol, a microbicidal candidate against HIV-1 transmission

L.M. Bedoya[1], M. Beltrán[2], P. Obregón[2], E. Gómez-Acebo[3], D. Auñon[3], L. Capa[2], J. Alcami[2]
[1]Pharmacy College, Universidad Complutense de Madrid, Department of Pharmacology, Madrid, Spain, [2]Centro Nacional de Microbiología, Instituto de Salud Carlos III, AIDS Immunopathology Department, Majadahonda, Spain, [3]Seprox Biotech, Madrid, Spain
Presenting author email: ppalcami@isciii.es

Background: Microbicides are currently one of the main strategies to prevent HIV infection that is especially important in developing countries. The objective of this work is to study the anti-HIV *in vitro* activity and *in vivo* toxicity of 5-hydroxytyrosol (5-HT), an anti-inflammatory and antiviral natural compound, in order to develop an effective low-cost microbicide.
Methods: The antiviral activity of 5-HT was assessed against SIV and several HIV-1 strains including founders viruses, strains resistant to other antiretrovirals using different experimental models: cell lines, lymphocytes and monocytes from human peripheral blood, autologous co-culture of DC-SIGN expressing cells and lymphocytes and infection through epithelial layers. Anti-HIV activity of 5-HT was also assessed in combination with Tenofovir or Lamivudine. Synergism was analyzed according to T-C Chou and P. Talalay method. Mechanism of action was studied using VSV pseudotyped HIV-1, RT-PCR and transfection experiments. Toxicity was tested *in vitro* and *in vivo,* through evaluation of local tolerability at vaginal mucosa in New Zealand White rabbits (n=6) at three different concentrations
(30, 100 y 200 mM or 4.6, 15.4 y 30.8 mg/L) during 14 consecutive days by topical route.
Results: 5-HT was active against SIV and all the HIV-1 strains and scenarios tested with IC_{50} ranging between 20-60 µM. *In vitro* toxicity was only observed at doses greater than 250 µM. A strong synergistic effect was displayed by combination of 5-HT and Tenofovir (Combination index as low as 0.24) while an additive effect was observed with Lamivudine. The mechanism of action of 5-HT is not related to viral entry, retrotranscription or integration. 5-HT was able to diminish viral transcription through NF-kB and Sp-1 inhibition. Topical administration of 5-HT did not cause inflammatory responses or morphological alteration in the vaginal mucosa of rabbit.
Conclusions: 5-HT was active against SIV and different HIV-1 strains in a variety of scenarios *in vitro*. A strong synergistic activity with Tenofovir was found being viral transcription the main target of 5-HT through NF-kB and SP-1 inhibition. In summary 5-hydroxytyrosol is a new class of microbicide combining both anti-inflammatory and anti-HIV properties and represents a potential candidate for clinical trials.

TUPEA084

Protection from HIV-1 infection by S-layer mediated display of anti-HIV proteins on *Caulobacter crescentus*

C. Farr Zuend, J.F. Nomellini, J. Smit, M.S. Horwitz
University of British Columbia, Microbiology and Immunology, Vancouver, Canada
Presenting author email: farrc@mail.ubc.ca

Background: Despite effective prevention options, more than 2.7 million new HIV-1 infections occur each year. Due to societal and biological factors, women are 2-6 times more likely to acquire HIV-1 through sexual transmission, suggesting that female controlled prevention options are urgently needed. We have previously proposed the development of an HIV-1 specific microbicide using the non-pathogenic freshwater bacterium *Caulobacter crescentus*.
Methods: *C. crescentus* has a Surface or S-layer, which is a repeating layer of the protein RsaA that coats the surface of the bacterium. We have developed a technique to insert foreign protein sequences into the RsaA protein, which leads to high-density display of recombinant proteins on the surface of *C. crescentus.* Recombinant *C. crescentus* have been tested for the ability to prevent HIV-1 infection *in vitro* using a virus blocking assay and *in vivo* with humanized mice.
Results: We have successfully expressed 17 different anti-HIV-1 proteins on the surface of *C. crescentus* including CD4, MIP1α, fusion inhibitors and anti-viral lectins. Using an *in vitro* viral blocking assay we have demonstrated that 12 of the recombination *C. crescentus* are able to provide significant protection from HIV-1 infection, with protection levels reaching 97% when recombinant *C. crescentus* are used in combination. Studies with immune-competent mice have demonstrated that *C. crescentus* does not induce the production of inflammatory cytokines or the recruitment of immune cells to the vaginal tract. We have continued *in vivo* experiments utilizing the humanized Bone marrow-Liver -Thymus (BLT) mouse model. The implantation of human liver and thymus tissue is combined with the intravenous injection of autologous human CD34+ cells into NOD-*scid* IL2Rg^{null} mice to create the BLT mice. The peripheral blood of these mice contains 40% human CD45+ cells including human CD4+ T cells, CD8+ T cells, B cells, NK cells and myeloid cells and the mice are susceptible to intravaginal infection with HIV-$1_{JR\text{-}CSF}$. We have demonstrated significant protection from vaginal HIV-$1_{JR\text{-}CSF}$ infection when recombinant *C. crescentus* is applied intravaginally at the time of HIV-1 infection.
Conclusions: Taken together these results suggest that a *C. crescentus* based microbicide could be a safe and effective method for HIV-1 prevention.

Targeting HIV persistence during ART (cure strategies)

TUPEA085

MG1 and VSVΔ51 viruses target and kill latently HIV-infected myeloid cells

N. Ranganath[1], S. Côté[2], T. Sandstrom[1], J. Angel[2,3]
[1]University of Ottawa, Biochemistry, Microbiology, Immunology, Ottawa, Canada, [2]Ottawa Hospital Research Institute, Infectious Disease, Ottawa, Canada, [3]The Ottawa Hospital, Infectious Disease, Ottawa, Canada
Presenting author email: nrang027@uottawa.ca

Background: Latent HIV reservoirs represent a major barrier to eradication. We propose a novel strategy to eliminate this reservoir using a class of oncolytic viruses (OV) that include Maraba (MG1) and Vesicular Stomatitis Virus (VSVΔ51). These recombinant OV target cancer cells by exploiting defects in type I interferon (IFN)-signaling. Similar alterations in IFN-mediated antiviral responses are also seen in HIV-infected cells, providing a crucial link between cancer cells and cells that constitute the HIV reservoir. We hypothesize that MG1 and VSVΔ51 selectively target and kill latently HIV-infected cells.
Methods: Latently HIV-infected myeloid (U1 and OM10.1) cell lines, as well as their respective parental uninfected controls (U937 and HL60) were infected with GFP-expressing MG1 or VSVΔ51. Productive OV infection was quantified by flow cytometry. PI, MTT, and Alamar Blue assays were used to assess cell viability. Type I IFN response to OV infection was characterized by measuring IFNα secretion by ELISA, as well as PKR expression by Western blot. OV infection of primary monocytes, MDMs, and CD4$^+$ T cells from HIV-uninfected donors was also assessed.
Results: U1 and OM10.1 cells were significantly more susceptible to MG1 and VSVΔ51 infection and killing than their respective HIV-uninfected U937 and HL60 parental controls. IFNα secretion significantly increased in response to OV infection in control cell lines, but not in the latently HIV-infected cells. In parallel, PKR expression in response to OV infection was significantly higher in the HIV-uninfected controls than in the latently HIV-infected cells. Primary monocytes, MDMs, and CD4+ T cells from HIV-uninfected individuals were relatively resistant to OV infection and killing.
Conclusions: Latently HIV-infected myeloid cells are preferentially targeted and killed by MG1 and VSVΔ51 when compared to their uninfected parent cells. Underlying defects in type I IFN-responses in latently HIV-infected cells may facilitate selective targeting by OV. Therefore, our results suggest that the use of OV may represent a novel and potentially safe approach to selective elimination of the latent HIV reservoir.

TUPEA086

Risk of virologic rebound in HIV-infected patients on HAART with very low-level viraemia

S.-Y. Chan, T.H.-C. Tang, W. Lam, T.-S. Kwong, M.-Y. Chu, Y.-T. Chan, M.-P. Lee, P.C.-K. Li, T.-C. Wu
Queen Elizabeth Hospital, Medicine, Kowloon, Hong Kong
Presenting author email: helenchansy@gmail.com

Background: Current guidelines recommend suppression of plasma human immunodeficiency virus type 1 (HIV-1) RNA viral load to below the limit of assay detection. Newer generations of viral load assays are now able to detect and quantify viral load at very low levels, but the significance of this very low-level viraemia (VLLV) remains unclear.
Methods: A retrospective cohort study was conducted to analyse the association between VLLV and virologic rebound in 820 HIV-1 infected patients on highly active anti-retroviral therapy (HAART). Patients with viral load < 50 copies/ml were stratified into "VLLV" group (20-49 copies/ml) and "suppressed" group (< 20 copies/ml) according to the viral load tested by Roche Molecular Systems COBAS AmpliPrep/COBAS Taqman HIV-1 Test version 2.0. Independent effects of viral load groups, demographic, clinical and laboratory variables on risk of virologic rebound at 104 weeks were investigated by a Cox proportional hazard model.
Results: There were 626 patients in the "suppressed" group and 194 patients in the "VLLV" group. Median follow-up time was 96 weeks (interquartile range (IQR) 90-101 weeks), virologic rebound rate were 1.8% and 3.6% in the "suppressed" and "VLLV" group respectively at 48 weeks and 3.2% and 7.2% at 104 weeks. Time to virologic rebound at 104 weeks is significantly shorter in "VLLV" group (log-rank test, $p < 0.005$). Cox proportional hazard model demonstrated that adjusted hazard ratio for virologic rebound for VLLV at 104 weeks was 3.351 (95% confidence interval, 1.411-7.957, $p < 0.01$), which is independent of adherence levels. Another independent predictor was suboptimal HAART adherence.
Conclusions: HIV-1 infected patients on HAART with very-low level viraemia were associated with virologic rebound and this finding was independent of other recognized determinants. The clinical significance of VLLV warrants further study.

TUPEA087

Minimal HIV-1 Gag epitope presentation in a T cell line during reactivation

X.T. Kuang[1], G. Anmole[1], P. Mwimanzi[2], M.A. Brockman[1,2,3]
[1]Simon Fraser University, Molecular Biology and Biochemistry, Burnaby, Canada, [2]Simon Fraser University, Health Sciences, Burnaby, Canada, [3]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada
Presenting author email: xtk@sfu.ca

Background: "Shock and kill" methods are being tested as a strategy to cure HIV infection. Various agents can reactivate latent provirus; however, immune-mediated killing of these cells appears to be inefficient. To investigate whether this is due in part to poor antigen presentation, we developed a reporter T cell assay to detect HIV epitopes on latent cells following reactivation.
Methods: A latent Jurkat-GFP (J-Lat) cell line stably expressing HLA-A*02+ was constructed and used as target cells. HIV was reactivated using anti-latency agents (TNFα and HDAC inhibitors). Enhancers of antigen processing (IFNγ and ATRA) were also tested. Effector T cells were generated by transfection of Jurkats with TCRα/β specific for the A*02-restricted Gag FK10 epitope, CD8α and NFAT-driven luciferase reporter plasmids. Reactivation of J-Lat cells was measured by assessing GFP and Gag-p24 expression using flow cytometry. Live GFP+ and GFP-negative target cells were collected by FACS and FK10 presentation on these cells was detected following co-culture with TCR+ effector cells as an increase in luciferase signal.
Results: Co-culture of FK10-pulsed J-Lat-A*02 targets with TCR+ effectors resulted in a dose-dependent increase in luciferase signal. Anti-latency agents reactivated ~5% to 40% of live J-Lat cells, versus TNFα (30%) and DMSO (0%), and expression of Gag-p24 correlated with higher GFP fluorescence. Despite robust Gag expression, no difference in TCR-driven luciferase signal was observed between GFP+ and GFP-negative J-Lat targets. Addition of IFNγ enhanced the ability of TNFα-treated J-Lat target cells to induce luciferase signal; and a further increase in signal was observed when IFNγ and all-trans retinoic acid (ATRA) were added in combination. However, these effects were not observed when HDACi-treated target cells were used.
Conclusions: These results indicate that J-Lat cells present endogenous viral peptides poorly, but this activity could be enhanced by IFNγ and ATRA. Lack of TCR-mediated stimulation by HDACi-treated target cells, even in the presence of IFNγ and ATRA, suggests that these drugs further impaired peptide presentation. Altered antigen presentation intrinsic to latent cells/cell lines or as a side-effect of anti-latency drugs should be considered as a potential barrier to HIV eradication.

TUPEA088

Vorinostat, panobinostat and romidepsin nonselectively activate transcription from quiescent HIV-1 proviruses in HIV-infected individuals on long-term suppressive antiretroviral therapy

K. Barton[1], T.A. Rasmussen[2], M. Tolstrup[2], W. Shao[3,4], B. Hiener[1], R. Olesen[2], A. Winckelmann[2], A. Solomon[5,6,7], L. Østergaard[2], S.R. Lewin[5,6,7], O.S. Søgaard[2], S. Palmer[1]
[1]University of Sydney, Westmead Millennium Institute, Westmead, Australia, [2]Aarhus University Hospital, Department of Infectious Diseases, Aarhus, Denmark, [3]Leidos Biomedical Research, Inc, Advanced Biomedical Computing Center, Reston, United States, [4]Frederick National Laboratory for Cancer Research, Frederick, United States, [5]Monash University, Department of Infectious Diseases, Alfred Hospital, Melbourne, Australia, [6]Burnet Institute, Centre for Biomedical Research, Melbourne, Australia, [7]The University of Melbourne, Doherty Institute for Infection and Immunity, Melbourne, Australia
Presenting author email: kirston.barton@sydney.edu.au

Background: Clinical trials in HIV-infected individuals on long-term anti-retroviral therapy (ART) using histone deacetylase inhibitors (HDACis) to reverse HIV-1 latency have demonstrated a measurable increase in HIV-1 transcription in CD4 T cells in blood. However, for effective viral clearance, it is important that these compounds activate transcription from a broad range of integrated proviruses.
In this study, we used sequencing to determine whether vorinostat, panobinostat, and romidepsin selectively or nonselectively target HIV-1 proviruses.
Methods: CD4 T cells were obtained from 36 participants before, during, and after HDACi treatment using vorinostat (n=15), panobinostat (n=15), and romidepsin (n=6). We used single-proviral/genome sequencing to characterize the genetic composition of the env region of cell-associated HIV-1 DNA and RNA to determine which HIV-1 proviruses were being transcribed in response to HDACi therapy within CD4 T cells. Additionally, for the panobinostat trial, we sequenced plasma HIV-1 RNA from samples collected during a post-HDACi ART interruption. Maximum-likelihood trees were constructed for each participant and the average-pairwise distance of the sequences was calculated using MEGA 6.0.
Results: The average-pairwise distance of the cell-associated HIV-1 RNA that was detected following administration of the HDACis was not significantly different from that of the cell-associated HIV-1 DNA (2.9% vs. 3.1%, p=0.79). Furthermore, upon phylogenetic analysis, the HIV-1 RNA sequences intermingled with the HIV-1 DNA sequences throughout the phylogenetic trees, supporting a broad and nonselective activation of HIV-1 proviruses. The plasma-derived sequences from the ART interruption samples contained expansions of identical sequences, which in three cases were identical to cell-associated DNA sequences. Additionally, cell-associated HIV-1 RNA had a significantly higher percentage of dead-end virus (hypermutated and/or containing stop codons) than the cell-associated HIV-1 DNA (40.1% vs. 7.8%, p=0.0004).
Conclusions: We found that vorinostat, panobinostat, and romidepsin nonselectively induce transcription from HIV-1 proviruses in HIV-infected individuals on long-term suppressive therapy, which is promising for the development of future therapies that aim to activate quiescent HIV-1 proviruses as part of an eradication strategy. Although, a large amount of cell-associated HIV-1 RNA was replication incompetent, we did identify cell-associated HIV-1 DNA that contributed to rebound virus during a post-HDACi ART interruption.

TUPEA089

Combinatorial CRISPR/Cas9 approaches targeting different steps in the HIV life cycle efficiently limits viral reactivation and halts viral replication

M. Nijhuis, D. de Jong, F. Wolters, E. Wiertz, R.J. Lebbink
University Medical Center Utrecht, Virology, Utrecht, Netherlands
Presenting author email: m.nijhuis@umcutrecht.nl

Background: Currently available combination antiretroviral therapy can successfully control HIV replication. However, conventional treatment lacks the ability to stop viral production and clear the latent reservoir, which remains the major obstacle towards a cure. Novel strategies are required to permanently disrupt the HIV genome in the latently infected cells. In this study we have investigated the potential of the CRISPR/Cas9 system to prevent HIV re-activation from latently infected cells and to target different steps in the viral lifecycle to halt viral replication.
Methods: The CRISPR/Cas9 system is comprised of a Cas9 protein, which in combination with a guideRNA (gRNA), is able to cleave a complementary dsDNA sequence. gRNAs were designed to target HIV LTR, protease, reverse transcriptase, integrase and the structural matrix protein. The CRISPR/Cas9 system was cloned in a lentivirus vector and used to transduce SupT1 and Jurkat cells. The latter contains near full-length HIV and expresses GFP upon TNFα stimulation. SupT1 cells were transduced with the lentiviral constructs and subsequently infected with HIV using different MOIs and viral replication was monitored by HIV DNA quantification and HIV CA-p24 production. On and off targeting efficiency (three genes per CRISPR) was assessed by deep sequencing.

Results: Lentiviral transduction in SupT1 and Jurkat cells resulted in stable expression of the CRISPR/Cas9 system. Deep sequence analysis demonstrated efficient HIV genome editing (75-99%) and an off-target efficiency ranging between 0.4-1.7%. TNFα-induced HIV reactivation from latently infected T cells was significantly reduced after transduction with gRNAs. Single gRNA resulted in 50-95% loss of HIV expression and in cells targeted by a combination of two LTR gRNAs >98% loss of expression was shown. Subsequently, we investigated the potential of gRNAs to inhibit viral replication. HIV DNA quantification demonstrated up to 40-fold reduction in intracellular HIV DNA and a significant reduction in virus production. Most combinations of two gRNAs resulted in complete abrogation of viral replication, which could not even be rescued after months of in vitro selection.
Conclusions: The newly discovered CRISPR/Cas9 system is able to target HIV efficiently in both primary infection and latency models and may provide a specific, efficacious prophylactic and therapeutic anti-viral approach.

TUPEA090

Universal Tre-recombinase (uTre) specifically targets the majority of primary HIV-1 isolates

I. Hauber[1], J. Karpinski[2], C. Schäfer[1,3], J. Chemnitz[1], H. Hofmann-Sieber[1], J. van Lunzen[3,4], F. Buchholz[2], J. Hauber[1,3]
[1]Heinrich Pette Institute, Antiviral Strategies, Hamburg, Germany, [2]TU Dresden, Medical Systems Biology, Dresden, Germany, [3]German Center for Infection Research (DZIF), Hamburg, Germany, [4]University Medical Center Hamburg-Eppendorf, Section Infectious Diseases, Hamburg, Germany
Presenting author email: v.lunzen@uke.de

Background: HIV-1 integrates into the host chromosome and persists as a provirus flanked by long terminal repeats (LTR). To date, treatment regimens primarily target virus attachment, virus-cell fusion or the virus enzymes, but not the integrated provirus. Thus, current antiretroviral therapy (cART) cannot eradicate HIV-1, a fact that highlights the urgency of pursuing new strategies to find a cure for HIV/AIDS. Previously, we engineered an experimental HIV-1 LTR-specific recombinase (Tre-recombinase) that can efficiently excise integrated proviral DNA from infected human cell cultures. Subsequently, we demonstrated highly significant antiviral activity of this HIV-1 subtype A-specific Tre in humanized mice. Broad clinical application, however, requires availability of a Tre-recombinase that recognizes a majority of clinical HIV-1 isolates.
Methods: We employed substrate-linked protein evolution to engineer universal Tre-recombinase (uTre), recognizing the LTRs in a majority of clinical HIV-1 isolates (≥94% of HIV-1 subtype A, B, and C). The activity of uTre was subsequently analyzed in cell lines and primary cell cultures, as well as in HIV-infected humanized mice.
Results: Here we demonstrate the absence of cytopathic and off-target effects, as well as pronounced antiviral uTre activity. In particular, uTre expression resulted in decline of viral loads below the detection limit (< 20 HIV-1 RNA copies/ml) in "personalized" mice, which were engrafted with $CD4^+$ T cells from HIV-infected patients.
Conclusions: The presented data suggest that uTre technology may become a valuable component of future eradication strategies to reverse infection and thereby provide a cure for HIV/AIDS.

TUPEA091

Polyvalent immune responses correlate with lower number of HIV-infected CD4 T cells in chronically infected subjects treated with autologous RNA pulsed DC therapy

I. Tcherepanova, J. Krisko, J. Harris, A. Gamble, W. Lewis, M. DeBenedette, C. Nicolette
Argos Therapeutics Inc, R&D, Durham, United States

Background: AGS-004 immunotherapy consists of autologous DCs electroporated with autologous amplified HIV RNAs (Gag, Vpr, Rev and Nef). AGS-004 was administered every four weeks to chronic HIV patients while on standard antiretroviral therapy (ART). At week 14, after 4 administrations a 12-week analytical treatment interruption (ATI) began, during which AGS-004 dosing continued every four weeks. Thirty six participants completed ATI, 23 of whom received AGS-004. This study evaluated the impact of AGS-004 on the level of integrated HIV DNA (pDNA) in CD4 T cells and its correlation with the immune response.
Methods: Peripheral blood samples were collected during a clinical study at baseline, week 8 during ART treatment and week 18 and week 26 during ATI. PBMCs were isolated using Ficoll separation and CD4 T cells were isolated using negative selection with a human CD4+ T Cell Isolation kit (Miltenyi). Genomic DNA was isolated using the Gentra Puregene kit (Qiagen). 15,000 genomes were used in a repetitive Alu-Gag based PCR. pDNA analysis was conducted on 35 subjects. Immunomonitoring data was available on 32 subjects. Levels of pDNA were correlated with the magnitude and quality of immune responses for 31 subjects. Immunomonitoring was conducted to determine if HIV-specific immune responses were generated. The analysis was conducted against all four or individual antigens used in AGS-004.
Results: There were no differences in pDNA levels in immunized versus placebo subjects (N=35). However, in an analysis of AGS-004-treated subjects (N=21), HIV pDNA levels were significantly lower in those subjects who developed multifunctional memory T cell responses (N=14) after two, five or seven doses of AGS-004 (weeks 8, 18 and 26) but not at baseline. The attenuation of pDNA levels were not associated with immune response to any individual antigen. These data taken together indicate that a polyvalent immune response directed against multiple antigens is important for the control of pDNA levels in CD4 T cells.
Conclusions: The results of this study provide a rationale to combine AGS-004 with ART and a latency reversing agent for the purpose of boosting the immune response to eliminate HIV reservoirs in infected individuals.

TUPEA092

Latency reversal Agent (LRA) romidepsin reactivates latent virus in two rhesus macaque (RM) models of controlled SIV infection in the absence of antiretroviral therapy (ART)

B. Policicchio[1,2], E. Brocca-Cofano[1], C. Xu[1], D. Ma[1], T. He[1,3], H. Li[4], G. Haret-Richter[1], T. Dunsmore[1], G. Shaw[4], R. Ribeiro[5], I. Pandrea[1,3], C. Apetrei[1,6]
[1]University of Pittsburgh, Center for Vaccine Research, Pittsburgh, United States, [2]University of Pittsburgh, Graduate School of Public Health, Infectious Diseases and Microbiology, Pittsburgh, United States, [3]University of Pittsburgh, School of Medicine, Cellular and Molecular Pathology, Pittsburgh, United States, [4]University of Pennsylvania, School of Medicine, Philadelphia, United States, [5]Los Alamos National Laboratory, Los Alamos, United States, [6]University of Pittsburgh, School of Medicine, Microbiology and Molecular Genetics, Pittsburgh, United States

Background: Viral reservoirs represent a major obstacle for HIV cure research. A reservoir reactivation strategy is the "flush and kill", in which LRAs reactivate latent virus and CTLs eliminate it. LRAs have limited efficacy, while immunosuppression impairs CTL ability to eliminate reactivated virus. Our goals were to assess *in vivo* romidepsin ability to reactivate SIV in two different models of controller RMs with functional immune responses and its effect on CTLs and viral control.
Methods: Three SIVsmmFTq-infected RMs received ART (PMPA; FTC; L-870812) for 9 months. After treatment discontinuation, the RMs controlled virus rebound and received 3 rounds of romidepsin, followed by $CD8^+$ cell depletion. Two SIVsab-infected RM spontaneous controllers received two rounds of romidepsin. Plasma viral loads were monitored with single copy assays. PBMC histone acetylation, IFN-γ production by CTLs and changes in T cells counts and their immune activation/proliferation status were assessed by flow cytometry. Romidepsin toxicity was monitored clinically and biologically; T-cell apoptosis post-RMD was assessed flow-cytometrically and by LDH ELISA.
Results: Romidepsin administration resulted in significant virus rebounds (up to 10^4 copies/ml for SIVsmmFTq and 10^3 copies/ml for SIVsab) followed by gradual viral decline. Romidepsin was well-tolerated and induced a massive surge in T-cell activation and transient lymphopenia during the first week post-treatment. Lymphopenia resulted from cell redistribution and down-regulation of surface markers rather than T-cell destruction. $CD8^+$ cell depletion resulted in robust viral rebound (up to 10^7 copies/ml) that was controlled upon $CD8^+$ T-cell recovery. Romidepsin did not significantly affect CTL antiviral functions *in vivo*. Using mathematical modeling, we showed that a small fraction of latently infected cells were at the origin of virus rebound.
Conclusions: Using two different *in vivo* models of SIV control, we demonstrated romidepsin can reactivate the reservoir virus. The levels of virus replication, timing of virus rebound and rapid control of virus replication after romidepsin administration suggest the reactivated virus is replication-competent and romidepsin does not persistently alter CTL function. $CD8^+$ cell depletion resulted in higher viral rebound compared to romidepsin administration, suggesting that romidepsin does not completely ablate CTL function. Altogether, our results show romidepsin can effectively reverse SIV latency.

TUPEA093

Robust HIV-specific T cells in post-treatment controllers from the VISCONTI cohort

A. Samri[1], V. Avettand-Fenoel[2,3], L. Hocqueloux[4], C. Bacchus-Souffan[5], A. Cheret[6], A. Emarre[7], B. Descours[8], A. Saez-Cirion[9], C. Rouzioux[2,3], B. Autran[10,11], VISCONTI Study Group
[1]Centre d'Immunologie et Maladies Infectieuses, UMR-S Inserm UPMCU 1135, Paris, France, [2]Paris-Descartes University, Sorbonne Paris-Cité, Virology Laboratory, EA 3620, Paris, France, [3]Necker Enfants-Malades Hospital, Virology Laboratory, Paris, France, [4]Regional Hospital Center, Infectious and Tropical Diseases Department, Orléans, France, [5]Université Pierre et Marie Curie, Sorbonne Universités, Centre d'Immunologie et Maladies Infectieuses, CIMI, UMR-S 1135, Paris, France, [6]CHU Druon, Infectious Diseases Department, Tourcoing, France, [7]Université Pierre et Marie Curie, Centre d'Immunologie et Maladies Infectieuses, CIMI, UMR-S 1135, Paris, France, [8]Université Pierre et Marie Curie, Laboratoire Immunité et Infection UMR-S-945, Paris, France, [9]Institut Pasteur, Unité de Régulation des Infections Rétrovirales, Paris, France, [10]Université Pierre et Marie Curie, Sorbonne Universités, Centre d'Immunologie et Maladies Infectieuses, CIMI, Paris, France, [11]Pitié-Salpétrière, C. Foix University Hospital, AP-HP, Immunology Department, Paris, France
Presenting author email: brigitte.autran@psl.aphp.fr

Background: Post-Treatment-Controllers (PTCs) represent models of functional HIV remission with an exceptional HIV control years after interruption of an early-initiated antiretroviral therapy. The enrichment in the HLA-B35 allele, associated with symptomatic primary-infection and poor prognosis, instead of the protective HLA alleles reported in Elite Controllers (ECs) questions the role mechanism of this HIV control and the role of anti-HIV T cell responses, particularly those driven by HLA-B35. We therefore compared the PTCs HIV-specific CD4 and CD8 T cells to those from continuously early-treated patients (CETs) and ECs.
Methods: We included 12 PTCs from the VISCONTI study*, half HLA-B35+, 10 CETs under a cART initiated within 10 weeks post-infection and 8 ECs from the ANRS-Co15 cohort. Multiparametric flow-cytometry assessed HIV-specific IFNg, IL2, TNFα, MIP1β or CD40L producing CD4 and CD8 T cell stimulated with HIV-p24 protein and peptides. The cell-associated HIV-DNA was measured in PBMCs and naïve and memory sorted resting CD4 T cell subsets.
Results: High frequencies of HIV-p24 specific CD4+ cellswere observed in PTCs and did not differ from the ECs or CETs ones. A third of these PTCs HIV-p24 specific CD4 cells were highly polyfunctional producing 2, 3 and 4 functions, similarly to from CETs and ECs. HLA-B35 did not influence these results. In contrast frequencies of PTCs CD8+ cells producing against HIV-p24 peptides IFNg (p=0.015) or MIP1b (p=0.001) were lower than ECs but equivalent to CETs ones, without differences in poly-functionality between the 3 groups. Among the functions tested here-in there were 20-fold less IFN-g producing HLA-B35+ CD8 T cells than HLA-B35- ones (0.006% versus 0.130%, p=0.041*)* against HIV-p24 peptides.
Conclusions: The model of HIV remission represented by VISCONTI PTCs is characterized by robust polyfunctional HIV-specific CD4+ T cells similar to those from Elite Controllers and from continuously early-treated patients, independently from the HLA-B35 allele which negatively impacts IFN-g producing CD8 T cells. These results illustrate differences between ECs and PTCs linked to HLA background and suggest early initiation of treatment allows maintenance of robust HIV-p24 specific CD4 T cells in PTCs.

TUPEA094

Nef inhibition for enhanced NK cell killing of cells expressing reactivated HIV-1

E. Scully[1,2], A. Lockhart[1], W. Garcia Beltran[1], A. Bodair[1], M.-C. Rouyez[3], S. Benichou[3], D. Kuritzkes[2], M. Altfeld[4]
[1]Ragon Institute of MGH, MIT and Harvard, Cambridge, United States, [2]Brigham and Women's Hospital, Division of Infectious Disease, Boston, United States, [3]Institut Cochin, Paris, France, [4]Heinrich Pette Institute, Leibniz Institute for Experimental Virology, Hamburg, Germany
Presenting author email: escully@partners.org

Background: Functional cure of HIV-1 infection obligates near complete eradication of cells carrying latent provirus. Early studies suggest that endogenous immune responses are insufficient and new strategies are needed to enhance immune recognition. The HIV-1 Nef protein mediates immune evasion by downregulating surface expression of CD4, HLA class I, and NKG2D receptor ligands. NKG2D is a receptor expressed on several classes of lymphocytes, and is a potent trigger of cytotoxicity on NK cells. We investigated the potential for inhibition of Nef to enhance NK cell killing of cells harboring latent HIV-1 after reactivation.
Methods: The J89 T cell line containing an integrated copy of HIV-1 with an eGFP reporter was used as a model of latency. HIV-1 expression was induced by treatment with 20 nM of panobinostat. Nef inhibitors included (1) a single-domain antibody fragment (sdAb19) previously shown to inhibit Nef-induced CD4 downregulation (2) a fusion of this antibody fragment to the SH3 domain of Hck, (Neffin), that blocks both CD4 and HLA class I downregulation. The sdAb19 and Neffin were stably expressed in the J89 cell line through transduction of lentiviral constructs. Their inhibitory activity was tested on Nef-induced downregulation of CD4, HLA class I, and NKG2D ligands. The killing activity of NK cells purified from HIV infected individuals was also assessed by coculture with varying ratios of J89 cells expressing the Neffin.
Results: In J89 cells, panobinostat induced expression of HIV-1 as measured by both GFP expression and intracellular p24. Concurrent expression of the sdAb inhibited Nef-mediated CD4 downregulation in reactivated cells, while expression of Neffin inhibited both CD4 and HLA class I downregulation. Both sdAb and Neffin blocked NKG2D ligand downregulation in reactivated J89 cells. There was a significant decline in the ratio of $HIV^+Neffin^+$:$HIV^+Neffin^-$ in the NK cell killing assay. Mean ratio $HIV^+Neffin^+$:$HIV^+Neffin^-$ was: 2.975 for no NK cells, 2.396 for 5:1 NK:target, and 1.087 for 10:1 NK:target (p=0.025 paired t test between no NK and 10:1).
Conclusions: These data indicate that Nef inhibition can enhance expression of NKG2D ligands after reactivation of HIV-1. The presence of Nef inhibitors enhances NK cell-mediated killing of cells expressing HIV-1 after reactivation.

TUPEA095

Emergence of infectious treatment-resistant HIV after provirus-directed endonuclease therapy

H.S. De Silva Feelixge[1], M. Aubert[1], D. Stone[1], K.R. Jerome[1,2]
[1]Fred Hutchinson Cancer Research Center, Seattle, United States, [2]University of Washington, Seattle, United States
Presenting author email: hdesilva@fhcrc.org

Background: Chronic viral infections that do not respond to treatment with antiviral drugs are a major cause of morbidity and mortality worldwide. As an approach to combat persistent viral infections targeted endonucleases have been pioneered as potentially curative agents. Recent studies have shown that endonucleases of several different classes can be engineered to cleave a number of virus genomes including HIV, and this can inhibit viral replication and subsequently persistence.
However, a major concern for endonuclease-based antiviral therapies has been that treatment-resistant infectious virus may arise.
Methods: Zinc finger nucleases (ZFNs) targeting the HIV protease, reverse transcriptase and integrase genes were generated and tested as antiviral therapeutics using *in vitro* models of HIV replication.
Results: Here we demonstrate the emergence of an endonuclease-resistant infectious virus. While testing the antiviral activity of HIV *pol*-specific ZFNs we identified a provirus encoding a treatment-resistant and infectious mutant that was likely derived from a chance disruption within a ZFN target site in reverse transcriptase. Although ZFN-mediated disruption of target sites in protease, reverse transcriptase and integrase inhibited viral replication, an insertion within the thumb region of the mutants reverse transcriptase produced a virus that efficiently replicated and could not be cleaved by its corresponding reverse transcriptase specific ZFN. Furthermore, the treatment-resistant mutant was 4-fold more infectious than wild type virus in SupT1 cells.
Conclusions: These observations show that although endonuclease therapy for HIV is highly promising, caution should be exercised in the development of endonuclease-based antiviral therapies for persistent viral infections.

Novel approaches in Immunotherapeutics (including bnAbs and anti-inflammatory mediators)

TUPEA096

Selection and evaluation of specific single chain antibodies against gp41 of HIV

F. Nejatollahi[1,2], H. Joulaei[1], R. Robati[2]
[1]Shiraz HIV/AIDS Research Center, Shiraz University of Medical Sciences, Shiraz, Iran, Islamic Republic of, [2]Recombinant Antibody Laboratory, Department of Immunology, Shiraz University of Medical Sciences, Shiraz, Iran, Islamic Republic of

Background: HIV -1 envelop glycoprotein gp41 is involved in virus- mediated membrane fusion which leads to HIV-entry into target cells. The C-domain of gp41 has been introduced as an important site implicating in the process of virus entry. The monoclonal antibody 2F5 recognizing the C-domain of gp41 has been able to inhibit binding of gp41 to monocytes and lymphocytes and neutralize many HIV strains. Single-chain variable fragment (scFv) antibodies which are composed of VH and VL domains offer several advantages over monoclonal antibodies. Due to scFvs properties including human origin, small size, high affinity, high specificity and exhibiting better tissue penetration, these antibodies have been introduced as highly effective agents for virus-targeted therapy. The aim of this study was to select and evaluate specific scFvs against gp41 of HIV-1.
Methods: A phage antibody display library of scFv was used to select specific scFvs against conserved neutralizing epitope of C-terminal part of gp41 by the panning process. DNA fingerprinting was applied to reveal the common patterns. The selected clones were tested by ELISA. The soluble form of the specific antibody was produced using Ecoli HB2151 and sonication process. The soluble scFv was evaluated in western blot analysis.

Results: one predominant fingerprinting pattern with frequency 55% was detected.
The OD obtained from reaction of the antibody with the corresponding epitope was significantly higher than the negative controls and showed the specificity of the isolated scFv. The western blot analysis demonstrated the presence of reactive soluble anti-gp41 scFv.
Conclusions: Targeted therapy using specific antibodies has been used to design novel antiviral therapy. Several studies have demonstrated that HIV-1 particles in blood of patients could be cleared by neutralizing antibodies. In this study we used a phage display technology to select specific scFvs against a conserved neutralizing epitope on gp41 of HIV-1. The results demonstrated successful panning process and selection of a specific scFv which was reactive in ELISA test against the corresponding epitope. The selected scFv was produced in soluble reactive form. The isolation of such a specific anti-gp41 scFv suggest further evaluation of the scFv for its application in the clinical use.

TUPEA097

Antibody-dependent cellular cytotoxicity against cells latently infected with HIV

W.S. Lee, M. Lichtfuss, M.S. Parsons, S. Kent
University of Melbourne, Department of Microbiology and Immunology, Peter Doherty Institute, Melbourne, Australia

Background: Current treatments for HIV infection are life-long as they do not diminish latent replication-competent HIV in long-lived resting CD4+ T cells. A major approach to an HIV cure is to reactivate the integrated HIV genome from latency and subsequently eliminate the cells harbouring reactivated HIV. We hypothesised that antibody-dependent cellular cytotoxicity (ADCC) could be a possible immune response to kill reactivated latently infected cells.
Methods: We established assays to measure ADCC-mediated killing by modifying the LDH release assay and ADCC-induced NK cell activation following reactivation of latently infected cell lines.
Results: ADCC-mediated killing and NK cell activation was detected following exposure of a chronically infected CD4+ T cell lines or cell lines pulsed with the HIV envelope glycoprotein gp120. However, we found that reactivated latently infected T cell lines, although they elicited higher background levels of killing and NK cell activation, were not susceptible to ADCC-mediated killing and did not elicit HIV-specific antibody-mediated NK cell activation. The reactivated cells expressed high levels of gp120 (as high or higher than gp120 pulsed cells), but did not express CD4, likely due to down-modulation by the HIV accessory proteins Vpu and Nef.
Conclusions: Our studies suggest the hypothesis that reduction in CD4-induced ADCC epitopes at least partially protects reactivated latently infected cells from ADCC recognition. These studies need to be confirmed in primary CD4+ T cell models of latency and will need to assess whether inhibition of Vpu and/or Nef can restore the susceptibility of reactivated latently infected cells to ADCC. Our results highlight a previously under-appreciated problem for the proposition that ADCC antibodies can assist in an HIV cure.

TUPEA098

Potent and broad neutralizing activity of small antibody fragments targeting CD4i (CD4-induced) epitope

K. Tanaka, T. Kuwata, Y. Maruta, K. Ramirez, M. Alam, Y. Egami, Y. Kawanami, S. Matsushita
Matsushita Project Laboratory, Center for AIDS Research, Kumamoto University, Kumamoto, Japan
Presenting author email: 130r5138@st.kumamoto-u.ac.jp

Background: CD4-induced (CD4i) epitope is exposed on the surface of trimeric HIV-1 envelope glycoprotein (Env) after conformational changes of gp120 by binding to CD4. The CD4i epitope is highly conserved because the N-terminal region of CCR5 binds to this epitope. Therefore, the CD4i epitope is a favorable target for antibodies to neutralize a broad range of HIV-1 strains. However, most of primary HIV-1 isolates are resistant to anti-CD4i antibodies because the CD4i epitope is hidden inside trimeric Env before binding to CD4.
In this study, we aim at developing more potent anti-CD4i neutralizing antibody than the original IgG form by constructing antigen-binding fragment (Fab) and single-chain variable fragment (scFv).
Methods: We constructed six Fabs and three scFvs from monoclonal antibodies (mAb) targeting CD4i epitope (16B2, 17B11, 4E9C, 5D6, 25C4b and 12G10). These anti-CD4i Fabs and scFvs were examined for their abilities to bind trimeric Env by flow cytometry. Neutralizing activities of these antibody fragments were examined by infection of TZM-bl cells with the pseudoviruses with various sensitivities to neutralizing antibodies, which were categorized to very high (tier 1A), above-average (tier 1B), moderate (tier 2), and low (tier 3).
Results: Three anti-CD4i scFvs (16B2, 4E9C and 25C4b) efficiently bound trimeric Env of HIV-1_{JRFL} without sCD4, while the addition of sCD4 was necessary for the binding of the corresponding anti-CD4i IgG antibodies to Env. In addition, the binding activities of these scFvs were significantly higher than those of the corresponding anti-CD4i Fabs. These three scFvs neutralized tier 2, and tier 3 clade B viruses which were resistant to the corresponding IgGs, and the neutralizing activities were significantly higher than those of the corresponding Fabs. Moreover these scFvs effectively neutralized non-clade B viruses, including clade A, C, and CRF01_AE.
Conclusions: Taken together, the anti-CD4i scFvs are accessible to CD4i epitope hidden inside trimeric Env before binding to CD4, and effectively neutralize multi-clade HIV-1. The small fragment of anti-CD4i antibodies will be useful for a potent and broadly neutralization of HIV-1.

TUPEA099

A novel TLR-9 agonist (MGN1703) activates NK-cells and enhances NK-cell mediated viral killing of HIV-1 infected CD4+ T cells ex vivo

R. Offersen, M. Tolstrup, S.K. Nissen, T. Rasmussen, L. Østergaard, P.W. Denton, O.S. Søgaard
Aarhus University Hospital, Dept. of Infectious Diseases, Aarhus, Denmark
Presenting author email: rasmus.offersen@gmail.com

Background: Toll-like receptor (TLR) agonists may have dual favorable effects in the context of 'kick and kill' HIV eradication approaches. First, as enhancers of anti-viral immunity via stimulation of immune effector cells and second as direct latency-reversing agents. To hasten the inclusion of a TLR agonist into an HIV cure strategy, we have performed extensive preclinical testing of a novel, specific and potent TLR-9 agonist, MGN1703. Classical TLR-9 agonists (e.g. CpG-ODN) exhibit toxicity and backbone-dependent activity associated with phosphorothioate modifications. In contrast, such chemical modifications are not required to maintain the structure of MGN1703, which greatly enhances the safety profile of this molecule.
Methods: PBMCs from HIV-patients were stimulated with MGN1703 or media. Unspliced HIV-1 RNA (usHIV-RNA) in subsequently enriched CD4+ T cells was quantified using RT-qPCR. NK-cell activation, intracellular IFN-gamma production and degranulation were assessed by flow cytometry. NK-mediated viral inhibition of HIV-1 (HBX2) infected, autologous CD4+ T cells was assessed using HIV-1 P24 ELISA and intracellular HIV-1 P24 staining of CD4+ T cells. Supernatant cytokines were quantitated by QuickPlex (MSD). Statistical analyses included one-sample and paired t-tests on log-transformed data.
Results: Regarding the ability of MGN1703 to improve antiviral immune responses, we found that MGN1703-stimulation led to: (i) increased CD69-expression on $CD56^{dim}CD16^{+}$ NK-cells (4.75-fold; p=0.0014); (ii) a higher proportion of CD107a+ NK-cells (1.50-fold; p=0.0016); and (iii) a higher proportion of $CD107a^{+}$IFN-gamma^{+} NK-cells (2.04-fold; p=0.13). Furthermore, MGN1703-stimulated NK-cells suppressed supernatant HIV-1 p24 levels by 76% versus 51% for unstimulated NK-cells (culture day 5; p=0.03). PBMCs stimulated with MGN1703 exhibited significant increases in cytokine production from (e.g. IP-10 increased 6.16-fold; p=0.024). Regarding the potential of MGN1703 to activate transcription of latent HIV-1, we found that MGN1703 increased transcription of usHIV-RNA in CD4+ T cells by 1.51-fold over media alone (p=0.036).
Conclusions: MGN1703 stimulation activated and enhanced the degranulatory capacity of NK-cells. In addition, NK-cells stimulated with MGN1703 exhibited a significantly increased capacity to control HIV-1 replication in autologous CD4+ T cells. These findings combined with the observation that MGN1703 induced an increase in usHIV-RNA transcription in CD4+ T cells supports the incorporation of the TLR9-agonist MGN1703 into HIV eradication trials.

HIV testing (including new algorithms, rapid/point of care testing and strategies)

TUPEB216

What individual and contextual factors are associated with rapid HIV test utilization in the U.S.?

R. Serrano, M. Philyaw, D. Lodin
Emory University, Health Policy and Management, Atlanta, United States
Presenting author email: ray.serrano@stanfordalumni.org

Background: Rapid HIV tests (RT) can improve access to screening for high-risk populations. This is the first known nationwide U.S. study to explore correlates of RT utilization.
Methods: This study includes 13,392 HIV-tested participants (ages 18-64) from the 2010 Behavioral Risk Factor Surveillance System with linked contextual data from the 2009 Area Health Resource File and state-level sources. Adjusted multilevel logistic models with scaled survey weights and clustered errors were estimated using GLLAMM to explore the association of RT receipt with individual, county and state fixed effects.
Results: 25.96% of individuals received a RT for their last HIV test. RT users were significantly more likely to be young adults (age 18-24, AOR=1.68, 95% CI: 1.39, 2.03; Ref=25 to 34) or middle-aged (e.g. age 55-64, AOR=1.32, 95% CI: 1.11, 1.58); of minority race/ethnicity (e.g. Black/African American, AOR = 1.62, 95% CI: 1.37, 1.90; Ref=White); uninsured (AOR=1.41, 95% CI: 1.20, 1.67); of lower household income (e.g. income < $15,000, AOR: 1.69, 95% CI: 1.42, 2.02; Ref=$50,000); and live in counties with above-median adult poverty rates

(rate>13.04%, AOR: 1.18, 95% CI: 1.02, 1.35) and higher minority rates (e.g. rate>52.07%, AOR: 1.38, 95% CI: 1.11, 1.73, Ref=1.45% - 19.88%). RT users were also significantly more likely to have been tested at counseling/testing sites (AOR: 2.87, 95% CI: 2.17, 3.78, Ref=clinic) or hospitals (AOR: 1.57, 95% CI: 1.31, 1.88). Individuals living in states with above-median uninsured rates (rate>19.20%) were significantly less likely to receive a RT (AOR: 0.78, 95% CI: 0.67, 0.90). RT receipt was not associated with county safety net capacity, Expanded Testing Initiative funding, or state HIV testing policies.

Conclusions: Rapid tests are being used by traditionally under-tested populations living in higher-risk communities. RT benefits may be limited in states which opted out of Medicaid expansion and have higher uninsured rates. Scaling up RT at counseling/testing sites and safety net clinics may be effective to increase early HIV detection among hard-to-reach populations. Future assessment should focus on the impact of expanded healthcare coverage, routine HIV testing, and other contextual factors that may affect RT uptake.

TUPEB217

High acceptability of rapid HIV test in Argentina: experience during a seroprevalence study in vulnerable groups

A. Duran[1], D. Rossi[2], R. Marone[3], G. Orellano[4], M. Romero[5], C. Petracca[6], E. Benedetti[7], M.M. Avila[8], H. Salomón[8], M.A. Pando[8]
[1]Coordinación Sida, Ministerio de Salud, Buenos Aires, Argentina, [2]Intercambios AC, Buenos Aires, Argentina, [3]Nexo AC, Buenos Aires, Argentina, [4]Asociación de Mujeres Meretrices de Argentina (AMMAR), Buenos Aires, Argentina, [5]Asociación de Travestis Transexuales y Transgéneros de Argentina (ATTTA), Buenos Aires, Argentina, [6]Programa de VIH-Sida e ITS, Municipalidad de San Martín, San Martín, Argentina, [7]Hospital en Red Especializado en Salud Mental y Adicciones (ex CENARESO), Buenos Aires, Argentina, [8]Instituto de Investigaciones Biomédicas en Retrovirus y SIDA (INBIRS), Buenos Aires, Argentina
Presenting author email: mpando@fmed.uba.ar

Background: The Ministry of Health in Argentina recently updated the HIV diagnosis algorithm, incorporating the rapid HIV test (RHT) and the confirmation of reactive cases with HIV viral load instead of Western blot. This new algorithm was implemented for the first time in Argentina to evaluate acceptability and accuracy of the RHT in a seroprevalence HIV study among vulnerable groups from Buenos Aires Metropolitan Area.

Methods: From September 2013 to May 2014, a cross-sectional HIV seroprevalence survey was conducted at different settings (non-governmental organizations, hospitals and field visits). Men who have sex with men (MSM), female transgender/travesties, drug users (DU) and female sex workers (FSW) were included in the study. HIV diagnosis was performed with Allere Determine HIV-1/2. All samples were also tested with Genscreen Ultra HIV Ag&Ab. Reactive cases were confirmed with viral load (bDNA Versant HIV RNA). CD4 cell count was also performed.

Results: Between September 2013 and May 2014, 1517 individuals were tested. Regarding RHT acceptability, 99.5% of participants reported that proceedings had been "good" or "very good" and 91.2% preferred to know results in the same day. For 19% of the participants this was the first time they tested for HIV. Prevalence of HIV infection was 11.5% (116/1015, 95% CI 9.5-13.5) for MSM, 31.5% (52/165, 95% CI 24.1-38.9) for female transgender/travesties, 3.5% (9/259, 95% CI 1.1-5.9) for DU and 5.1% (4/78, 95% CI 1.4-12.6) for FSW. Comparison of RHT with standard laboratory diagnosis showed 10 discordant results (0.66%). RHT sensitivity and specificity was 97.3% and 99.6%, respectively (PPV: 96.7%, NPV: 99.7%). Acute HIV infection was detected in the laboratory in four MSM with a negative RHT. Fifty eight percent of HIV positive individuals had less than 500 CD4/µl at diagnosis.

Conclusions: Implementation of RHT was successful, revealing that its implementation could be a useful tool to facilitate access to diagnosis in vulnerable groups, where prevalence of HIV remains extremely high. RHT expansion, improving early diagnosis, would diminish the frequency of individuals that are diagnosed at advanced stages of the infection.

TUPEB218

Novel diagnostic peptide epitope biomarkers for detection and identification of recent and longstanding HIV infection using the Europium Nanoparticle Immuno Assay (ENIA)

M.K. Haleyur Giri Setty[1], Z. Panhe[1], J. Liu[1], B. Du[1], S.M. Keating[2], M.P. Busch[2], C. Pilcher[2], M. Cohen[3], B.F. Haynes[4], M. Vermeulen[5], I.K. Hewlett[1]
[1]United States Food and Drug Administration, CBER, Silver Spring, United States, [2]University of California-San Francisco, Blood Systems Research Institute, San Francisco, United States, [3]University of North Carolina-Chapel Hill, Chapel Hill, United States, [4]Duke Human Vaccine Institute, Durham, United States, [5]South African National Blood Service, Weltevreden Park, South Africa
Presenting author email: mohan.haleyurgirisetty@fda.hhs.gov

Background: Accurate and early detection of HIV infection is critical for timely initiation of therapy and help prevent transmission. Estimation of HIV incidence is necessary to evaluate impact of HIV prevention measures, and to identify populations for recruitment into clinical trials designed to prevent infection or treat early infection. Many incidence tests have been developed in the last decade but several limitations exist and improved tests are needed. We sought to evaluate disease-stage specific viral immune responses using a peptide epitope screening method to identify diagnostic biomarkers that distinguish recent and chronic infection.

Methods: We synthesized 20-mer peptides for consensus sequences for HIV-1 p24, gp41 and gp120 proteins using overlapping by 15 amino acids. Peptides were evaluated for binding of antibodies using plasma samples from 40 recent and 40 longstanding HIV -1 infected patients. Peptides were coated onto microtiter plate wells to capture anti-p24, anti-gp41 and anti-gp120 antibodies followed by binding to an anti-human antibody labeled with biotin molecules and streptavidin (SA)-conjugated Eu^{3+} nanoparticles (NPs) through biotin-SA interaction.

Results: We have identified three gp41 peptides which elicit strong reactivity with samples from chronically infected patients and very low or no reactivity with samples from recently infected patients. These gp41 peptides showed consistent positive reactivity in chronically infected patient samples and negative or very low response in recently infected plasma. We also have identified three gp120 peptides which showed strong reactivity with samples from recently infected plasma but negative response in chronic patients.

Conclusions: We have identified novel peptide epitopes in gp120 and gp41 proteins that could serve as diagnostic biomarkers for recent or longstanding infection. Together with HIV p24 antigen, the inclusion of appropriate peptide epitopes could enhance accuracy and specificity of identifying recent HIV infection cases. The Europium Nanoparticle Immunoassay platform eliminates background fluorescence thus enhancing sensitivity. It will be useful to evaluate other HIV epitopes to improve assay sensitivity for identification of recent infection and develop suitable testing format for use in a variety of settings. This work will contribute to development of new assays for distinguishing recent vs. chronic infection, improving current status of assays in this field.

TUPEB219

Performance of the determine HIV 1/2 Ag/Ab combo rapid test for detecting acute HIV infection: a systematic review and Bayesian meta-analysis

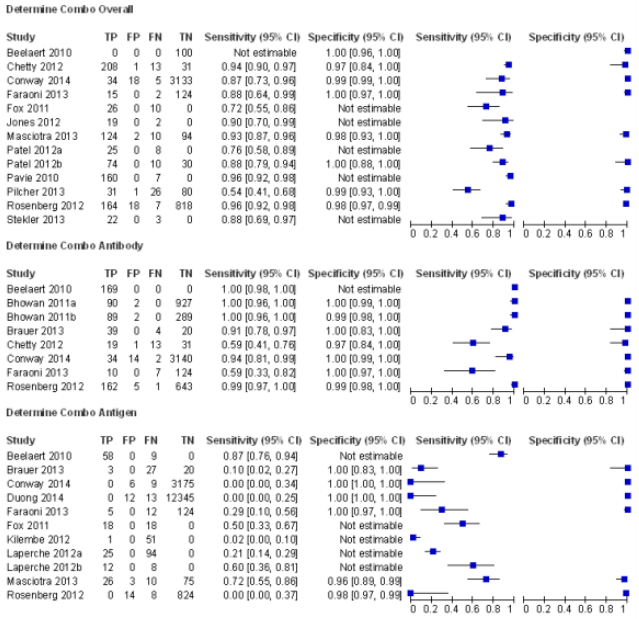
M. Smallwood[1], R. Vijh[2], B. Nauche[3], B. Lebouché[4], L. Joseph[1], N. Pant Pai[4]
[1]McGill University, Epidemiology, Biostatistics and Occupational Health, Montreal, Canada, [2]McGill University Health Centre, Division of Clinical Epidemiology, Montreal, Canada, [3]McGill University Health Centre, Medical Library (Royal Victoria Hospital), Montreal, Canada, [4]McGIll University, Medicine, Montreal, Canada
Presenting author email: megan.smallwood@mail.mcgill.ca

Background: Fourth generation HIV point of care assays (Ag/Ab combo) offer a huge potential for timely detection of acute HIV infection, which is important for test and treat initiatives, but data on their field performance has not been synthesized to date. To fill this gap, we synthesized evidence on the diagnostic performance of the only FDA-approved fourth generation rapid test (the Determine HIV 1/2 Ag/Ab Combo) in adults, using Bayesian methods for meta-analysis.

Methods: Two reviewers searched seven databases (Medline, Embase, PubMed, BIOSIS, The Cochrane Library, LILACS, and African Index Medicus) and gray literature, independently extracted data, and assessed study quality with QUADAS-2. Included studies evaluated the rapid test in adults, against a reference standard. From 17 studies, data on sensitivity and specificity of assay components (i.e., antigen, antibody, overall) were pooled using a Bayesian hierarchical random effects meta-analysis model. Subgroup analyses by blood sample and study design was performed.

Results: The pooled sensitivity of the antigen component was 12.3%, 95% credible interval (CrI) [1.1 - 44.2], while pooled antigen specificity was 99.7%, 95% CrI [96.8 - 100]. Pooled sensitivity of the antibody component was 97.3%, 95% CrI [60.7 - 99.9], while pooled antibody specificity was 99.6%, 95% CrI [99.0 - 99.8]. The overall pooled sensitivity for the device was 88.5%, 95% (CrI) [80.1 - 93.4], and overall pooled specificity was 99.1%, 95% CrI [97.3 - 99.8],

(refer to Table 1; Figure 1). Individual study limitations included weak study designs, poor patient case mixes, and variable reference standards. Detection bias, selection bias (selecting patients or samples based on HIV status), verification bias, and incorporation bias limited further analyses. Data limitations prevented statistical exploration of the effect of patient case-mix on accuracy.



[Forest plots: performance of Determine]

Overall	Sensitivity	95% CrI	Specificity	95% CrI
Total	88.5	80.1 - 93.8	99.1	97.3 - 99.8
Serum	84.3	65.0 - 94.2	99.3	94.7 - 100.0
Whole blood	93.8	84.4 - 97.3	98.8	0.00 - 100.0
Case-control	84.9	65.0 - 94.5	99.6	79.1 - 100.0
Cross-sectional	93.2	83.9 - 96.9	98.8	37.2 - 100.0

[Results from Bayesian hierarchical meta-analysis]

Conclusions: Although the specificities of the antigen and antibody components of the Determine Combo rapid test were high; the antigen sensitivity calls for an improvement. Future research with improvements in study designs, patient sampling, and case mixes (to avoid biases), is pertinent. The Determine Combo assay has potential for timely and affordable detection of HIV post-seroconversion at point of care, but accuracy parameters need improvement for widespread global use.

TUPEB220

Roll-out of a national early infant diagnosis program in Papua New Guinea, 2008-2013

I. Silas[1], P. Desai[2], E. Lavu[1], M. Kiromat[2]
[1]Central Public Health Laboratory, Health Department, Port Moresby, Papua New Guinea, [2]Clinton Health Access Initiative, Health Department, Port Moresby, Papua New Guinea
Presenting author email: ivn.silas@gmail.com

Background: In 2007, Papua New Guinea (PNG) had an HIV vertical transmission rate of 30%, with a national prevention of parent to child transmission (PPTCT) coverage less than 3% and no laboratory method to confirm infant HIV status, a prerequisite for early infant HIV treatment (EIT). With support from Clinton Health Access Initiative, the Central Public Health Laboratory implemented HIV DNA PCR testing, and, in collaboration with the PPTCT program, rolled out an Early Infant Diagnosis (EID) program to 158 sites in 21 provinces with 396 health care workers trained to collect dried blood spots (DBS). Here, we report the EID program data from 2008 through 2013.
Methods: The prevalence of HIV was determined among infants (6 weeks to 18 months age) in PNG, whose DBS samples were collected from any of the trained sites and the proportion of infants tested who were less than 2 months of age. HIV testing was conducted using either the Roche Amplicor manual assay or the automated Roche HIV qualitative assay. The national EID coverage rate defined as the percentage of infants born to HIV-positive women receiving a virological test for HIV within 2 months of birth was calculated.
Results: A total of 3293 infants were tested in the EID program between 2008 and 2013, of whom 667 (20.3%) were confirmed to be HIV positive. The number of infants tested in the program increased from 122 in 2008 to 828 in 2013. The HIV prevalence among those tested declined from 36.1% to 13.7% during these years. Fifty percent of infants tested had their DBS collected within the first 2 months of birth and 40% of infants tested were between 2 to 12 months of age. National EID testing coverage was 32% in 2012, and 41% in 2013.
Conclusions: PNG has made progress in EID thus making Early Infant Treatment (EIT) possible. Looking forward, the EID program needs to focus on addressing barriers to participation of trained sites and patients as well as strengthening linkages with PPTCT and pediatric ART services to improve EID and EIT coverage.

TUPEB221

Performance of the Trinity Biotech Uni-Gold HIV 1/2 rapid test as a first-line screening assay for gay and bisexual men compared with 4th generation immunoassays

P. Keen[1], D.P. Conway[1,2], P. Cunningham[3,4], A. Mcnulty[5,6], D.L. Couldwell[7,8], S.C. Davies[9,10], D.E. Smith[6,11], J. Gray[12], M. Holt[13], C. O'connor[1,14,15], R. Finlayson[1,16], J. Mcallister[17], B. Hughes[18,19,20], C. Carmody[20], R. Varma[7,21], D. Smith[22], P. Read[1,23], D. Callander[1], R. Pickles[19], R. Guy[1]
[1]The Kirby Institute for Infection and Immunity in Society, Sexual Health Program, Sydney, Australia, [2]Short Street Sexual Health Centre, Kogarah, Australia, [3]NSW State Reference Laboratory for HIV, St Vincent's Hospital, Darlinghurst, Australia, [4]St Vincent's Centre for Applied Medical Research, University of New South Wales, Sydney, Australia, [5]Sydney Sexual Health Centre, Sydney Hospital, Sydney, Australia, [6]School of Public Health and Community Medicine, University of New South Wales, Sydney, Australia, [7]Western Sydney Sexual Health Centre, Western Sydney Local Health District, Sydney, Australia, [8]The Marie Bashir Institute for Infectious Diseases, University of Sydney, Sydney, Australia, [9]North Shore Sexual Health Service, Royal North Shore Hospital, St Leonards, Sydney, Australia, [10]Sydney Medical School, University of Sydney, Sydney, Australia, [11]Albion Centre, Surry Hills, Sydney, Australia, [12]AIDS Council of NSW, Surry Hills, Sydney, Australia, [13]Centre for Social Research in Health, University of New South Wales, Sydney, Australia, [14]RPA Sexual Health, Community Health, Sydney LHD, Camperdown, Sydney, Australia, [15]Central Clinical School, Sydney Medical School, University of Sydney, Sydney, Australia, [16]Taylor Square Private Clinic, Darlinghurst, Sydney, Australia, [17]Immunology & Infectious Diseases Unit, St. Vincent's Hospital, Sydney, Australia, [18]Faculty of Health and Medicine, University of Newcastle, Callaghan, Australia, [19]HNE Sexual Health Services, Hunter Street, Newcastle, Australia, [20]Liverpool Sexual Health, Liverpool, Australia, [21]Nepean and Blue Mountains Sexual Health Clinics, Penrith, Australia, [22]Lismore Sexual Health, Lismore, Australia, [23]Kirketon Road Centre, Kings Cross, Australia
Presenting author email: pkeen@kirby.unsw.edu.au

Background: There is a strong public health need to increase HIV testing in gay and bisexual men (GBM). Rapid testing is preferred by the majority of GBM over conventional testing. The Trinity Uni-Gold HIV 1/2 rapid test (Uni-Gold) is an antibody-only test used in some countries for HIV screening but not yet approved in Australia. Most evaluations of the Uni-Gold have compared its performance to 3rd generation antibody-only immunoassays (EIA) and/or nucleic acid tests, however 4th generation combination antigen/antibody EIAs are increasingly used in laboratory HIV testing algorithms. We evaluated the operational performance of the Uni-Gold test as a first-line screening assay in GBM in NSW compared to 4th generation EIAs.
Methods: GBM clients attending any of 17 clinical and community sites were offered the Uni-Gold test. We assessed the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of Uni-Gold compared with conventional laboratory serology including a 4th generation EIA. Individuals were classified as having acute HIV infection if they had reactive 4th generation EIA AND negative or indeterminate western blot (WB) pattern, AND positive p24antigen OR HIV-1 RNA tests OR a previous HIV-negative test in the past 3 months. Established infections were defined by a positive 4th generation EIA and WB.
Results: Of 9277 specimens tested with Uni-Gold and conventional serology, 82 (0.9%) were confirmed as HIV-positive by conventional serology and 67 were Uni-Gold reactive (sensitivity=81.7%,95% CI:71.6-89.4). Of these, 30 (36.6%) were acute infections, of which 16 were Uni-Gold reactive (sensitivity=53.3%,95%CI:34.3-77.7) and 52 (63.4%) were established infections, of which 51 were Uni-Gold reactive (sensitivity=98.1%,95%CI:89.7-100.0). Of 9195 specimens confirmed as HIV-negative, 9189 were Uni-Gold negative (specificity=99.9%,95% CI:99.9-100.0). PPV overall was 91.8% (95%CI:83.0-96.9) and NPV was 99.8% (95%CI:99.7-99.9).
Conclusions: The sensitivity of Uni-Gold in acute and established HIV infection versus results on 4th generation EIAs appears comparable to other rapid tests used in the same population and setting, though PPV and specificity of Uni-Gold is higher. When using any rapid test for screening, we recommend men at risk of acute HIV infection also have conventional serology including 4th generation EIA or direct detection (p24 or nucleic acid) performed.

TUPEB222

Evaluation of SD bioline HIV Ag/Ab assay for detection acute HIV infection (AHI)

A. Drake[1], D. Matemo[2], J. Kinuthia[2], S. McClelland[1,3,4], J. Klausner[5,6], G. John-Stewart[1,3,4]
[1]University of Washington, Global Health, Seattle, United States, [2]University of Nairobi, Obstetric and Gynecology, Nairobi, Kenya, [3]University of Washington, Epidemiology, Seattle, United States, [4]University of Washington, Medicine, Seattle, United States, [5]University of California, Medicine, Los Angeles, United States, [6]University of Los Angeles, Global Health, Seattle, United States
Presenting author email: daniel.matemo@gmail.com

Background: Early detection of acute HIV infection (AHI) among pregnant and postpartum women can enable timely initiation of antiretrovirals and prevent mother-to-child HIV transmission (PMTCT). Rapid HIV tests used for antenatal screening only detect antibody and fail to detect AHI in the "window period". We evaluated a 4th generation assay for detecting AHI during pregnancy and postpartum.
Methods: HIV negative women seeking antenatal care in Nyanza, Kenya were enrolled in a cohort study of HIV acquisition during pregnancy and postpartum. Blood samples were collected for nucleic acid amplification testing (NAAT) at enrolment, 28, and 36 weeks gestation; and at 6, 14, 24 and 36 weeks postpartum. Women with positive NAAT results were classified as AHI. The Abbott Determine HIV-1/2 Test and SD Bioline HIV Ag/Ab Combo Rapid Test (4th generation) were conducted on blood specimens at time of first HIV RNA detection. Median time to HIV detection was calculated for women who were non-reactive Determine but had positive NAATs and had samples available at subsequent visits.
Results: Among 27 women with AHI detected by NAAT, 19 (70%) were reactive by Determine and 21 (78%) were reactive by Bioline. Among 8 women with initial Determine non-reactive results, 6 (75%) were also Bioline non-reactive. Four of 6 AHI initially Determine non-reactive had samples available for serial testing: 2 (50%) were simultaneously reactive by Bioline and Determine, 1 was only reactive by Bioline reactive, and 1 was only reactive by Determine. Overall, Bioline detected 3 (38%) AHI missed by the Determine assay, whereas Determine detected 1 (13%) AHI not detected by Bioline. Half (n=2) of Bioline reactive samples detected p24 antigen. Median time to HIV detection using Determine was 18 days (IQR:14-21), and 12 days (IQR:2-20) using Bioline (n=6). Among 5 AHI detected first by Bioline, AHI were detected a median of 6 days earlier with Bioline than Determine (IQR:0-13).
Conclusions: While the Bioline detected 38% of infections missed by Determine, 13% of infections detected by Determine would have been missed in antenatal screening programs using Bioline. Rapid and inexpensive assays are needed to reliably detect AHI in PMTCT programs.

CD4 measurement (including point of care diagnostics)

TUPEB223

A meta-analysis of the performance of the Pima™ CD4 for point of care testing

L. Scott[1], J. Campbell[2], L. Kestens[3], L. Vojnov[2], T. Peter[2], W. Stevens[1,4]
[1]University of the Witwatersrand, Molecular Medicine and Haematology, Johannesburg, South Africa, [2]Clinton Health Access Initiative, Boston, United States, [3]University of Antwerp, Belgium and Laboratory of Immunology, Department of Biomedical Sciences, Institute of Tropical Medicine, Department of Biomedical Sciences, Antwerp, Belgium, [4]National Priority Program, NHLS, Johannesburg, South Africa
Presenting author email: lescott.ac@gmail.com

Background: The Alere point-of-care (POC) Pima™ CD4 analyzer allows for decentralized testing and expansion to testing antiretroviral therapy (ART) eligibility. A consortium conducted a pooled multi-data technical performance analysis of the Pima CD4.
Methods: The study used primary data (11,803 paired observations) comprised from 22 independent studies between 2009-2012 from the Caribbean, Asia, Sub-Saharan Africa, USA and Europe, using 6 laboratory-based reference technologies. Data was analyzed as categorical (including binary) and numerical (absolute) observations using a bivariate and/or univariate random effects model when appropriate.
Results: At a median reference CD4 of 383cells/µl the mean Pima CD4 bias is -23cells/µl (average bias across all CD4 ranges is 10% for venous and 15% for capillary testing). Sensitivity of the Pima CD4 is 93% (95% confidence interval [CI] 91.4%-94.9%) at 350cells/µl and 96%(CI-95.2%-96.9%) at 500cells/µl, with no significant difference between venous and capillary testing. Sensitivity reduced to 86% (CI-82%-89%) at 100cells/µl (for *Cryptococcal antigen* (CrAg) screening), with significant difference between venous (88%, CI-85%-91%) and capillary (79%, CI-73%-84%) testing. Total CD4 misclassification is 2.3% cases at 100cells/µl, 11.0% at 350cells/µl and 9.5% at 500cells/µl, due to higher false positive rates resulting in more patients identified for treatment. Misclassification increased by 1.2%, 2.8% and 1.8% respectively for capillary testing. There was no difference in misclassification between the full dataset and a population subset of HIV+ ART naïve individuals, nor in misclassification among operator cadres. The Pima CD4 was most similar to Beckman Coulter PanLeuocgated CD4, Becton Dickinson FACSCalibur and FACSCount, and less similar to Partec CyFlow reference technologies.
Conclusions: The Pima CD4 may be recommended using venous-derived specimens for screening (100cells/µl) for reflex CrAg screening; and for HIV ART eligibility at 350cells/µl and 500cells/µl thresholds using both capillary and venous derived specimens. These meta-analysis findings add to the knowledge of acceptance criteria of the Pima CD4 and future POC tests, but implementation will require full costing analysis.

Viral load measurement (including point of care diagnostics)

TUPEB224

Assessment of new technology for the scale up of HIV viral load monitoring in South Africa

S. Carmona[1,2], Z. Mahlumba[3], B. Seiverth[4], E.G. Marins[5], B.R. Cobb[5], C. Simon[4], W. Stevens[1,2]
[1]University of the Witwatersrand, Molecular Medicine and Haematology, Johannesburg, South Africa, [2]National Health Laboratory Service, Johannesburg, South Africa, [3]NHLS, Molecular Medicine and Haematology, Johannesburg, South Africa, [4]Roche Diagnostics International, Rotkreuz, Switzerland, [5]Roche Molecular Systems, Pleasanton, United States
Presenting author email: sergio.carmona@nhls.ac.za

Background: To reduce the global HIV incidence, scale up efforts are required to diagnose and treat patients in order to suppress the virus and reduce transmission, in line with the UNAIDS effort to increase access to viral load monitoring. South Africa has a centralized HIV-1 viral load (VL) testing model that supports scale up initiatives which relies on the laboratory to managed the increasing demand. New tools are required to be able to address this demand, handle reduced input volume without compromising performance and provide comprehensive coverage of diverse HIV-1 variants.
Here, we present data using a new high throughput system designed to detect and quantify HIV-1.
Methods: The **cobas**® HIV-1 test (CE-IVD) performance was evaluated on the fully automated **cobas**® 8800 System (CE-IVD) for method correlation to the COBAS®AmpliPrep/COBAS®TaqMan® HIV-1, version 2.0 (TaqMan® HIV-1 v2) using 168 residual clinical samples from routine testing at NHLS. Subtype inclusivity and two input volumes (200uL & 500uL) were assessed. Reproducibility (> 50 samples) and throughput capability of the system were analysed. The dynamic range and analytical sensitivity were also defined.
Results: The new assay compared well with the TaqMan® HIV-1 v2 (mean titer difference of -0.05 $\log_{10}$ with a 95% CI of -0.11 to -0.01 $\log_{10}$). Accurate quantification of HIV-1 group M subtypes, HIV-1 group N and O isolates in EDTA plasma was demonstrated. Input volume of 200 ul correlated well (R^2 = 0.9) to 500 uL. The new platform released the first 96 tests in 3.5 hours followed by additional 96 results every 30 minutes achieving a total of 960 results in 8 h. The **cobas**® HIV-1 test is reproducible over the dynamic range (20-10,000,000 cp/mL) with an improved sensitivity of 13.2 cp/mL. At a 200 uL sample input volume, the dynamic range was 50-10,000,000 cp/mL.
Conclusions: The new HIV-1 test and system are well suited to support centralized laboratory model for HIV-1 VL monitoring which is key to enable rapid scale up efforts in Sub-Saharan Africa. The availability of two lower sample input volumes optimizes the sample utilization and reduces the blood draws in patients where sample volume is a limiting factor.

TUPEB225

Alere ™q HIV-1/2 POC assay on plasma rather than whole blood, yields adequate viral load results

L. Hans[1,2], N. Ndongwane[2], L. Gonzales[3], S. Carmona[1,2]
[1]University of the Witwatersrand, Department of Molecular Medicine and Haematology, Johannesburg, South Africa, [2]National Health Laboratory Service, Johannesburg, South Africa, [3]Alere Healthcare, Johannesburg, South Africa
Presenting author email: lucia.hans@nhls.ac.za

Background: The need for HIV viral load tests has increased globally in response to the UNAIDS call for universal access to HIV treatment. The centralised HIV viral load testing model in South Africa can result in prolonged turnaround times at remote ARV clinics which may adversely affect patient management. These clinics may benefit from access to onsite viral load tests as well as specialised centres of care where a prompt viral load result may improve adherence. We assessed the performance of Alere ™ q HIV-1/2 assay on plasma rather than whole blood against the local standard; Roche CAP/CTM HIV-1 V.2 assay.

Methods: Freshly spun plasma from routine patient samples was tested on the two assays within 24hrs of arrival in the Johannesburg General Hospital HIV PCR laboratory. The input volume of Alere™ q assay was 25µl as compared to the 1000µl used in the Roche assay (gold standard). Virological failure was regarded as greater than 1000 copies/ml.
Results: Sixty-nine samples ranging from 400 (2.63 log_{10}) to 675670 (5.83 log_{10}) RNA copies/ml were analysed. Fifty- two samples had a viral load >1000 RNA copies/ml. The Alere ™ assay correctly classified 75 % of virological failure. Alere™ q assay missed 13.5% (7/52) of virological failures and over read 11.5 %(6/52). A Bland-Altman assessment for agreement where the range of agreement was defined as mean bias ± 2 SD, showed agreement for values greater the 3.5log_{10} (bias 0.67) which is similarly reflected in linear regression analysis (R^2 = 0.5). According to ROC analysis, 3.995 log_{10} is the correct threshold for classifying virological failure using the Alere ™ assay (75.4%).
Conclusions: Alere ™ q assay correctly identified virological failure in 75% of cases but lacked sensitivity in the 13.5% of the remaining samples. This lower sensitivity of the Alere ™ q assay may be attributed to the low input volume. A simple modification to the cartridge input volume may result in improved sensitivity and should be considered in the next assay version. This evaluation demonstrates progress in POC VL assays and may soon be a viable option for use in remote sites.

TUPEB226

Accuracy of HIV viral load testing with dried plasma spot (DPS) samples for identifying virological failures: primary data from 11 field studies

L. Vojnov[1], C. Zeh[2], M. Prescott[3], C. Boeke[3], T. Peter[4], C. Yang[5],
DPS for VL Diagnostics Investigation Consortium
[1]Clinton Health Access Initiative, Dar es Salaam, Tanzania, United Republic of, [2]US Centers for Disease Control, Kisumu, Kenya, [3]Clinton Health Access Initiative, Boston, United States, [4]Clinton Health Access Initiative, Gaborone, Botswana, [5]US Centers for Disease Control, Atlanta, United States

Background: Routine HIV viral load testing using plasma samples requires cold chain and expedited transport to laboratory testing facilities. Dried plasma spots (DPS), possessing longer stability and no cold chain requirements, may be more practical in field settings.
Methods: We combined primary datasets with paired viral load values of DPS and plasma sample types from standard blood drawn from 1,688 patients from 11 field studies in 15 countries. Sensitivity, specificity, and other diagnostic accuracy parameters were assessed for DPS samples using the Abbott m2000, Biocentric, bioMerieux NucliSens, and Roche Cobas TaqMan technologies at multiple virological failure thresholds compared to the current WHO recommended plasma threshold of 1,000 copies/mL. We used hierarchical logistic regression with a univariate random effects model to account for inter-study heterogeneity.
Results: The mean DPS value (2.63 log copies/mL) was lower than the mean plasma value (2.82 log copies/mL). Overall sensitivity was highest (Se=92.8%; 95% CI: 88.8%, 95.4%) and total misclassification was lowest (5.4%; 3.9%, 7.4%) at the DPS threshold of 1,000 copies/mL when all technologies were analyzed together. The overall specificity at the 1,000 copies/ml threshold was 93.6% (95% CI: 86.8%, 97.0%). At the 1,000 copies/ml threshold, each technology had a sensitivity of approximately 90% or higher. Though the specificities were often highest at the highest threshold tested (10,000 copies/ml), Abbott, bioMerieux, and Roche TaqMan technologies had a specificity of approximately 85% or higher at the 1,000 copies/ml threshold. At 1,000 copies/mL, the overall positive and negative predictive values (PPV and NPV) were high at 94.1% (95% CI: 90.7%, 96.4%) and 92.8% (95% CI: 85.3%, 96.6%), respectively.
Conclusions: The DPS samples performed comparably to paired plasma samples when tested on each of the currently available viral load platforms, particularly at a cutoff of 1,000 copies/ml. Due to the need for a centrifuge on-site to separate the blood into plasma prior to spotting, DPS may not be a feasible sample option in all resource-limited settings; however, facilities with the capacity to separate plasma from whole blood on-site may consider DPS samples as the preferred sample type due to longer stability and strong performance compared to plasma samples.

Drug resistance testing

TUPEB227

Alarming levels of drug resistance in HIV-1-infected patients failing treatment in Cuba

L. Pérez[1], Y. Alemán[1], C. Correa[1], J. Perez[2], C. Fonseca[2], C. Aragonés[2], J. Campos[2], D. Álvarez[2], Y. Schrooten[3], L. Vinken[3], D. Pérez[2], A. Álvarez[1], Y. Soto[1], C. Limia[1], A.-M. Vandamme[3], K. Van Laethem[3], V. Kourí[1]
[1]Tropical Medicine Institute, Virology, La Habana, Cuba, [2]Tropical Medicine Institute, Hospital, La Habana, Cuba, [3]Rega Institute for Medical Research, Department of Microbiology and Immunology, Leuven, Belgium
Presenting author email: jorge.perez@ipk.sld.cu

Background: By the end of 2013, Cuba had 16,479 patients living with HIV-1 of whom 9,662 (58.6%) were receiving antiretroviral therapy (ART). The objectives of this study were to analyze the levels and patterns of drug resistance in HIV-1 patients failing ART.
Methods: Demographic, clinical and laboratory data were collected from 588 ART-experienced HIV-1 patients attending a clinical center in Havana from January 2009 to September 2013. HIV-1 drug resistance genotyping was performed using Sanger sequencing of the pol gene. Drug resistance mutations and levels were determined using Rega version 8.0.2. Full-class resistance was defined as no antiviral drug fully susceptible in a respective drug class. Multidrug resistance was scored if the virus strain was interpreted as susceptible to at most one drug belonging to the 3 commonly available drug classes in Cuba.
Results: The majority of patients were male (76.5%), men who have sex with men (68.5%) with a median age of 40.4 years and 67.2% of the patients were from La Habana province. The median CD4 cell count and viral load at genotyping were 205 cells/mm^3 and 24,713 RNA copies/mL, respectively. The median of ART exposure was 2.9 years and patients were exposed to 1-13 ART regimens. Sequencing revealed the highest drug resistance levels against 3TC/FTC (79.3%), NVP (73.0%) and EFV (72.6%). The most frequent NRTI and NNRTI mutations were M184VI (77.2%), T215YFIDS (43.6%), D67NEG (29.2%), K219QNER (29.4%), M41L (27.5%) and K103N (27.8%), Y181ICV (28.0%), G190AS (22.2%), respectively. The most frequent PI mutations were V82ATI (33.1%), M46IL (18.8%), I54VML (17.8%), L90MV (19.9%). Full-class resistance to NRTI, NNRTI, PI and multidrug resistance were detected in 25.0%, 33.7%, 11.4% and 6.3%, respectively.
Conclusions: Our study reveals a high level of drug resistance in HIV-1 patients failing ART and supports the need for appropriate laboratory monitoring in clinical practice, as infrequent viral load monitoring and limited access to drug resistance testing might have contributed to this high prevalence. Additionally, there is an urgent need for potent drug regimens that can be prescribed upon virological failure.

TUPEB228

Prevalence of primary HIV drug resistance by short reverse transcriptase genotypic resistance assay in Thailand

S. Kiertiburanakul[1], S. Pinsai[1], W. Chantratita[2], E. Pasomsub[2], M. Leechawengwongs[3], N. Siriyakorn[4], S. Sungkanuparph[1]
[1]Faculty of Medicine Ramathibodi Hospital, Department of Medicine, Bangkok, Thailand, [2]Faculty of Medicine Ramathibodi Hospital, Department of Pathology, Bangkok, Thailand, [3]Vichaiyut Hospital, Bangkok, Thailand, [4]Maharat Nakornrachasima Hospital, Department of Medicine, Nakornrachasima, Thailand
Presenting author email: sasisopin.kie@mahidol.ac.th

Background: The emergence and transmission of HIV drug resistance (HIVDR) has raised concern after rapid scaling up of antiretroviral therapy (ART). Currently HIVDR testing prior to ART is not routinely recommended in Thailand due to cost, effectiveness and low reported prevalence.
Methods: A prospective cohort study was conducted in naïve HIV-infected patients. Blood samples were tested for drug resistance (DR) by detection of codon 99-191 on the RT gene. We selected this region to cover 8 major mutations which were K103N, V106A/M, V108I, Q151M, Y181C/I, M184V/I, Y188C/L/H and G190S/A for lowering the cost of testing to approximately 35 USD. The HIVdb program of Stanford HIV database was used to classify the DR mutations. The association between the presence of primary HIVDR and HIV RNA < 50 copies/mL after 6months of ART was determined by logistic regression.
Results: A total of 265 HIV-infected patients were included with median age of 35.2 (range, 16.8-75.2) years and 62.6% males. Risks of HIV infection included heterosexual (63.4%) and homosexual (30.2%). Median [interquartile range (IQR)] CD4 count was 292 (87-466) cells/mm^3 and median HIV RNA (IQR) was 65,700 (17,306-211,256) copies/mL. The overall prevalence of primary HIVDR was 7.9%. The prevalence of each mutation were K103N (6.0%), V106A/M (1.1%), V108I (0.4%), Q151M (0%), Y181C/I (3.4%), M184V/I (4.5%), Y188C/L/H (0%) and G190S/A (2.3%). After 6 months of ART, patients who had primary HIVDR had lower median CD4 cell counts (76 vs. 232 cells/mm^3, p=0.010) and lower proportion of HIV RNA < 50 copies/mL (46.1% vs. 53.8%, p=0.077). By multiple logistic regression, factors associated with HIV RNA < 50 copies/mL after 6 month of ART were having M184V/I [odds ratio (OR) 0.11; 95% con-

fidence interval (CI) 0.02-0.62, p=0.013], condom usage (OR 2.38; 95% CI 1.12-5.06, p=0.024) and adherence (OR 1.16 per 5% increment; 95% CI 1.00-1.35; p=0.044).
Conclusions: Primary HIVDR was approximately 8% detected by a low cost of short RT genotypic resistance assay in naïve HIV-infected Thai patients. Presence of primary HIVDR is associated with HIV RNA >50 copies/mL at 6 months after ART. Routine short RT genotypic resistance assay for detection of primary HIVDR should be considered in Thailand.

TUPEB229

Establishment of an Illumina MiSeq-based HIV drug resistance testing platform

H. Ji[1,2], T. Taylor[1], E. Enns[3], M.-K. Gauthier[1], R. Capina[1], B. Liang[3], G. Van Domselaar[2,3], P. Sandstrom[1,2], J. Brooks[1]
[1]Public Health Agency of Canada, National HIV & Retrovirology Laboratories, Winnipeg, Manitoba, Canada, [2]University of Manitoba, Department of Medical Microbiology, Winnipeg, Canada, [3]Public Health Agency of Canada, National Microbiology Laboratory, Winnipeg, Manitoba, Canada
Presenting author email: hezhao.ji@phac-aspc.gc.ca

Background: Accountable HIV drug resistance(DR) testing represents a key component in effective HIV/AIDS management. We had previously developed a tagged pooled pyrosequencing (TPP)-based HIV DR testing method which offers improved sensitivity, data throughput and cost-efficiency as compared to conventional Sanger sequencing (SS). However, the limited TPP accountability in detecting mutation residing in homopolymeric regions, such as K103N, remains unresolvable due to its intrinsic technical limitation. Here we present a fully validated, Illumina MiSeq-based platform that addresses SS and TPP limitations including homopolymer issue.
Methods: MiSeq-based DR testing starts with HIV RNA extraction followed by two rounds of PCR amplications of the HIV protease and partial RT genes. The derived amplicons are then indexed and sequenced using Illumina MiSeq sequencer. A proprietary web-based HIV DR analysis (HyDRA) pipeline was used for MiSeq data processing and all HIV DRMs were inferred based on Stanford SDRM lists. The accuracy, sensitivity, precision and HIV subtype coverage of this platform was assessed using 6 pedigreed plasmids, 15 EQAPOL controls and a cohort of clinical specimens.
Results: The protocol performs well on all examined HIV-1 subtypes including A1, B, C, D, F2, G, CRF01_AE and CRF-02_AG. The overall error rate was determined as 0.0042 (0.0021 and 0.0050 for homopolymeric and non-homopolymeric areas respectively). The analytical sensitivity varied amongst HIV subtypes in range of 200~500 copies/ml. MiSeq reliably detects minor variants at frequencies as low as 1%. MiSeq consensus sequences with a mixed-base identification threshold at 20% ($MBIT_{20}$) showed high identity with matching SS sequences (99.82% and 99.77% for nucleotide and amino acid respectively). All examined HIV DRMs were consistently detected among all replicates at comparable frequency readouts. All DRMs identifiable by SS were readily and quantitatively detected by MiSeq while low abundance DRMs were detectable only by MiSeq.
Conclusions: MiSeq platform offers considerably enhanced sensitivity, accountability and accessibility of HIV DR monitoring for either patient care or surveillance proposes. It not only deciphers intra-host HIV diversity with high resolution, but also renders fully packaged, customizable HIV DR surveillance data with ease. The MiSeq platform holds the promise of becoming a new standard HIV DR testing in this NGS era.

TUPEB230

Validating the World Health Organization HIV drug resistance early warning indicators

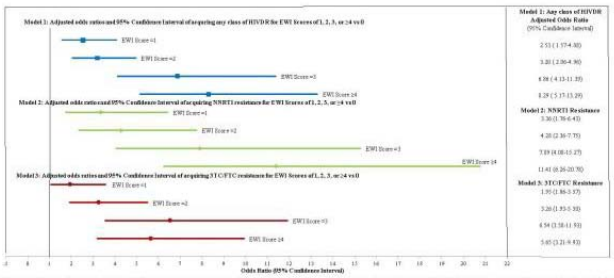
L. Lourenco[1], H. Ma[2], R. Harrigan[1,3], P. Sereda[1], J. Montaner[1,3], V. Lima[1,3]
[1]British Columbia Centre for Excellence in HIV/AIDS, Vancouver, Canada, [2]University of British Columbia, Department of Statistics, Vancouver, Canada, [3]University of British Columbia, Faculty of Medicine, Vancouver, Canada
Presenting author email: llourenco@cfenet.ubc.ca

Background: In 2006, the WHO released the HIV Drug Resistance (HIVDR) Early Warning Indicator (EWI) Monitoring system as a part of the WHO Global Strategy for the Surveillance and Monitoring of HIVDR. EWIs measure ART site factors associated with HIVDR prevention, without the use of HIVDR laboratory testing. However, there is a dearth of published studies validating EWIs. Thus, we validated WHO EWIs (from the April 2010 update) using data from British Columbia, Canada, a high-income setting with universal access to HIV treatment and routine HIV laboratory and resistance.
Methods: Eligible individuals were ART-naïve, ≥19 years old, initiated ART between January 1st, 2000-December 31st, 2012, had ≥15 months of follow-up post-ART initiation, and were without baseline transmitted HIVDR. Individuals were followed for acquired HIVDR until March 31st, 2014, the last contact date, or death. We tested the associations between EWIs and acquired HIVDR. We built multivariable logistic regression models to explore associations between the EWI Score (the number of EWIs an individual failed to meet the targets of) and acquiring: i) any class of HIVDR (either a non-nucleoside reverse-transcriptase inhibitor (NNRTI), 3TC/FTC, any other nucleoside reverse-transcriptase inhibitor (NRTI), or protease inhibitor resistance), ii) NNRTI, and iii) 3TC/FTC resistance, during follow-up. A predictive logistic regression model was built to assess whether the EWI Score predicted acquiring any class of HIVDR (yes/no).
Results: We included 3,082 individuals (82% males, median age: 42 years (25th -75th percentile: 34-49) in our analysis. All explored EWIs, except for EWI1 (ART prescribing practices) were associated with having any class of HIVDR or a NNRTI resistance during follow-up. All EWIs except for EWI1 and EWI2 (patients lost to follow-up 12 months post-ART initiation) were associated with a 3TC/FTC or any other NRTI resistance (Table 1).

	Any class of HIVDR Unadjusted OR (95% CI)	3TC/FTC Unadjusted OR (95% CI)	NNRTI Unadjusted OR (95% CI)	NRTI Unadjusted OR (95% CI)	PI Unadjusted OR (95% CI)
EWI1 Target Met (No vs Yes)	1.11 (0.73-1.69)	0.87 (0.49-1.56)	1.15 (0.69-1.94)	1.14 (0.52-2.52)	2.20 (0.75-6.48)
EWI2 Target Met (No vs Yes)	2.18 (1.62-2.94)	1.14 (0.73-1.76)	2.39 (1.67-3.43)	1.48 (0.81-2.73)	1.73 (0.64-4.67)
EWI3a Target Met (No vs Yes)	2.42 (1.88-3.12)	2.01 (1.46-2.78)	2.29 (1.67-3.15)	2.59 (1.61-4.15)	2.06 (0.90-4.73)
EWI3b Target Met (No vs Yes)	3.01 (2.30-3.94)	3.04 (2.18-4.23)	3.99 (2.90-5.50)	3.46 (2.14-5.61)	0.76 (0.23-2.56)
EWI4b Target Met (No vs Yes)	3.33 (2.60-4.25)	3.37 (2.47-4.59)	3.80 (2.80-5.17)	2.03 (1.27-3.26)	1.72 (0.73-2.56)
EWI7b Target Met (No vs Yes)	3.83 (2.99-4.92)	3.18 (2.32-4.34)	4.33 (3.14-5.96)	2.53 (1.59-4.03)	2.37 (1.06-5.31)
EWI8 Target Met (No vs Yes)	6.73 (5.03-9.00)	6.52 (4.61-9.24)	7.15 (5.07-10.08)	6.70 (4.01-11.17)	5.32 (2.18-12.95)

[Unadjusted odds ratios (OR) relating HIVDR to EWIs]

The adjusted odds ratio for acquiring any class of HIVDR resistance for an EWI Score≥4 (worst score) versus 0 (best score) was 8.29 (95%CI 5.17-13.29);predictive model concordance index=0.848.



Note: Results from three multivariable logistic regression models relating the EWI Score to either: i) any class of HIVDR (either a 3TC/FTC resistance, any other nucleoside reverse-transcriptase inhibitor resistance, non-nucleoside reverse-transcriptase inhibitor resistance (NNRTI), or protease inhibitor resistance), ii) a NNRTI resistance, and iii) a 3TC/FTC resistance. Multivariable models were adjusted for the covariates: age at ART initiation, CD4 cell count at baseline, viral load at baseline, and study follow-up time. EWI Score: the number of EWIs an individual failed to meet the targets of, categorized as 0, 1, 2, 3, and ≥4. This variable includes the following WHO EWIs from the April 2010 Update: EWI 2; EWI 3a; EWI 3b; EWI 4b; EWI 7b; and EWI 8. Follow-up time=first resistance date (of either any HIVDR or NNRTI or 3TC/FTC)–first ARV date.

[Figure 1. Adjusted odds ratios relating the Early Warning Indicator (EWI) Score (categorized as 0, 1, 2, 3, ≥4) with acquired HIV drug resistance (any class of HIVDR or NNRTI or 3TC/FTC resistance)]

Conclusions: Several EWIs were found to be associated with and predictive of HIVDR. Also, failing to meet the target of ≥1 EWI (except for EWI1) was predictive of acquiring any class of HIVDR.

TUPEB231

High prevalence of NNRTI HIV drug resistance in children under 18 months of age recently diagnosed with HIV: results from a national survey in South Africa

S. Carmona[1,2], K. Steegen[1], G. Hunt[3], L. Morris[3,4], I. Sanne[5], W. Stevens[1,2], G. Sherman[6]
[1]University of the Witwatersrand, Molecular Medicine and Haematology, Johannesburg, South Africa, [2]National Health Laboratory Service, Johannesburg, South Africa, [3]National Institute of Communicable Diseases, Centre for HIV and STIs, Johannesburg, South Africa, [4]University of the Witwatersrand, Johannesburg, South Africa, [5]Right to Care, University of the Witwatersrand, Johannesburg, South Africa, [6]University of the Witwatersrand, Department of Paediatrics and Child Care, Johannesburg, South Africa
Presenting author email: sergio.carmona@nhls.ac.za

Background: The number of children infected with HIV in 2013 was 240 000, notably less than previous periods. The decline is attributed to the success of PMTCT programs. With the expansion of maternal and infant prophylaxis regimens, the early vertical transmission rate in South Africa has decreased to ±2% however, HIV-infected infants are at risk of harbouring resistant HIV-1 strains prior to initiation of ART. This study aimed to assess the prevalence of resistance profiles in infants under 18 months of age across South Africa.

Methods: This retrospective cross sectional survey was based on the WHO protocol to assess HIVDR in children < 18 months. Stored remnant DBS for routine HIV early infant diagnosis (EID) were collected from September 2014 to January 2015 from all 9 NHLS EID laboratories in South Africa. *Pol* sequences were obtained using RT-PCR and Sanger sequencing and submitted to Stanford Calibrated Population Resistance tool v6.0 which uses 2009 WHO surveillance drug resistance mutation (SDRM) list. Pol subtyping was performed using Rega HIV subtyping tool v2.0. Statistical analyses were performed using GraphPad Prism 6.
Results: The cohort comprised of 226 cases of which 52,6% were females infants with median age of 74,5 (IQR 45-228) days at the time of diagnosis. Sequence data revealed 98.2% to be subtype C. Drug resistance to NNRTIs was present in 143 of 226 infants (63.3 %, 95% CI 56.8-69.3%) with K103N, Y181C and V106M being the most common mutations (Table 1). NRTI resistance was observed in 11.1% of infants (n=25, 95% CI 7.6-15.9%); most often caused by M184I/V and K65R (Table 1). Only three infants presented with a single PI related mutation.

	#	%	95% CI
No SDRM	81	35,8	29.9-42.3
Any SDRM	145	64,2	57.7-70.1
NRTI SDRM only	1	0,4	0.0-2.7
NNRTI SDRM only	117	51,8	45.3-58.2
PI SDRM only	1	0,4	0.0-2.7
NRTI +NNRTI SDRM	24	10,6	7.2-15.4
PI + NNRTI SDRM	2	0,9	0.0-3.4

[Table 1: Frequency of drug resistance mutation]

Conclusions: The results reported here show frequent prevalence of NNRTI mutations in infants under 18 months of age. The presence of NRTI and PI mutations were less frequent. Due to the high frequency of resistance, an NNRTI-based 1st-line regimen is not recommended for these children. The results are relevant for countries in the region using similar PMTCT regimens but without access to PIs. The availability of PIs for these newly diagnosed infants should be prioritised as is the case in South Africa now.

TUPEB232

Moderate levels of pre-treatment HIV-1 antiretroviral drug resistance observed in a national survey in South Africa

K. Steegen[1], S. Carmona[1,2], M. Bronze[2], M.A. Papathanasopoulos[1], G. Van Zyl[2,3], D. Goedhals[2,4], W. Macleod[5,6], I. Sanne[7], W.S. Stevens[1,2]
[1]University of the Witwatersrand, Department of Molecular Medicine and Haematology, Johannesburg, South Africa, [2]National Health Laboratory Services, Johannesburg, South Africa, [3]Tygerberg and Stellenbosh University, Department of Medical Virology, Stellenbosh, South Africa, [4]University of the Free State, Department of Medical Microbiology and Virology, Bloemfontein, South Africa, [5]Boston University School of Public Health, Center for Global Health and Development, Boston, United States, [6]University of the Witwatersrand, Health Economics and Epidemiology Research Office, Department of Internal Medicine, School of Clinical Medicine, Johannesburg, South Africa, [7]Right to Care, Johannesburg, South Africa
Presenting author email: sergio.carmona@nhls.ac.za

Background: In order to assess the level of transmitted and/or pre-treatment drug resistance WHO recommends regular surveys to be conducted. This study assessed the frequency of HIV-1 antiretroviral drug resistance in patients initiating ART in South Africa.
Methods: A prospective cross-sectional survey was conducted between March 2013 and October 2014, using probability proportional to size sampling. This method ensured that samples, from all 9 South African provinces, were proportionally collected, based on the number of patients receiving ART in each region. Samples were collected from 45 health care facilities in 34 districts. *Pol* sequences were obtained using RT-PCR and Sanger sequencing and submitted to Stanford Calibrated Population Resistance tool v6.0 which uses 2009 WHO surveillance drug resistance mutation (SDRM) list. *Pol* subtyping was performed using Rega HIV-subtyping tool v2.0. Statistical analyses were performed using GraphPad Prism 6.
Results: A total of 277 sequences were available for analysis and 98.2% were found to be subtype C. Most volunteers were female (58.8%) and the median age was 34 years (IQR: 29-42). The median baseline CD4-count was 149 cells/mm^3 (IQR:62-249) and, based on self-reporting, volunteers had been diagnosed to be HIV-positive for a median of 44 days prior to sample collection (IQR: 23-179). Overall, 25 out of 277 patients presented with ≥1 SDRM (9.0%, 95% CI: 6.1-13.0%). NNRTI mutations were most often detected (n=23). Only two patients presented with a PI mutation. In four patients ≥4 SDRMs were detected, which might indicate they were not truly ART naïve, yet they presented at the clinic for ART initiation. Provided all patients would be initiated on TDF-3TC-EFV/NVP, as per national guidelines, 17 patients (6.1%) would receive a dual NRTI regimen; one patient (0.4%) would receive TDF mono-therapy and for five patients (1.8%) none of the antiretrovirals would have full activity.
Conclusions: These results show that the level of antiretroviral drug resistance in ART-naïve South Africans has reached the upper margin of moderate levels as per WHO classification. Therefore, regular assessment of pre-treatment drug resistance levels in all regions of South Africa are highly recommended to monitor changing levels of pre-treatment drug resistance.

TUPEB233

Prevalence of HIV-1 cross-resistance against dolutegravir and elvitegravir in raltegravir-experienced patients in Germany over the past five years

F. Wiesmann[1], T. Goodarzi[2], P. Braun[2], H. Knechten[2]
[1]PZB Aachen, HIV and Hepatitis Research, Aachen, Germany, [2]PZB Aachen, Aachen, Germany
Presenting author email: pab@pzb.de

Background: This evaluation focussed on the prevalence of cross-resistance against RAL, EVG and/or DTG in RAL-experienced patients with detectable HIV viremia between 2009 and 2014.
Methods: 202 RAL-experienced patients from Germany (76% with subtype B) were tested for resistance mutations in HIV-1 integrase between 2009 and 2014 (33 pts. in 2009-2010 / 49 pts. in 2011-2012 / 120 pts. in 2014). Data of mutations within the integrase, reverse transcriptase and protease were analyzed in relation to prescribed therapy regimens. Resistance interpretation results were assessed by using the HIV-Grade, ANRS, Rega and Stanford interpretation algorithms and results were compared concerning the degree of concordance.
Results: The rate of patients tested positive for integrase inhibitor resistance decreased from 2009 to 2014 from 45% - 51% between 2009 and 2012 to 19.2% in 2014. N155H, Q148H/R and T97A were the most frequent mutations. Q148H/R was less frequently detected in 2014 (13.0%) as compared to 2009-2010 (26.6%) and 2011-2012 (20.0%) while the prevalence of N155H increased over the time from 16.7% (2009), 22.2% (2010), 33.6% (2011), 56.2% (2012) to 47.8% in 2014. There was a high degree of concordance between the interpretation systems concerning EVG and RAL cross-resistance. However, prediction of DTG resistance showed a higher discrepancy. HIV-Grade predicted 67%/88%/65% to show at least intermediate resistance 2009-2010, 2011-2012 and 2014. ANRS predicted resistance in 33%/20%/13% of cases and the Stanford interpretation system predicted 53%/76%/52% and REGA predicted 33%/24%/9% to be at least partly resistant.
Conclusions: Integrase resistance analysis is now part of the routine testing. This has changed since the approval of raltegravir where resistance analysis was performed late in the process of viral breakthrough due to difficult reimbursement procedures. This might explain the decrease of total detected resistance mutations over the years. It also might explain an increase of observed early N155H substitutions as compared to the Q148H mutation, which represents a later event in resistance pathways. There is a high concordance between the interpretation systems in EVG and RAL cross-resistance prediction. However, there is a higher discordance in predicting DTG resistance, which might make it difficult to decide about the use of DTG in ongoing therapies.

TUPEB234

High frequency of genotypic resistance in HIV-1-infected patients on highly active antiretroviral therapy with persistent low viremia

D. Pellegrino[1], J. Souza Cavalcanti[2], J.L. Ferreira[2], L.F. Brígido Macedo[3]
[1]Medical School of the University of São Paulo, Infectious Diseases Division, São Paulo, Brazil, [2]Institute Adolfo Lutz, São Paulo, Brazil, [3]Institute Adolfo Lutz, Virology, São Paulo, Brazil
Presenting author email: lubrigido@gmail.com

Background: Resistance is a major cause of virologic failure in HIV-1 infected patients; genotypic analyses optimize salvage therapy but technical constraints limit testing in plasma viral load (pVL) below 1000 copies/ml. Nevertheless a great amount of patients are failing therapy with a persistent low-level viremia, and in this context it is possible to obtain genotypic information although slight modifications are required during genotype standard procedures. The aim o this study was to assess genotypic resistance in HIV-1 infected patients with persistent low level viremia and virologic response after switching to genotype-guided salvage therapy.
Methods: Cohort prospective study in which eligible HIV infected patients were at least 18 years old, provided informed consent, were on HAART for at least 12 months with two consecutive pVL between 50 - 999 copies/ml after achieving and maintaining viral suppression (two pVL < 50 copies/ml). Modifications in genotype standard procedures included a larger volume of starting plasma, concentrating the sample by centrifugation and higher viral RNA input. Resistance was defined as the detection of any NRTI, NNRTI or PI major resistance mutations. Virologic response was assessed 8 weeks after salvage therapy.
Results: Hundred patients, 53% male, median age 49, median CD4 508 cells/mm^3, median pVL 240 copies/ml, average number of previous regimens 5, 87% with successful genotype. Resistance mutations were detected in 63 patients (72,4%) 61% were receiving a PI-based regimem. All patients had NRTI mutations, 20% had NNRTI mutations and 45% had PI mutations, most common mutations were M41L, D67N, M184V, K103N, M46I, I47V, I54V and L90M. Of these 63 patients 61 started a genotype-guided salvage regimen and presented a pVL< 50 copies/ml after 8 weeks of follow up. For seven patients there was previous genotypic information highlighting the selection and accumulation of resistance mutation during persistent low-level viremia.

Conclusions: In this group of heavily pretreated patients with persistent low viremia, a high frequency of genotypic resistance was observed; obtaining genotypic information may prevent further accumulation of resistance mutation and preserve future therapeutic options.

Diagnostics of co-infections (including syphilis, TB, Cryptococcus, hepatitis B, C and other)

TUPEB235

Global performance of GeneXpert (Xpert MTB/RIF, Cepheid) using standardized verification and external quality assessment material

L. Scott[1], V. Magida[2], A. David[2], V. Deyde[3], A. Adelekan[3], C. Gilpin[4], R. Coombs[5], W. Stevens[1,2], Xpert MTB/RIF EQA consortium
[1]University of the Witwatersrand, Molecular Medicine and Haematology, Johannesburg, South Africa, [2]National Priority Program, NHLS, Johannesburg, South Africa, [3]CDC, Pretoria, South Africa, [4]Global TB Programme, World Health Organization, Geneva, Switzerland, [5]AIDS Clinical Trial Group, University of Washington, Seattle, United States
Presenting author email: lescott.ac@gmail.com

Background: The dried MTB culture spot (DCS) proficiency testing matrix has been endorsed by the WHO to verify GeneXpert instruments (Cepheid, Sunnyvale,CA) upon initial installation or relocation, module replacement and cartridge calibration when performing the Xpert MTB/RIF assay. A DCS external quality assessment (EQA) program is available and has been expanded worldwide to 295 testing sites. We report the performance of this globally distributed matrix on Xpert MTB/RIF.
Methods: DCS material used for verification consisted of inactivated *Mycobacterium tuberculosis* (*M.tb*) susceptible to Rifampicin (RIF). DCS for EQA consisted of 3 panels/year comprising 4 DCS of *M.tb* with RIF susceptible, RIF resistant and non-TB mycobacteria. Submission and reporting of results is managed through an in-house software program *www.tbgxmonitor.com*.
Results: Global participants (>1site) in the DCS quality program (verification and EQA) include: South Africa's National Health Laboratory Service (207 sites), AIDS Clinical Trial Group (13 countries world-wide), Ghana National Tuberculosis Program, Walter Reed Army Institute of Research (4 countries), Namibia Institute of Pathology and Swaziland Health Laboratory Services. Sites using DCS verification material have increased rapidly from 66 (2011), 92 (2012), 143 (2013) and26 (2014). By the end of 2014, 4,317 verification DCS were performed globally with 97.4% of the modules functioning correctly. EQA uptake increased from 17 participants in 2012 to 295 in 2014 i.e. currently 392 devices in 18 countries (throughout Africa, Asia, Europe and the Caribbean). Timely submission of EQA panel results fluctuated from 68-100%, with incorrect results accounting for **1.2%** and **0.6%** for device error (including invalid tests)**.** Verification and EQA reports provided detailed analyses of results as well as possible reasons for observed failures and guidance for corrective action.
Conclusions: The DCS quality program highlights the successful, rapid implementation of quality assured Xpert MTB/RIF testing globally. The standardization of testing material and minimal variation of testing sites illustrates stability and robustness of instruments. High quality assay performance over time as well as consistency among sites and users was demonstrated.

TUPEB236

Routine eye screening by an ophthalmologist is clinically useful for HIV-1-infected patients with CD4 count less than 200 /μL

T. Nishijima[1], S. Yashiro[2], K. Teruya[1], Y. Kikuchi[1], N. Katai[2], H. Gatanaga[1,3], S. Oka[1,3]
[1]National Center for Global Health and Medicine, AIDS Clinical Center, Tokyo, Japan, [2]National Center for Global Health and Medicine, Department of Ophthalmology, Tokyo, Japan, [3]Kumamoto University, Center for AIDS Research, Kumamoto, Japan

Background: The revised 2013 American CDC guidelines for opportunistic infections did not state recommendations for routine eye screening by ophthalmologists for patients with HIV-1 infection.
This study aims to investigate clinical usefulness of routine ophthalmologic screening for HIV-1-infected patients.
Methods: We conducted a single-center observational study in Tokyo. HIV-1-infected patients with age over 17 who visited our clinic for the first time between January 2004 and December 2013 and underwent full ophthalmologic examination within one year from the first visit were enrolled. Patients who were already diagnosed of ophthalmologic diseases at the time of referral to our clinic were excluded. At our clinic, ophthalmologic examination, including dilated retinal examination by indirect ophthalmoscopy was routinely conducted by ophthalmologists on the first visit. The prevalence of ophthalmologic diseases and associated factors including the existence of ocular symptoms were analyzed. Diagnosis of CMV retinitis (CMV-R) was based on "confirmed CMV retinitis" of the ACTG criteria.
Results: The 1,515 study patients were mostly Asian men who have sex with men, with the median CD4 count and HIV-1 load of 210 /μL (IQR 66-353 /μL) and 4.76 $\log_{10}$copies/mL (IQR 4.04-5.28 $\log_{10}$copies/mL), respectively. 87% were treatment-naïve for HIV-1 infection. CMV-R was diagnosed in 24 (2%) patients, HIV retinopathy (HIV-R) in 127 (8%), cataract in 31 (2%), ocular syphilis in 4 (0.3%), uveitis with unknown cause in 8 (0.5%). Other ocular diseases were diagnosed in 14 patients. All CMV-R cases and 87% of HIV-R were with CD4 count < 200 / μL. The prevalence of any ocular diseases, CMV-R, and HIV-R in patients with CD4 < 200 / μL were 22%, 3%, and 15%, respectively, whereas for those with CD4 ≥200 /μL, they were 5%, 0%, and 2%.

	All patients n=1515	CD4 <50/uL n=308	CD4 <100/uL n=490	CD4 <200/uL n=731	CD4 >200/uL n=784
Any ocular diseases	201 (14)	81 (26)	130 (27)	162 (22)	42 (5)
Any ocular diseases without ocular symptoms	161	68	108	132	14
CMV retinitis	24 (2)	14 (5)	20 (4)	24 (3)	0
CMV retinitis without ocular symptom	16	10	12	16	0
HIV retinopathy	127 (8)	62 (20)	97 (20)	111 (15)	16 (2)
HIV retinopathy without ocular symptoms	114	54	86	100	14

[Prevalence of Ocular Diseases According to CD4]

No ocular symptoms were reported by 71% of CMV-R cases and 82% of patients with any ocular diseases.
Conclusions: Routine ophthalmologic screening is recommended for HIV-1-infected patients with CD4 < 200 /μL in resource-rich settings based on the high prevalence of ocular diseases within this CD4 count category and most patients with ocular diseases, including those with CMV-R, were free of ocular symptoms.

TUPEB237

Association between transient elastography (TE) scores and AST to platelet ratio index (APRI) among HIV/HCV co-infected patients

M. Harris[1,2,3], M. Hull[3,4], A. Moghadam[1], G. Larsen[1], W. Zhang[4], B. Ganase[1], T. Kozai[1], B. Yip[4], R. Hogg[3,4,5], J. Montaner[3,4]
[1]St. Paul's Hospital/University of British Columbia, HIV/AIDS Research Program, Vancouver, Canada, [2]University of British Columbia, Department of Family Practice, Vancouver, Canada, [3]University of British Columbia, Department of Medicine, Division of AIDS, Vancouver, Canada, [4]British Columbia Centre for Excellence in HIV/AIDS, Vancouver, Canada, [5]Simon Fraser University, Faculty of Health Sciences, Burnaby, Canada
Presenting author email: mharris@cfenet.ubc.ca

Background: Evaluation of hepatic fibrosis stage is critical in the management of HIV/HCV co-infected patients, and can be done non-invasively using TE or serum biomarkers. TE is the most accurate non-invasive method for distinguishing cirrhosis (F4) from non-cirrhosis (F0/1/2/3), but APRI is more widely available.
We examined agreement between APRI and TE scores in an HIV/HCV co-infected outpatient clinic population.
Methods: Fibrosis was assessed using TE following a 2-hour fast in sequential HIV/HCV co-infected individuals between October 2013 and December 2014. TE scores were interpreted as: < 7.6 kPa, F0/1; 7.6-8.9 kPa, F2; 9.0-12.3 kPa, F3; >12.3 kPa, F4. APRI was calculated using AST and platelet counts from blood drawn ≤90 days of TE. APRI >1.5 and >1.0 were evaluated as potential indicators of significant fibrosis (≥F2) or cirrhosis (F4). McNemar's test and sensitivity/specificity calculations were conducted to measure the agreement between the two methods.
Results: HIV/HCV co-infected individuals (n=101, 89% male, median age 51 years) underwent both TE and APRI. The median durations of HIV and HCV infections were 14 and 10 years, respectively. Median current and nadir CD4 counts were 540 and 130 cells/ mm^3, respectively; 98% received ART at time of TE, and 85% had plasma HIV RNA< 40 copies/mL. By TE, fibrosis scores were F0/F1 in 55%, F2 in 10%, F3 in 12%, and F4 in 23%. APRI >1.5 was seen in only 11% overall, and in 35% of those with F4 on TE; 23% overall and 65% of F4 on TE had APRI >1.0. The proportion of patients having "high" APRI (>1.5) is different from the proportions with either ≥F2 or F4 on TE (p< 0.001 and 0.005, respectively). For the APRI cutoff of 1.0, the proportion having "high" APRI is different from the proportion with ≥F2 on TE (p< 0.001); however, the proportion having "high" APRI is not significantly different from the proportion with F4 on TE (p=0.999). APRI >1.0 predicted F4 on TE with a sensitivity of 65% and a specificity of 90% (see Table 1).

APRI	TE Score F0/1/2/3	TE Score F4	Total N
"normal", ≤1.0	70	8	78
"high", >1.0	8	15	23
Total N	78	23	101

[Table 1]

Conclusions: Where TE is not available, an APRI of >1.0 could be considered suggestive of cirrhosis in HIV/HCV co-infected patients.

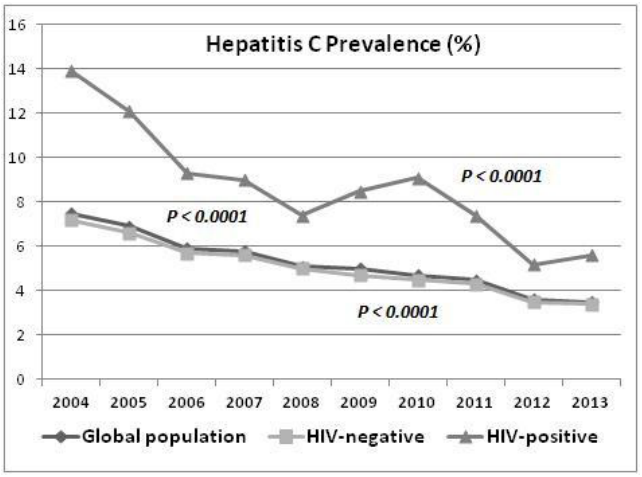
Hepatitis C

TUPEB238

Decreasing prevalence of HCV-HIV co-infection (2004-2013) in Madrid, Spain

A. Díaz-De Santiago[1], S. Serrano[1], B. Sastre[1], C. Gómez-Ayerbe[1], S. Bañón-Escandell[1], E. Loza[2], C. Quereda[1], A. Moreno[1], J.L. Casado[1], M.J. Pérez Elíaz[1], S. Moreno[1]
[1]Ramon y Cajal University Hospital, Infectious Diseases, Madrid, Spain, [2]Ramon y Cajal University Hospital, Microbiology, Madrid, Spain
Presenting author email: ddsalbertorubio@hotmail.com

Background: Since HIV and HCV share common routes of transmission, HIV/HCV coinfection has traditionally been frequent. Nevertheless, whereas HIV can be highly contagious by sexual contact, the efficiency of HCV by this route is low. While HCV infection seems to be expanding among HIV-infected men who have sex with men (MSM), the rate of coinfection in intravenous drug users (IDU) is assumed to remain constant. We evaluated the serial prevalence of HIV/HCV coinfection across all risk groups for HIV infection at our Healthcare Area in Madrid (Spain).
Methods: We examined the serial prevalence of HCV infection in HIV-infected/uninfected subjects using data from the Microbiology Department registry of our tertiary hospital (HCV antibodies samples sent between 2004 and 2013). Risk factors for HIV/HCV coinfection were analyzed in 676 newly HIV-positive diagnosed subjects at our centre during the study period by logistic regression analysis. We further examined tendencies in anti-HCV treatment use and community HCV RNA.
Results: The prevalence of HIV/HCV coinfection at our Healthcare Area decreased from 13.04% (95%CI, 11.54-15.65) in 2004-05 to 5.39% (95%CI, 4.51-6.38) in 2012-13, $P < 0.0001$. The prevalence of HCV infection among HIV-negative subjects decreased from 6.90% (95%CI, 6.63-7.17) in 2004-05 to 3.47% (95%CI, 3.29-3.64) in 2012-13, $P < 0.0001$. Among HIV-infected subjects the trend from 2004 to 2013 among each risk group was: IDU, 85.72% to 100%, $P = 0.67$; MSM, 5.45% to 5.26%, $P = 0.45$; heterosexual, 8.91% to 4.17%, $P = 0.47$. Strongest associated factors for HIV/HCV coinfection were IDU (OR, 75.7; 95%CI, 33-172), birth decade 1971-80 (OR, 0.18, 95%CI, 0.07-0.44), birth decade >1980 (OR, 0.07, 95%CI, 0.01-0.39), and high educational level (OR, 0.66, 95%CI, 0.46-0.95). During the same period no association was observed between HCV prevalence and the use of treatment for HCV or community HCV RNA load.



[HCV prevalence 2004-2013]

Conclusions: The prevalence of HIV/HCV coinfection decreased in Madrid between 2004 and 2013. This decline was not consistently observed across any risk group and is likely to be explained by a declining burden of HCV in the general population.

TUPEB239

No difference in safety profiles comparing 12- and 24-week HCV treatment durations in HCV genotype 1 and HIV-1 co-infected patients: results from TURQUOISE-I

J.J. Eron[1], J. Slim[2], R. Elion[3], R. D'Amico[4], R. Trinh[4], Y.B. Hu[4], M. Co[4], D. Wyles[5]
[1]University of North Carolina, Chapel Hill, United States, [2]St. Michael's Medical Center, Newark, United States, [3]Whitman-Walker Health, Washington DC, United States, [4]AbbVie Inc., Chicago, United States, [5]University of California San Diego, San Diego, United States
Presenting author email: jeron@med.unc.edu

Background: The 3 direct-acting antiviral (3D) regimen of ombitasvir (OBV), paritaprevir (identified by AbbVie and Enanta; co-dosed with ritonavir; PTV/r), and dasabuvir (DSV) with ribavirin (RBV) is approved to treat HCV infection in patients with HIV-1 co-infection. In the TURQUOISE-I trial, response rates were 91 and 94% in this population when treated for 24 or 12 weeks, respectively. We report the safety profiles of the two treatment durations.
Methods: Patients were randomized to receive OBV/PTV/r + DSV + RBV for 12 (N=31) or 24 weeks (N=32). Eligible patients in this open-label study were treatment-naïve or pegIFN/RBV-experienced patients, with or without cirrhosis, who had CD4+ count ≥200 cells/mm^3 or CD4+ % ≥14%, and plasma HIV-1 RNA suppressed while receiving a stable atazanavir- or raltegravir-inclusive antiretroviral (ART) regimen. Treatment-emergent adverse events (AEs) from the time of study drug administration until 30 days after last dose for all patients who received ≥1 dose of study drug are reported.
Results: The percentage of patients experiencing any AE, severe, or serious AEs were similar in both arms. The majority of AEs were mild or moderate, and no serious AE or discontinuation due to an AE was reported. The most common AEs in the 12- and 24-week arms respectively, were fatigue (58 vs 38%), insomnia (16 vs 22%), and nausea (16 vs 19%). Seven patients experienced an anemia-related AE, all deemed RBV-related, though no patient interrupted study drugs. Among patients receiving atazanavir or raltegravir-inclusive ART, 53% and 6% experienced grade 3+ total bilirubin elevations, respectively. Median declines in CD4+ T-cell counts of 47 and 62 cells/mm^3 were observed at the end of 12 and 24 weeks of treatment, respectively, and returned to above baseline levels by post-treatment week 4. Mean CD4+ percentages remained stable throughout the study. No patient had a confirmed HIV-1 breakthrough ≥200 copies/mL during treatment or experienced an AIDS-related opportunistic infection.
Conclusions: In GT1 HCV/HIV-1 co-infected patients, treatment duration did not appear to influence the rate or severity of AEs or laboratory abnormalities and no patient discontinued HCV treatment due to AE. HIV-1 suppression remained stable throughout the course of HCV treatment.

	12-Week OBV/PTV/r + DSV + RBV (N=31)	24-Week OBV/PTV/r + DSV + RBV (N=32)
Any AE	28 (90)	28 (88)
Severe AE	1 (3)	1 (3)
Serious AE	0	0
AE leading to study drug discontinuation	0	0
AE leading to RBV dose modification	5 (16)	6 (19)
AIDS-associated opportunistic infection	0	0
Laboratory abnormalities		
Hemoglobin <10 g/dL	4 (13)	3 (9)
Hemoglobin <8 g/dL	0	0
Total bilirubin >3 x ULN	11 (35)	6 (19)
ALT >5 x ULN	0	0

[Treatment-Emergent Adverse Events (AEs), n (%)]

TUPEB240

Low incidence of reinfection with hepatitis C virus after successful treatment in Montreal

N. Machouf, B. Trottier, C. Galanakis, E. Huchet, M. Poliquin, S. Vézina, S. Lavoie, D. Longpré, D. Legault, R. Thomas
Clinique Médicale L'Actuel, Montreal, Canada

Background: The incidence rate of HCV infection is estimated at 26/100 py among Montreal IDU. Though HCV reinfection has been reported in IDU and MSM patients, the extent to which it occurs is unknown. Given the high treatment costs, HCV reinfection in cured patients may limit future access to treatment. We therefore aimed to evaluate the incidence of reinfection in a clinical cohort of HCV treated patients.
Methods: HCV patients with a sustained virological response (SVR) were included. Censoring date was the date of HCV reinfection or the date of the last negative HCV RNA test. Reinfection was defined as detectable HCV RNA. The rate of reinfection was calculated using the number of person-years of observation after the end of treatment (EoT). Time from SVR to reinfection was estimated using Kaplan-Meier analyses.

Results: 338 patients were included. The sample was 77% male; mean age was 46 years; and the main risk factor for HCV infection was IDU (n=275, 82%). Patients were followed for a median of 2.7 years after EoT (IQR=1.7-4.8), for a total of 1175 person-years. 316 (94%) patients remained HCV-negative, while 22 (6%) became reinfected during follow-up with an overall reinfection rate of 1.7/100py [95% CI 1.07-2.58]. Median time to reinfection was 14.7 years (95%CI 13.6-15.7). Cumulative incidence of seroconversion within 2 years of SVR was 4% (9/210) and 11% (10/88) within 5 years. When controlling for drug use, the incidence rate of HCV reinfection was 0.43/100py [95% CI 0.02-0.11] for non-IDU; 1.90/100py [95% CI 1.13-3.14] for past IDU and 3.60/100py [95% CI 1.44-7.39] for present IDU.
Conclusions: HCV reinfection after successful treatment in our cohort is low. Although the rate of HCV reinfection is higher in IDU than non-IDU, it is much lower than the overall incidence rate of the first HCV infection among IDU in Montreal.

TUPEB241

Fibrosis regression is possible after a successful treatment of hepatitis C even with cirrhosis

B. Trottier, E. Huchet, M. Poliquin, M.-M. Bellon, S. Vézina, C. Galanakis, D. Longpré, S. Lavoie, R. Thomas, N. Machouf
Clinique Médicale L'Actuel, Montreal, Canada
Presenting author email: benoit.trottier@lacutel.ca

Background: Liver fibrosis was considered a long-term, irreversible damage. Despite the scaling up of HCV treatment and evidence of an HCV cure, there have been few encouraging results showing fibrosis regression. The aim of this study was to determine the factors associated with fibrosis regression.
Methods: Patients treated for HCV from a single-site clinical cohort with pre-treatment METAVIR score ≥ F2 and available post-treatment measures, were included. Liver fibrosis staging was assessed using elastometry (fibroscan) or biopsy. Clinical and laboratory data were routinely collected. Fibrosis regression and progression were defined as reduction and augmentation of ≥ 1 METAVIR score during follow-up. The determinants of fibrosis regression were analysed by multiple logistic regression using SPSS17.0.1©.
Results: A total of 92 patients were included with baseline METAVIR scores of F2 (26%), F3 (19%), F4 (55%). 21 (23%) patients were HIV co-infected, 12 (13%) were diabetics. 71 (77%) were infected with HCV-geno1,4, 18 (20%) with HCV-geno2,3 and 3% had multiple genotypes. 32 patients (35%) were treated with DAA and 59 (65%) with peginterferon/ribavirin. Overall, 56 (61%) had a sustained virological response (SVR) to treatment, while 36 (39%) were non-responders/relapsers. Overall, fibrosis regression was observed in 45 (49%) patients, which was greater when SVR was achieved (68% vs. 19% in non-SVR; p< 0.001). In SVR patients, fibrosis regression occurred regardless of baseline METAVIR score: 67% in patients with METAVIR=F2, 83% in F3 and 66% in F4 (p=0.219). Based on logistic regression analyses, controlling for age, sex, alcohol consumption, HCV genotype, baseline METAVIR score, diabetes and HIV co-infection, the only determinants of fibrosis regression were successful treatment, and no prior diabetes diagnosis. Compared to non-responders/relapsers, fibrosis regression was greater after SVR [OR=11.6 (3.7-36.7); p< 0.001]; and diabetes seems to preclude fibrosis regression [OR=0.1 (0.1-0.8); p=0.033]. Regression was equally observed in HCV mono-infected and HIV-HCV co-infected patients [OR=2.3 (0.7-7.8); p=0.177], and in those with or without cirrhosis at baseline [OR=0.5 (0.2-1.5); p=0.218].
Conclusions: Fibrosis regression was observed in 61% of patients after SVR was achieved. Regression was even observed in cirrhotic patients. Diabetes seems to preclude fibrosis regression. Fibrosis regression was equally observed in HCV mono and HIV-HCV co-infected patients.

TUPEB242

HCV continuum of care among sex workers living with and affected by HIV, 2010-2013: need for increased access to HCV services alongside HIV prevention efforts

M.E. Socías[1,2], K. Shannon[1,3], J. Montaner[1,3], S. Guillemi[1], S. Dobrer[1], P. Nguyen[1], S. Goldenberg[1], K. Deering[1,3]
[1]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada, [2]University of British Columbia, Interdisciplinary Studies Graduate Program, Vancouver, Canada, [3]University of British Columbia, Department of Medicine, Vancouver, Canada
Presenting author email: esocias@cfenet.ubc.ca

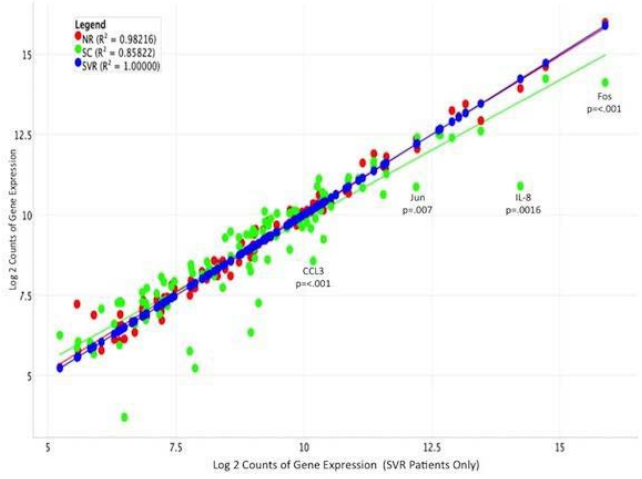
Background: HCV cure leads to reduced morbidity and mortality, and decreased HCV transmission. Therefore, there is growing enthusiasm about HCV Treatment as Prevention. However, this needs to be tempered by the potential for HCV reinfection. Despite increased vulnerability to HCV through dual sex/drug use routes, research on access to HCV testing and care among female sex workers (FSWs) remains negligible.
Methods: Baseline data were drawn from an ongoing prospective cohort of 723 FSWs recruited across Vancouver ("An Evaluation of Sex Workers' Health Access") between 01/2010-08/2013. We assessed the prevalence of HCV and self-reported engagement in the HCV continuum of care. Bivariate and multivariable logistic regression analyses were used to evaluate correlates of recent HCV testing (ie, in the last year).
Results: Among 705 FSWs with valid laboratory tests, 302 (42.8%) tested HCV+ at baseline, of whom 23.2% were co-infected with HIV. Among HCV+ participants, 77.5% were aware of their infection, 45.7% reported having accessed HCV-related care, 15.9% being offered treatment, and only 1.0% receiving treatment. Among FSWs who self-reported being HCV-seronegative within one year of enrolment, only 52.9% reported being recently tested. In multivariable analysis, FSWs who reported recent HCV testing were more likely to identify as a sexual/gender minority (AOR=1.89, 95%CI 1.11-3.24), and currently use injection (AOR=2.00, 95%CI 1.19-3.34) or non-injection drugs (AOR=1.95, 95%CI 1.00-3.78). Immigrants to Canada (AOR=0.24, 95%CI 0.12-0.48) and women living outside the Downtown Eastside (Vancouver's primary drug scene, AOR=0.31, 95%CI 0.18-0.56) or homeless (AOR=0.32, 95%CI 0.15-0.72) had reduced odds of having a recent HCV test.
Conclusions: Our results show that despite high HCV prevalence, hardly any of FSWs with HCV accessed treatment. Further, almost half of self-reported HCV-seronegative FSWs did not receive a recent test. These findings likely reflect a combination of structural and individual barriers to healthcare. In a setting with universal access to healthcare and increasing availability of safer and more efficacious HCV drugs, these findings highlight the need for comprehensive interventions to facilitate and sustain access to HCV testing and care, including harm reduction and addiction management, among FSWs. This will be critical to the success of an HCV Treatment as Prevention strategy.

TUPEB243

Pro-inflammatory gene expression remains altered after successful HCV treatment

P. Waldron[1,2], M. Holodniy[1,2]
[1]Stanford University School of Medicine, Division of Infectious Diseases and Geographic Medicine, Stanford, United States, [2]Palo Alto Veteran's Affairs Health Care System, Office of Public Health Surveillance and Research, Palo Alto, United States
Presenting author email: pwaldron@stanford.edu

Background: Inflammatory gene expression in peripheral blood mononuclear cells (PBMC) is altered in chronic Hepatitis C virus (HCV) infection. However duration of these changes after pegylated-Interferon (peg-IFN) based HCV treatment is unclear. We investigated PBMC gene expression in treated patients to determine if differences persisted despite successful treatment.
Methods: PBMC Gene expression of 184 genes involved in inflammatory response pathways were assayed using the nCounter GX Human Inflammation Kit (Nanostring). HCV or HCV/HIV infected patients were categorized as treatment non-responders (NR, n=17), sustained virologic responders (SVR, n=22) and spontaneous clearers HCV (SC, n=23). Patients in NR and SVR groups had received peg-IFN -based regimens in the preceding 5 years. Pair-wise analyses were performed to assess differences.
Results: There were no differences in race or gender between groups. Mean time from last treatment was 2.6 and 3 years in SVR, NR respectively (p=.47). SC mean age was 5 years younger than SVR or NR (p=.02). Of 184 genes assessed, 120 had expression levels above background (mean counts greater than 50). Using a significance threshold of p < .01, mRNA counts were significantly different for 63 genes comparing SVR v SC patients, 54 genes comparing NR v SC, and 12 genes comparing SVR to NR. Differential expression of 45 genes was significantly different in both SVR and NR groups when compared to SC. Of note, *IL-8* gene expression was 10 and 8-fold higher in SVR and NR v SC (p=.0016, p=0.02), respectively.*CCL3* gene expression was similarly upregulated (3-fold higher in both SVR and NR v SC, p < .001 for both) as were AP-1 components *Fos* (3.5 fold higher in both SVR and NR v SC, p < .001 for both) and *Jun (*2.5 fold higher in both SVR and NR vs SC, p=.007 and .003 respectively) [Fig 1].



[Figure 1: Comparative PBMC gene expression]

Conclusions: PBMC gene expression profiles from SVR patients were more similar to infected NR patients than SC patients, with transcriptional upregulation of cytokine/chemokine genes such as *CCL3* and *IL8* and pro-inflammatory transcription factors such as *Fos* and *Jun*. This suggests an inflammatory state persists in SVR patients despite successful peg-IFN-based treatment and plasma viral clearance.

TUPEB244

Genetic variation in *IL-6* and *HLA-DBQ1* genes are associated with spontaneous clearance of hepatitis C virus infection

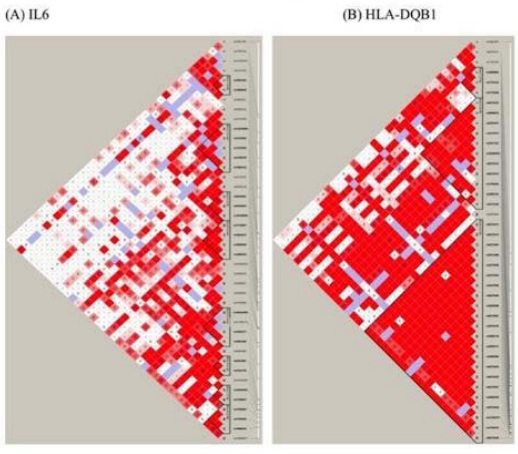
P. Waldron[1,2], I. Belitskaya-Levy[3], A. Chary[1,2], L.C. Lazzeroni[3,4], A. Monto[5,6], J. Ryan[5,6], M. Holodniy[1,2]
[1]*Stanford University School of Medicine, Division of Infectious Diseases and Geographic Medicine, Stanford, United States,* [2]*Palo Alto Veteran's Affairs Health Care System, Office of Public Health Surveillance and Research, Palo Alto, United States,* [3]*VA Palo Alto Health Care System, Cooperative Studies Program Coordinating Center, Palo Alto, United States,* [4]*Stanford University, Department of Psychiatry, Stanford, United States,* [5]*San Francisco VA Medical Center, San Francisco, United States,* [6]*University of California, San Francisco, United States*
Presenting author email: pwaldron@stanford.edu

Background: Worldwide, approximately 7 million patients with HIV are co-infected with hepatitis C. Approximately 30% have spontaneously cleared the infection without antiviral treatment for reasons that are not well understood. A recent genome-wide association study (GWAS) demonstrated an association between spontaneous HCV clearance and two single nucleotide polymorphisms (SNPs) in *IL28B* and *HLA-DBQ1*. Genetic variation in other genes, including *IL-6*, have been implicated in other studies. Whole gene analysis is an alternate technique for examining genetic variation that requires a relatively small sample size and can evaluate the impact of multiple SNPs in linkage disequilibrium on clinical outcomes.
Methods: Blood was collected for DNA analysis from patients with either chronic HCV infection or evidence of spontaneous clearance defined as confirmed serum HCV antibody and undetectable HCV viral load without treatment. Whole genome analysis was performed using Illumina Quad 610/660W chips. To overcome anticipated limitations of small sample size, primary analyses focused on 12 preselected candidate genes based on known association with host immunologic response to HCV infection. 150 SNPs across the 12 genes met criteria for analysis. Single whole-gene likelihood ratio tests were performed for each candidate further reducing impact of multiple testing on power. We also performed an untargeted, SNP-based, genome-wide association analysis. Step-down permutation analyses were used to adjust for multiple testing in both candidate gene and genome-wide analyses.
Results: Ninety-five patients with HCV chronic infection (including 29 co-infected with HIV) and Sixty-two patients with spontaneous clearance (including 14 co-infected with HIV) were included for analysis. *HLA-DBQ1*, ($p=1.76*10^{-5}$) and *IL-6* (p=0.0007) genes were significantly associated with spontaneous HCV clearance. *IL28B* was not significantly associated with spontaneous clearance (p=0.17). Results were similar when controlled for HIV [Table 1].

Gene Name	LRT p-value	5% Significance Threshold	LRT p-value (controlled for HIV status)	5% Significance Threshold (controlled for HIV status)
HLA-DBQ1	.0000176	0.0006	.0000184	0.0005
IL-6	0.0007	0.0117	0.0008	0.0110
IL-28B	0.1700	0.0347	0.1600	0.0324

[Likelihood Ratio Test (LRT) results for 3 genes]

40 and 42 SNPs were examined and linkage mapped for *HLA-DBQ1* and *IL-6*, respectively [fig. 1].



[Figure 1. Linkage Disequilibrium Maps of Significant Genes]

No individual SNP surpassed the multiple-testing correction in the broader genome-wide analysis.
Conclusions: Our whole-gene analytic strategy identified a previously unreported association of IL-6 with spontaneous clearance of HCV infection. We also confirmed an earlier finding that HLA-DBQ1 is associated with spontaneous resolution of HCV infection.

TUPEB245

Favourable IFNL3 genotypes and liver fibrosis in HIV-hepatitis C (HCV) co-infected individuals from the Canadian Co-infection Cohort

N. Moqueet[1], R. Platt[1], M. Hull[2], C. Cooper[3], S. Walmsley[4], J. Gill[5], M. Klein[1,6], Canadian Co-infection Cohort
[1]*McGill University, Epidemiology, Biostatistics, and Occupational Health, Montreal, Canada,* [2]*University of British Columbia, BC Centre for Excellence in HIV/AIDS, Vancouver, Canada,* [3]*University of Ottawa, Ottawa Hospital-General Campus, Ottawa, Canada,* [4]*University of Toronto, University of Toronto and University Health Network, Toronto, Canada,* [5]*University of Calgary, Calgary, Canada,* [6]*McGill University Health Centre, Division of Infectious Diseases and Chronic Viral Illness Service, Montreal, Canada*
Presenting author email: nsmoqueet@gmail.com

Background: Liver fibrosis progression is faster in HIV-HCV co-infected individuals due to an elevated inflammatory profile. Interferon Lambda-3 (IFNλ-3), encoded by the *IFNL3* gene (formerly *IL28B*), has antiviral and pro-inflammatory properties, though reports of its association with liver fibrosis are inconsistent. Homozygous recessive single nucleotide polymorphisms (SNPs rs12979860CC, rs8099917TT) in this gene are linked to spontaneous HCV clearance and better treatment response, possibly via functional variant rs8103142, which causes a lysine-arginine substitution at position 70 (K70R).
We examined the relationship between IFNL3 genotypes and significant liver fibrosis (AST-to-platelet ratio index (APRI) ≥1.5) in HIV-HCV co-infected Canadians.
Methods: HCV RNA-positive participants free of fibrosis, end-stage liver disease and chronic Hepatitis B at baseline (n=612) were included from the prospective Canadian Co-infection Cohort (n=1176). Cases developed an APRI≥1.5 over follow-up. Cox proportional hazards was used, adjusting for sex, ethnicity, alcohol use, age, CD4 count (≤350 vs. 350+, time-varying), HCV genotype 3 vs. non-3, baseline APRI, and a product term between rs8099917 and rs8103142. Multiple imputation accounted for missing data. Haplotype analysis was performed, adjusted for ethnicity.
Results: Overall 69% were male with median HCV duration=17 years; 126 participants developed fibrosis over 1346 person-years of risk (9.40/100 person-years, 95% CI: 7.90-11.20/100 p-y). Homozygous recessive genotype at rs8099917 and rs8103142 individually increased the risk of significant liver fibrosis, HR (95% CI) 1.96 (1.18, 3.26) and 3.51 (1.15, 10.70), respectively. When present together, each genotype modified the other (product term p-value=0.03), resulting in a protective effect, verified by haplotype analysis. Inheritance of TCT, a haplotype with beneficial alleles at all 3 SNPs, was protective (OR 0.52, 95% CI:0.39-0.70) against risk of developing significant fibrosis.
Conclusions: Our results suggest that rs8099917 and rs81013142 are individually linked to a higher rate of liver fibrosis among HIV-HCV co-infected Canadians. When present together, these SNPs reduce fibrosis risk, possibly via enhanced HCV clearance. Functional studies are needed to examine any potential biological interactions.

TUPEB246

The risk of cardiovascular disease and death over 10 years in HIV/HCV co-infected patients with and without steatosis

C. Down[1], N. Mehta[2], K. Marks[3]
[1]*New York Presbyterian Hospital, Weill Cornell, New York, United States,* [2]*Weill Cornell Medical College, New York, United States,* [3]*New York Presbyterian Hospital, Weill Cornell, Infectious Disease, New York, United States*
Presenting author email: cmd9008@nyp.org

Background: Co-infection with HIV/HCV is associated with more severe liver disease including increased frequency of steatosis and significant fibrosis compared to patients mono-infected with HCV or HIV. Hepatic steatosis has been associated with greater fibrosis in cross sectional studies. We sought to explore the impact of steatosis on fibrosis progression, cardiovascular (CV) disease, and survival over time.
Methods: An IRB-approved, single-center retrospective cohort study was undertaken to analyze 10-year clinical outcomes in patients co-infected with HIV and HCV previously studied by Marks et al in 2005. Patients included underwent liver biopsy between 1998-2003 for the evaluation of HCV disease. Biopsy samples were assessed by a study pathologist (blinded) for fibrosis and steatosis. Clinical outcomes including cardiac events, liver function, and survival were collected over 10 years. Liver fibrosis progression was assessed using Fib4 and APRI scoring systems.
Results: 105 patients met criteria for this study. At cohort entry, mean age 45 +/- 7 yrs, 70% male, 88% on ARVs, 61% had undetectable HIV VL, median CD4+ count was 410 and 12 patients had CD4+ < 200, mean BMI was 26.3, 10% had diabetes, and 20% had HTN. 10-year

CVD risk estimated by the Framingham Risk Score was 9.6%. Analysis of clinical outcomes showed non-significant trends towards DM (22%), decompensated liver disease (19%), MI (5%), CAD (5%), and PAD (5%) in the steatosis group compared to those without steatosis (11%, 15%, 2%, 4%, 4%, respectively) over the 10 year period. On average MELD, Fib4 and APRI scores were higher in the steatosis group at the 10 year timepoint, however this trend was not statistically significant. Survival analysis was performed which showed decreased survival in the steatosis group at the 5-year and 10-year timepoints with 5-year survival 88% and 10-year survival 65% in the steatosis group vs 93% and 73% at respective time points in the nonsteatosis group.

Conclusions: Given the prevalence of steatosis in approximately half of co-infected patients, the cardiovascular, fibrosis progression and survival differences observed over 10 years warrant further study. Furthermore, mortality for this population was very high; variables responsible for decreased survival in this population should be studied.

TUPEB247

Implications of baseline HCV RNA level and intrapatient viral load variability on OBV/PTV/r + DSV 12-week treatment outcomes

R. Brown[1], M. Puoti[2], C. Cooper[3], D. Wyles[4], T. Sepe[5], R. Nahass[6], M. King[7], E. Coakley[7], B. McGovern[7], J. Feld[8], R. Trinh[9]

[1]Columbia University Medical Center, Center for Liver Disease and Transplantation, New York, United States, [2]AO Ospedale Niguarda Ca Granda, Milan, Italy, [3]University of Ottawa, Ottawa, Canada, [4]University of California San Diego, La Jolla, United States, [5]Liver Center, University Gastroenterology, Providence, United States, [6]ID Care, Hillsborough, United States, [7]AbbVie Inc., Chicago, United States, [8]University of Toronto, Toronto, Canada, [9]AbbVie Inc., North Chicago, United States

Background: High levels of pre-treatment HCV RNA may impact the risk of virologic relapse post-treatment. Within the ombitasvir/paritaprevir*/ritonavir and dasabuvir (3D) development program, we examined the effect of viral load on the risk of virologic relapse within various HCV RNA strata.

Methods: Non-cirrhotic treatment-naïve HCV-infected patients who received 12 weeks of 3D (GT1b) or 3D+RBV (GT1a) were included in the analysis. Post-treatment relapse rates were summarized by pre-treatment HCV RNA thresholds. Intrapatient HCV RNA measurement variability was assessed by evaluating differences in HCV RNA levels between screening and baseline (median interval=3 weeks). Plasma samples were analyzed at a central laboratory using the Roche COBAS® TaqMan® RT-PCR assay v2.0.

Results: Among 618 patients, median baseline HCV RNA was 6.56 $\log_{10}$ IU/mL (3.6 million [M] IU/mL); 7/618 (1.1%) had post-treatment relapse. There was no association between baseline HCV RNA and relapse rate for any threshold (Table), with relapse rates of 1.2% and 0.9% below and above baseline HCV RNA of 10 million IU/mL, respectively. In patients who achieved SVR12 or relapsed, the median baseline HCV RNA was 6.55 and 6.66 $\log_{10}$ IU/mL, respectively (p=0.2). No relapses were observed for any patient with viral load < 2.5M IU/mL. Intrapatient variability in HCV RNA measurements increased with rising baseline viremia. Screening and baseline HCV RNA measurements differed by >1M IU/mL in 55%, by >2M IU/mL in 35%, and by >3M IU/mL in 26% of patients. In the subset of patients with a screening HCV RNA above 2M IU/mL, 79% differed by >1M IU/mL, 53% differed by >2M IU/mL, and 40% differed by >3M IU/mL. At the 6M IU/mL threshold, 18% of patients had discordant baseline and screening HCV RNA values.

Conclusions: With this multi-targeted regimen, we did not identify any viral threshold for risk of relapse, suggesting that 12 weeks of therapy is optimal for minimizing the risk of relapse in naïve, non-cirrhotic patients, regardless of underlying host or viral factors. Intrapatient variability in HCV RNA measurements was common, suggesting that a subset of patients may be misclassified if viral thresholds are important for clinical decision-making.

*Paritaprevir was identified by AbbVie and Enanta.

Threshold	Below threshold	Above threshold
1 million IU/mL	0/157 (0%)	7/461 (1.5%)
1.5 million IU/mL	0/201 (0%)	7/417 (1.7%)
2 million IU/mL	0/223 (0%)	7/395 (1.8%)
2.5 million IU/mL	0/248 (0%)	7/370 (1.9%)
3 million IU/mL	1/269 (0.4%)	6/349 (1.9%)
3.5 million IU/mL	1/302 (0.3%)	6/316 (1.7%)
4 million IU/mL	2/324 (0.6%)	5/294 (1.2%)
5 million IU/mL	4/373 (1.1%)	3/245 (1.2%)
6 million IU/mL	4/410 (1.0%)	3/208 (1.4%)
7 million IU/mL	5/443 (1.1%)	2/175 (1.1%)
8 million IU/mL	5/467 (1.1%)	2/151 (1.3%)
9 million IU/mL	5/489 (1.0%)	2/129 (0.9%)
10 million IU/mL	6/502 (1.2%)	1/116 (0.9%)
Total	7/618 (1.1%)	

[Table. Relapse rates according to baseline HCV RNA thresholds chosen based on recent FDA analysis]

TUPEB248

National trend and characteristics of acute hepatitis C among HIV-infected individuals: a matched case-control study - Taiwan, June 2001 - December 2014

Y.-C. Lo

Taiwan Centers for Disease Control, Office of Preventive Medicine, Taipei, Taiwan, Province of China

Presenting author email: loyichun@cdc.gov.tw

Background: Hepatitis C virus (HCV) infection has been recognized as an emerging sexually transmitted disease among HIV-infected men who have sex with men (MSM) in Europe, North America, and Australia. In Taiwan, a hospital-based study demonstrated increasing incidence of recent HCV infection among HIV-infected individuals. We determined the national trend and associated characteristics of acute hepatitis C (AHC) among HIV-infected individuals.

Methods: The National Disease Surveillance System collects characteristics of notifiable disease cases including AHC, HIV infection, syphilis, and gonorrhea through mandatory physician reports and patient interviews. Information on HCV seroconversion has been collected since June 2001. We defined an HIV/AHC case as AHC reported during June 1, 2001-December 31, 2014 in a previously reported HIV-infected individual with a positive HCV antibody ≤12 months after the last negative HCV antibody test. Each HIV/AHC case was matched to two HIV-infected, non-AHC controls on age (+/-5 years), sex, mode of transmission, date of diagnosis (+/-30 days), and county/city of residence. Logistic regression was used to identify characteristics associated with AHC.

Results: During the study period, 93 (1.4%) of 6,624 AHC reports met the HIV/AHC case definition; the case counts during 2001−2004, 2005−2008, 2009−2011, and 2012−2014 were 0, 6, 11, and 76. All HIV/AHC cases were males aged 21-49 years with AHC diagnosed 2-5,923 (median: 1,467) days after HIV diagnoses. All denied injection drug use and 81 (87%) self-reported as MSM. Sixty-nine (74%) lived in the Taipei metropolitan area. Before AHC diagnoses, syphilis and gonorrhea had been diagnosed in 72 (77%) and 19 (20%) of the cases, respectively. Eighty-one cases (99% MSM) were successfully matched to 162 controls. In logistic regression, AHC was associated with a syphilis diagnosis ≤12 months (adjusted odds ratio [AOR]: 4.6; 95% confidence interval [CI]: 2.5-8.5) and a previous diagnosis of gonorrhea (AOR: 2.2; 95% CI: 1.1-4.4).

Conclusions: AHC has been increasingly reported among HIV-infected men nationwide, predominantly among MSM in the Taipei metropolitan area. Physicians should suspect and monitor AHC in HIV-infected MSM with a diagnosis of recent syphilis or gonorrhea. We recommend continued surveillance and identification of behavioral and virologic characteristics contributing to AHC among HIV-infected individuals in Taiwan.

TUPEB249

High efficacy and low relapse rates observed with 8 or 12 weeks of LDV/SOF STR in GT1 HCV infected treatment-naïve, non-cirrhotic patients with pretreatment HCV RNA <6 million IU/mL

D.L. Wyles[1], P.Y. Kwo[2], S. Zeuzem[3], G. Foster[4], P.E. Sax[5], T. McLean[6], S. Seyedkazemi[6], C. Avila[6], B. Kreter[6], P.S. Pang[6], K. Kowdley[7]

[1]University of California, San Diego, Division of Infectious Diseases, La Jolla, United States, [2]Indiana University, Division of Gastroenterology/Hepatology, Indianapolis, United States, [3]J.W. Goethe University Hospital, Department of Medicine, Frankfurt, Germany, [4]Queen Mary, University of London, Hepatology, London, United Kingdom, [5]Brigham and Women's Hospital, Harvard Medical School, Division of Infectious Diseases, Boston, United States, [6]Gilead Sciences, Inc., Foster City, United States, [7]Swedish Liver Center, Department of Gastroenterology/Hepatology, Seattle, United States

Background: A shortened duration of ledipasvir/sofosbuvir (LDV/SOF) for 8 weeks (+/- RBV) was compared to 12 weeks LDV/SOF in genotype 1 (GT1) treatment-naïve, non-cirrhotic patients in ION-3, a Phase 3, randomized, open label study (N=647). Overall sustained virologic response (SVR) rates were non-inferior between the 8 and 12 week LDV/SOF arms (94% and 96% respectively), however relapse was numerically higher in those treated for 8 weeks (5.1%) compared to 12 weeks (1.4%). Addition of RBV did not improve SVR. A post-hoc analysis of the ION-3 trial was conducted to evaluate baseline factors that might be responsible for the differential in relapse rates between the 8 and 12 week arms of LDV/SOF.

Methods: Baseline historical negative predictors were evaluated in subjects who relapsed, including: age, gender, race, GT1 subtype, METAVIR fibrosis stage, BMI, IL28B status, and baseline HCV RNA. For baseline viral load, pre-defined cut-off of 800,000 IU/ml and subsequently up to 10 million IU/mL were assessed.

Results: In the ION-3 trial, approximately 60% of treatment-naïve, non-cirrhotic subjects had baseline HCV RNA of < 6 million IU/mL. For these subjects, there was no difference in SVR rates (97% and 96%) nor relapse rates (1.6% and 1.5%) between 8 and 12 weeks of LDV/SOF treatment. SVR rates were identical for the 8 week and 12 week arms (96%) in patients with pretreatment HCV RNA < 10 million IU/mL, and relapse occurred in 3.1% vs. 1.2%, respectively. The majority of failures in ION-3 who were treated for 8 weeks had a baseline HCV RNA greater

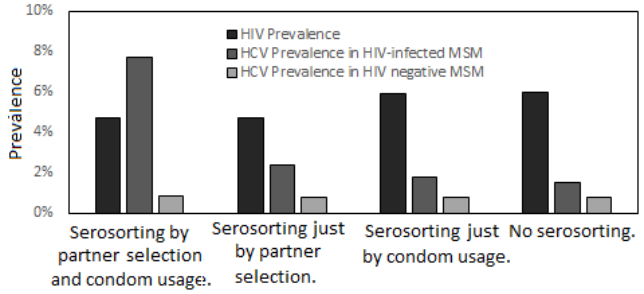
than 10 million IU/mL. Although higher overall rates of relapse were observed for males and subjects who were IL28B non-CC, sex and IL28B status had no effect on outcome among those with a pretreatment HCV RNA < 6 million IU/ml.
Conclusions: A baseline HCV RNA < 6 million IU/mL in treatment-naïve, non-cirrhotic GT1 patients correlated with similar SVR and relapse rates with 8 weeks or 12 weeks of LDV/SOF single tablet regimen regardless of other patient characteristics. This shortened duration could improve adherence and affordability of HCV treatment.

TUPEB250

The impact of serosorting on hepatitis C and HIV co-infection amongst men who have sex with men: a modelling analysis

L. MacGregor[1], N. Martin[1], A. Ganesh[2], F. Hickson[3], P. Weatherburn[3], P. Vickerman[1]
[1]University of Bristol, School of Social and Community Medicine, Bristol, United Kingdom, [2]University of Bristol, Mathematics, Bristol, United Kingdom, [3]London School of Hygiene and Tropical Medicine, Department of Social and Environmental Health Research, London, United Kingdom
Presenting author email: peter.vickerman@bristol.ac.uk

Background: Recent observations highlight a sexually driven emerging Hepatitis C (HCV) epidemic within HIV positive men who have sex with men (MSM). We use transmission modelling to explore the potential role of serosorting (modification of behaviours based on perceived HIV status between sexual partners) on both infections' prevalence within MSM.
Methods: We developed a deterministic HIV and HCV sexual transmission model amongst MSM parameterized to the UK. We used the European MSM Internet Survey (EMIS) 2010 UK dataset to parameterise serosorting behaviours, condom usage and frequency of sexual partners. Two serosorting behaviours were considered; firstly individuals preferring sexual partners of concordant HIV status, and secondly condom use being governed by the perceived HIV status of each partner. A parameter was included denoting the accuracy with which MSM decide an individual's HIV status. Consistent with UK data, the baseline model running from 2000-2010 was fit to a steady HIV prevalence of 4.7% among MSM and HCV prevalence increase from 0.63% to 7.7% amongst HIV-infected MSM while incorporating serosorting, run between 2000-2010. We examined the effect of serosorting and biological interactions (HIV increasing the susceptibility and infectiousness of HCV) on the observed patterns in disease prevalence.
Results:



[Modelled effect of different types of serosorting on HIV and HCV prevalence, with serosorting by partner selection and condom usage]

In the absence of biological interactions between HIV and HCV, the model could fit the observed pattern but not magnitude of observed HIV and HCV prevalence data. If HIV-positive MSM are more (2.88 fold) infective and (2-3 fold) susceptible to HCV, the degree to which serosorting elevates HCV prevalence amongst HIV-positive individuals is amplified, producing accurate fits to observed prevalence data. Compared to a model with no serosorting, accurate HIV serosorting (Figure) leads to moderate decreases in HIV prevalence (from 6.0% to 4.7%), but large increases in HCV prevalence among HIV-positive MSM (from 1.5% to 7.7%), and small increases in HCV among HIV negative MSM (from 0.8% to 0.83%). As serosorting becomes less accurate, HIV prevalence increases whereas HCV prevalence decreases in HIV-positive MSM but increases in HIV-negative MSM.
Conclusions: Serosorting practises decrease HIV prevalence regardless of errors in judgement, but can increase HCV among HIV-positive MSM. Discouraging serosorting could reduce HCV prevalence but increase HIV prevalence.

TUPEB251

Pending availability and affordability of new HCV regimens in resource-limited settings, should HIV-HCV co-infected patients start receive peg-interferon and ribavirin which just started to be affordable?

G. Jourdain[1,2,3], J. Figoni[1,2], K. Thetket[4], P. Leenasirimakul[5], V. Klinbuayaem[6], S. Khusuwan[7], C. Bowonwatanuwong[8,9], S. Chalermpantmetagul[1,2], T.R. Cressey[2,3], L. Decker[1,2], N. Durier[10], N. Salvadori[1,2], N. Ngo-Giang-Huong[1,2,3], PHPT HIV-HCV Treatment Group
[1]Institut de Recherche pour le Développement (IRD), PHPT-UMI 174, Marseille, France, [2]Chiang Mai University, Fac. Associated Medical Sciences, Chiang Mai, Thailand, [3]Harvard T.H. Chan Harvard School of Public Health, IID, Boston, United States, [4]Nakornping Hospital, Gastroenterology, Chiang Mai, Thailand, [5]Nakornping Hospital, Internal Medicine, Chiang Mai, Thailand, [6]Sanpatong Hospital, Internal Medicine, Chiang Mai, Thailand, [7]Chiangrai Prachanukroh Hospital, Internal Medicine, Chiang Rai, Thailand, [8]Chonburi Hospital, Internal Medicine, Chonburi, Thailand, [9]IRD-CMU, UMI 174 - PHPT, Chiang Mai, Thailand, [10]amfAR, TREAT Asia, Bangkok, Thailand

Background: In many limited resource settings, HIV-HCV co-infected patients with advanced fibrosis have not yet benefited from any HCV treatment. In Thailand, peg-interferon/ribavirin combination therapy, which remained unaffordable until 2013, has never been evaluated in real life for HIV-HCV co-infected patients. We initiated a peg-interferon/ribavirin-based treatment program for co-infected patients in four HIV clinics in Thailand.
Methods: Population is composed of HIV infected adults with chronic HCV infection, fibrosis stage of F2/3/4 by transient elastography, well controlled for their HIV infection, with no contra-indications. Treatment is prescribed by internists, with hepatologist advice as necessary: peg-interferon alpha 2-b (1.5 microgram/kg once a week) and ribavirin (dosing according to HCV genotype and bodyweight) for 48 weeks. Monitoring for safety is done at 2, 4, 8 and 12, 24, 36, 48 weeks (dosing adapted as needed). HCV RNA is assessed at 12, 24, 48 and 72 weeks (Abbott m2000) with complete early virological response (EVR) defined as undetectable HCV RNA (threshold 12 IU/mL) after 12 weeks and partial EVR as drop >2 $\log_{10}$ IU.
Results: Of the first 16 patients enrolled, 11 were males. At enrollment, median (interquartile range) age was 44.3 (40.4-51.1) years and HCV RNA 5.95 (5.53-6.75) $\log_{10}$ IU/mL. Eleven patients had fibrosis stage F4, 4 F3 and 1 F2. Two had HCV genotype (GT) 1a, 7 GT1b, 5 GT3a, and 2 GT6. Thirteen had IL28b CC and 3 CT. One patient discontinued treatment for intolerance after first peg-interferon injection. During the first 12 weeks, 4 patients experienced anemia (1 Grade 3 and 3 Grade 1), 5 neutropenia
(1 Grade 4, 3 Grade 3 and 1 Grade 1) and 3 thrombocytopenia (all Grade 2) but none discontinued treatment. 9/15 patients had complete EVR, 4 had partial EVR and 2 did not respond.

	IL28b			Total
HCV genotype	CC	CT	TT	
1a	1/1	0/1	0	1/2
1b	3/6	0/1	0	3/7
3a	3/3	0/1	0	3/4
6a or 6b	1/1	0	0	1/1
6c-l	1/1	0	0	1/1
Total	9/12	0/3	0	9/15

[Proportion with undetectable HCV RNA at week 12]

Conclusions: In these HIV-HCV co-infected patients with favorable IL28b but advanced fibrosis, this therapy appeared effective and relatively well tolerated. Hepatologists and HIV specialists collaboration is essential for patients with HCV co-infection. This treatment remains the only option for a significant number of patients who cannot wait longer for the availability and affordability of all oral HCV treatment regimens.

TUPEB252

Prevalence of HIV, HBV and HCV infections in Nigeria

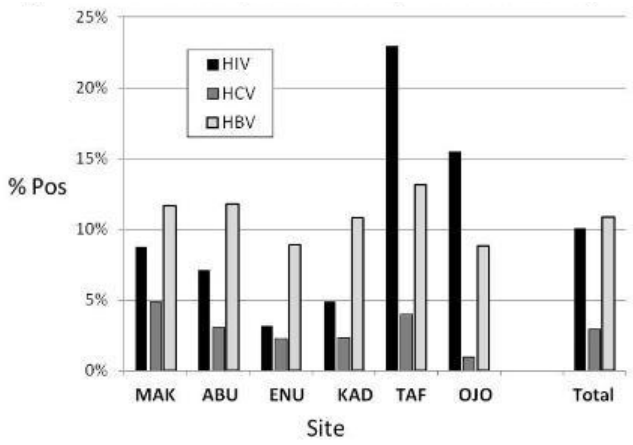
M. Manak[1], O. Njoku[2], A. Shutt[1], J. Malia[3], M. Milazzo[1], A. Suleiman[2], R. Nelson[2], O. Ayemoba[2], R. O'Connell[4], D. Singer[5], N. Michael[6], S. Peel[3]
[1]Henry Jackson Foundation, Laboratory Diagnostics and Monitoring, Silver Spring, United States, [2]Walter Reed Program, Abuja, Nigeria, [3]Walter Reed Army Institute of Research, Laboratory Diagnostics and Monitoring, Silver Spring, United States, [4]Armed Forces Research Institute of Medical Sciences, Bangkok, Thailand, [5]Uniformed Services University of Health Sciences, Bethesda, United States, [6]Walter Reed Army Institute of Research, Silver Spring, United States
Presenting author email: mmanak@hivresearch.org

Background: Nigeria has the world's second highest number of HIV/AIDS related deaths after South Africa and is highly endemic for viral hepatitis. Co-infection of HIV-1 positive individuals with HBV or HCV had previously been shown to lead to rapid decline of CD4, progression of HIV disease, increased risk of antiretroviral drug associated toxicity, and increased mortality

and morbidity. A study was conducted to estimate the prevalence and distribution of HIV-1, HBV and HCV infections at selected sites throughout Nigeria as part of evaluation of populations for HIV vaccine cohort development. Participants included workers in "Mammy Markets" adjacent to military barracks and general markets (Makurdi, Abuja, Enugu, Kaduna), as well as bar, hotel, restaurant and brothel workers in highway settlements (Tafa, Ojo Lagos), regarded as locations of increased risk for HIV infection.

Methods: Plasma samples from a total of 3,229 subjects from the six study sites were tested for HIV, HBV and HCV infection by standard laboratory tests: Bio-Rad GS HIV-1/2/O EIA, Ortho HCV v3.0 ELISA, Bio-Rad MONOLISA Anti-HBc EIA, and Bio-Rad GS HBsAg EIA 3.0. HIV repeat reactive samples were confirmed by Bio-Rad GS HIV-1 Western Blot, while HCV repeat reactives were confirmed by either Ortho HCV RIBA (sites 1-4) or INNO-LIA HCV Score (sites 5-6).

Results: Site-specific and aggregate proportion of HIV, HCV, and HBV infections are shown in Fig 1. The prevalence of HIV-1 and HCV ranged from 3.1 to 23.0%, and 1.0 to 4.8%, respectively. Prevalence of HBV, based on anti-HBc and HBsAg testing, ranged from 23.6 to 40.8%, and 8.9% to 13.2%, respectively. Infection with HIV did not correlate with HBV or HCV suggesting independent factors.



[Fig 1. Prevalence of HIV, HCV and HBsAg at select sites in Nigeria]

Conclusions: HIV-1 prevalence varied widely at study sites from 3.1 to 23.0%, with much lower and less variable HCV prevalence (averaging 2.9%). Lack of correlation between HIV and viral hepatitis prevalence suggests independent factors for these diseases. HBV antibody reactivity was high (32.5%), with 10.9% positive for HBsAg indicative of active infection. Understanding the complex HIV-1 geographic heterogeneity and prevalence of HCV and HBV co-infection among individuals associated with specific Nigerian sites may provide the basis for directed interventions against all three infections.

TUPEB253

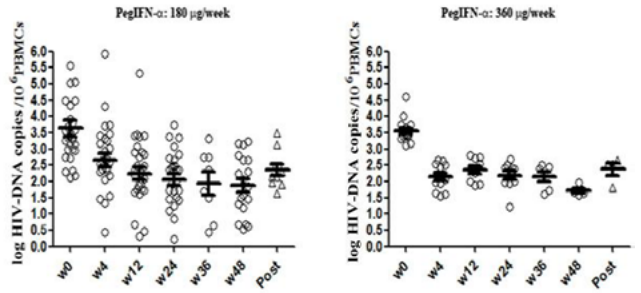
PegIFN-a 2a dose-dependent reduction in HIV-DNA levels during the first 4 weeks of treatment in HIV-1/HCV co-infected patients

O.-J. BenMarzouk-Hidalgo, A. Torres-Cornejo, A. Gutierrez-Valencia, R.M. Ruiz-Valderas, P. Viciana, L.F. López-Cortés
Hospital Universitario Virgen del Rocío, Instituto de Biomedicina de Sevilla (IBiS), CSIC/ Universidad de Sevilla, Unidad Clínica de Enfermedades Infecciosas, Microbiología y Medicina Preventiva, Sevilla, Spain
Presenting author email: benmarzouk@hotmail.com

Background: IFN-a has been shown to exert active antiviral activity against HIV-1, indeed its administration has been shown to reduce HIV-1 viraemia in untreated patients up to 5-10 fold. However, scarce data is available about the effects of exogenous IFN-a in the HIV reservoir of HAART treated patients. The aim of this study is to investigate whether or not there is a dose-dependent effect of IFN on the levels of HIV-DNA in a cohort of HIV/HCV co-infected patients.

Methods: Retrospective and longitudinal study that recruited HIV-infected patients who started a pegIFN-a 2a (either 180 or 360 mg/week) plus ribavirin-based (600-800 mg BID) anti-HCV therapy. PBMCs and plasma samples were obtained at baseline, weeks 4, 12, 24, 26 and 48 of bi-therapy and after 6-12 months after the end of the bi-therapy. All patients were HIV suppressed for the entire follow-up. Isolated PBMCs were digested to extract cellular DNA and total HIV DNA levels were quantified by real time-PCR.

Results: Forty-seven patients were recruited due to samples availability: 33 patients treated with 180 mg/week and 14 receiving 360 mg/week of pegIFN-a 2a. Patients showed similar characteristics at baseline. Similar baseline HIV-DNA levels were found in both groups of patients (single-dose: 3.37 vs. double-dose: 3.42 log HIV-DNAcopies/10^6PBMCs; p-value=0.551). Overall, HIV-DNA levels were significant higher at week 4 among patients with single-dose compared to those receiving double-dose of IFN (2.618 *vs.* 2.16 log HIV-DNAcopies /10^6BMCs, *p*-value=0.041). Comparing both dosages, the decrease on the HIV reservoir size was significantly higher in patients with the 360 mg dosage (single-dose:1.384 *vs.* double-dose: 0.583 log HIV-DNAcopies/10^6PBMCs, p-value=0.037). However, no differences between both dosages were found at week 48 of the follow-up (single-dose: 1.85 vs. double-dose: 1.68 log HIV-DNAcopies/10^6PBMCs, p-value=0.945). Moreover, after the end of the bi-therapy, HIV-DNA levels raised significantly compared to when IFN was administered (single-dose: 2.23 vs. double-dose: 2.54 log HIV-DNAcopies/10^6PBMCs, p-value=0.031), though without differences between both groups (p-value=0.539).



[Figure 1]

Conclusions: HIV reservoir decrease is affected upon pegIFN-a 2a administration during the first 4 weeks of treatment in a dose-dependent manner. After treatment interruption, a significant replenishment is observed with both doses.

TUPEB254

Global systematic review and meta-analysis of the seroprevalence of HBV and HCV infection in HIV-infected persons

P. Easterbrook[1], L. Platt[2], E. Gower[3], H. Razavi[3], K. Sabin[4], P. Vickerman[5]
[1]WHO, Geneva, Switzerland, [2]London School of Hygiene and Tropical Medicine, London, United Kingdom, [3]Centers for Disease Analysis, Boulder, United States, [4]UNAIDS, Geneva, Switzerland, [5]University of Bristol, Bristol, United Kingdom

Background: There is a paucity of country level data on the prevalence of HIV-hepatitis B (HBV) and hepatitis C (HCV) coinfection, especially from low and middle income countries. Reliable estimates are needed to inform the development of regional and national strategies for hepatitis screening and management.

Methods: We undertook a global systematic review and meta-analysis of the prevalence of HIV-HBV and HIV-HCV coinfection through a comprehensive search of 12 bibliographic databases and contact with WHO regional offices to access unpublished serosurveys. Eligible studies examined prevalence of HBV and HCV among HIV-infected adults at country level from 2002 to 2013, and stratified by population or risk group where available (Gen population (Genpop), PWID, MSMs, Heterosexuals (Hetero), and pregnant women (Preg)). Study quality was rated based on study design, sample size, potential for selection bias, and assay quality. Regional burden of coinfection was derived by applying HBV or HCV prevalence in HIV-infected gen pop/risk groups to 2014 UNAIDS regional estimates of no. HIV infected.

Results: The search identified 25,236 articles, and 1,606 met inclusion criteria after screening of abstracts. There were 833 country-level prevalence estimates of HCV from 86/193 (45%) countries, and 483 from 75/193 (39%) for HBsAg. Based on 314 estimates of HCVAb prevalence among 5 HIV-infected populations from 11 geographic regions, median prevalence ranged 1-7% (Genpop), 71-96% (PWID), 2-20% (MSM), 0.5-12% (Hetero), 0.6-10% (Preg). Based on 170 estimates HBsAg prevalence among 5 HIV-infected populations from 11 geographic regions, median prevalence ranged 1-11% (Genpop), 7-27% (PWID), 4-22% (MSM), 3-17% (Hetero), 0.5-9% (Preg). The estimated IQ range of global burden of HIV-HBsAg and HIV-HCV antibody co-infection is 1.5 to 5.5 million and 1.6 to 6.9 million, respectively. Key methodological challenges include lack of data from 23 countries or in certain risk groups from some regions; use of different generation HCVAb assays; and importance of stratification of prevalence estimates by risk behaviour, especially for HCV.

Conclusions: Sub-Saharan Africa has the highest regional burden of HIV-HBV and HIV-HCV co-infection, followed by eastern Europe and South-east Asia.There are several key methodological and analytic challenges in generating reliable estimates of country and regional prevalence of HIV-HBV and HCV coinfection.

TUPEB255

Safety of ledipasvir/sofosbuvir with and without ribavirin for the treatment of patients with chronic HCV genotype 1 infection: an analysis of the phase 3 ION trials

N. Bräu[1], S. Alqahtani[2], N. Afdhal[3], S. Zeuzem[4], S. Gordon[5], A. Mangia[6], J.C. Yang[7], X. Ding[7], P.S. Pang[7], M.S. Sulkowski[2]
[1]Mount Sinai School of Medicine, Division of Infectious Diseases and Liver Diseases, New York, United States, [2]Johns Hopkins Medical Center, Baltimore, United States, [3]Beth Israel Deaconess Medical Center, Boston, United States, [4]Johann Wolfgang Goethe University, Frankfurt, Germany, [5]Henry Ford Health System, Detroit, United States, [6]Casa Sollievo della Sofferenza Hospital, San Giovanni Rotondo, Italy, [7]Gilead Sciences, Inc., Foster City, United States

Background: The once-daily fixed-dose combination tablet of ledipasvir/sofosbuvir (LDV/SOF) was evaluated with and without ribavirin (RBV) for the treatment of HCV genotype 1 infection in three phase 3 studies (ION-1, ION-2, ION-3). Overall, SVR rates were high (97%) regardless of RBV use. The purpose of this analysis was to characterize the safety profile of RBV in an interferon-free regimen.
Methods: Treatment-naïve and -experienced patients with HCV genotype 1 infection, including those with compensated cirrhosis, were randomized to 8, 12, and 24 weeks of LDV/SOF ± RBV in the ION-1, ION-2, and ION-3 studies. Treatment-emergent adverse events (AEs) and laboratory abnormalities were assessed.
Results: 1952 patients (No RBV, n=1080; RBV, n=872) were treated in the phase 3 studies: 308 (16%) were African American, 224 (11%) had compensated cirrhosis, 501 (26%) had a BMI ≥30 kg/m^2, and 440 (23%) were treatment-experienced. Overall, 97% of all patients achieved SVR12. Treatment-related AEs occurred in 71% and 45% of patients treated with and without RBV (Table 1). For both groups, treatment-related serious AEs (≤0.4%) and treatment-discontinuations due to AEs (≤0.8%) were uncommon. More patients taking RBV than LDV/SOF alone required dose modification or interruptions of study treatment due to AEs (13.5% v 0.6%) and other medications during treatment (63% v 53%) including topical corticosteroids (73% v 3%), antihistamines (11% v 5%), and sleeping aids (17% v 10%). Anemia, defined as hemoglobin level < 10 g/dL, was observed in 7% (n=58) of patients taking RBV and < 0.01% (n=1) of patients taking LDV/SOF alone. Similar patterns of AEs were observed among cirrhotic patients. No deaths occurred during the studies.
Conclusions: The addition of RBV did not increase the rate of treatment discontinuation or treatment-related serious AEs, but was associated with greater incidence of AEs including fatigue, insomnia, irritability and rash/pruritus, and concomitant medication use. RBV use did not impact the efficacy of LDV/SOF.

Adverse event N (%)	% Difference	SOF/LDV 8, 12, or 24 weeks N=1080	SOF/LDV + RBV 8, 12, or 24 weeks N=872
Fatigue	-16	240 (22)	331 (38)
Headache	-5	222 (21)	228 (26)
Nausea	-7	112 (10)	152 (17)
Insomnia	-10	82 (8)	155 (18)
Irritability	-7	46 (4)	95 (11)
Rash	-7	47 (4)	94 (11)
Cough	-6	42 (4)	90 (10)
Pruritus	-6	33 (3)	78 (9)
Mean change in hemoglobin from baseline at end of treatment (8wk / 12wk / 24 wk) (g/dL)	N/A	-0.2 / -0.4 / -0.3	-1.9 / -2.3 / -2.0

[Table 1]

Other adverse reactions and complications of ART

TUPEB256

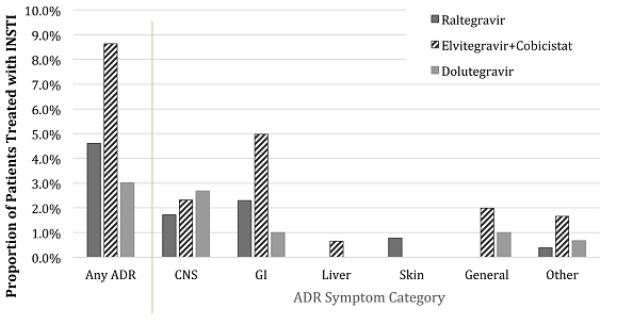
Adverse drug reactions associated with integrase strand transfer inhibitors (INSTI) in clinical practice: post-marketing experience with raltegravir, elvitegravir-cobicistat and dolutegravir

K.J. Lepik[1,2], A. Nohpal[1], B. Yip[1], K.J. Toy[2], L. Akagi[1,2], J.S.G. Montaner[1], S. Guillemi[1], R. Hogg[1], R. Barrios[1]
[1]BC Centre for Excellence in HIV/ AIDS, Vancouver, Canada, [2]St Paul's Hospital, Pharmacy, Vancouver, Canada
Presenting author email: klepik@cfenet.ubc.ca

Background: The integrase strand transfer inhibitors (INSTI) raltegravir, elvitegravir with pharmacokinetic booster cobicistat (elvitegravir-cobicistat) and dolutegravir have demonstrated safety and efficacy in clinical trials. This post-marketing, observational study describes and compares the incidence and type of INSTI adverse drug reactions (ADRs) reported during routine clinical use in British Columbia (BC) Canada.
Methods: HIV-1-infected persons age ≥19 years were included if their first prescription for raltegravir, elvitegravir-cobicistat or dolutegravir was dispensed between 01-Jan-2012 and 31-Aug-2014 through the BC Centre for Excellence in HIV/AIDS (BC-CfE) Drug Treatment Program. Patients could contribute data for more than one INSTI. All patients had ≥4 months follow-up opportunity until 31-Dec-2014. Clinical and demographic variables and ADR reports were abstracted from BC-CfE databases and summarized by descriptive statistics. The primary outcome was any ADR resulting in therapy discontinuation. ADR incidence density rates and 95% confidence intervals (CI95) were estimated by Poisson regression, adjusted for covariates. Adjusted relative ADR rates (RR) were calculated using raltegravir as the reference.
Results: The cohort included 1044 INSTI-treated patients, 75 (7.2%) of whom contributed data for ≥2 INSTIs, providing 1122 distinct patient-INSTI records: 522 raltegravir-treated, 301 elvitegravir-cobicistat-treated and 299 dolutegravir-treated patients. Table 1 summarizes patient and INSTI regimen characteristics.

Variable	Raltegravir N=522	Elvitegravir-Cobicistat N=301	Dolutegravir N=299
Age, median (IQR) yr	50 (43,56)	43 (34, 50)	49 (41,55)
Sex n(%): male female	 420 (80%) 102 (20%)	 225 (75%) 76 (25%)	 237 (79%) 62 (21%)
CD4, median (IQR) cells/microL	440 (230, 650)	470 (280, 650)	550 (380, 760)
Suppressed viral load <50 copies/mL n(%)	288 (55%)	126 (42%)	201 (67%)
Hepatitis C co-infection n(%)	239 (46%)	106 (35%)	74 (25%)
Previous ART, n(%): treatment naïve treatment experienced	 66 (13%) 456 (87%)	 67 (22%) 234 (78%)	 37 (12%) 262 (88%)
Concurrent ARVs: 2 NRTI: TDF+3TC/FTC 2 NRTI: ABC+3TC Other ARV combination	 185 (36%) 111 (21%) 226 (43%)	 263 (87%) 0 (0%) 38 (13%)	 61 (20%) 179 (60%) 59 (20%)
INSTI treatment duration: median (IQR) yr cumulative person-yr exposure	 1.15 (0.56, 1.79) 635 person-yr	 0.75 (0.44, 1.13) 233 person-yr	 0.50 (0.38, 0.63) 150 person-yr
Abbreviations: IQR: interquartile range, ARV: antiretroviral, ART: ARV therapy, INSTI: integrase strand transfer inhibitor, ABC: abacavir, 3TC: lamivudine, FTC: emtricitabine, TDF: tenofovir, NRTI: Nucleoside (nucleotide) Reverse Transcriptase Inhibitor			

[Table 1: Patient and Treatment Characteristics]



Abbreviations and definitions: Any ADR: Any adverse drug reaction resulting in therapy discontinuation, INSTI: Integrase strand transfer inhibitor, ADR Symptom Category: Counting 1 symptom per category per patient INSTI-ADR record; CNS: central nervous system, GI: gastrointestinal, General: non-specific symptoms e.g. fatigue, malaise, pain.

[Figure 1. INSTI adverse drug reactions by symptom category]

For each INSTI, the proportion of patients with an ADR leading to discontinuation was: Raltegravir 24/522 (4.60%), elvitegravir-cobicistat 26/301 (8.64%) and dolutegravir 9/299 (3.01%). As shown in Figure 1, the most commonly reported ADR symptoms were: Central nervous system (sleep disturbance, nightmares, headache), gastrointestinal tract (nausea, diarrhea, gastrointestinal discomfort) and general fatigue/ malaise. No serious ADRs (grade IV severity or leading to hospitalization) were reported.
After controlling for under-dispersion using robust Poisson regression and adjusting for sex, antiretroviral treatment experience and hepatitis C co-infection, adjusted ADR rates (CI95) per 100 person-years were: Raltegravir 1.88 (0.72-4.93), elvitegravir-cobicistat 5.76 (2.14-15.49), and dolutegravir 3.34 (1.19-9.40). The adjusted RR (CI95) of ADR relative to raltegravir was 3.06 (2.97-3.14) for elvitegravir-cobicistat and 1.78 (1.65-1.91) for dolutegravir.
Conclusions: All INSTI were generally well tolerated. The newer INSTIs elvitegravir-cobicistat and dolutegravir had shorter follow-up times than raltegravir, but had relatively higher rates of ADRs resulting in therapy discontinuation. Follow-up of this cohort is ongoing.

TUPEB257

Physiological concentrations of combination antiretroviral therapy drugs affect mitochondrial DNA (mtDNA) quantity and quality in cell culture models

S. Saberi[1,2], F. Valentino[1], A. Ziada[1], A. Hsieh[1], I. Gadawski[1], H.C. Côté[1,2,3], the CIHR Team in Cellular Aging and HIV Comorbidities in Women and Children (CARMA)
[1]University of British Columbia, Vancouver, Canada, [2]Centre for Blood Research, Vancouver, Canada, [3]Women's Health Research Institute, Vancouver, Canada

Background: NRTIs inhibit mitochondrial polymerase gamma, which can deplete mtDNA. However, mitochondrial dysfunction is not always associated with mtDNA depletion. PIs and NNRTIs can induce oxidative stress and mtDNA damage that can stimulate compensatory mitochondrial biogenesis. We evaluated the effects of individual ARVs and two cART regimens on mtDNA quantity and quality in cultured cells.
Methods: Immortalized human placental (JEG-3) and T lymphoblast (CEM) cells were cultured in the presence of NRTIs: ABC, AZT, FTC, TDF, 3TC, d4T (+control), NNRTIs: EFV, NVP, and PIs: LPV, NFV, all at 1x, 10x and 20× Cmax for 3 days, then harvested. The JEG-3 cells were also exposed to clinical (0.5x and 1× Cmax) concentrations of cART regimens used in HIV pregnancy: AZT/3TC/ LPVr and 3TC/TDF/EFV. After 21 days, the cells were returned to ARV-free medium for 10 days, to allow recovery. Cells were collected every 3 days. Growth rate, viability, mtDNA content and mtDNA apparent oxidative damage (AOD) were measured. Somatic mtDNA mutation burden was also quantified in a subset using an ultra-deep sequencing strategy.
Results: Both cells showed similar trends in response to ARVs. MtDNA content increased at 1x but depleted at 10x and 20x Cmax d4T while mtDNA content and AOD both increased in cells exposed to ABC, LPV and NFV. These effects were concurrent with substantially reduced growth rates. In cells exposed to EFV, a mixed effect was seen whereby mtDNA increased at 1× and 20x Cmax but decreased at 10× Cmax. Among all ARVs tested, EFV exerted the largest effect on growth rate, mtDNA content and AOD. Somatic mtDNA mutation burden (n=1, 20x Cmax ARV) was d4t>>EFV>NFV=control. In JEG-3 cART-exposed cultures, mtDNA increased significantly from day 3 to 21, followed by a rapid decline early in recovery phase. Both cART regimens led to increased mtDNA AOD.
Conclusions: The opposite effects of ARVs on mtDNA content illustrate the need to evaluate ARVs alone and in combinations, using multiple mtDNA measures, as various mtDNA alterations could affect mitochondrial function, cellular metabolism and aging. The mtDNA effects seen here with EFV, LPV and ABC warrant further research given their increasing use in pregnancy.

TUPEB258

Hearing loss in HIV-infected children in Lilongwe, Malawi

S. Hrapcak[1,2,3], H. Kuper[4], P. Bartlett[5], A. Devendra[2], A. Makawa[2], M. Kim[1,2,3], P. Kazembe[1,2,3], S. Ahmed[1,2,3]
[1]Baylor College of Medicine, Houston, United States, [2]Baylor College of Medicine - Children's Foundation - Malawi, Lilongwe, Malawi, [3]Baylor International Pediatric AIDS Initiative at Texas Children's Hospital, Houston, United States, [4]London School of Hygiene & Tropical Medicine, International Centre for Evidence in Disability, London, United Kingdom, [5]African Bible College, Lilongwe, Malawi
Presenting author email: susan.hrapcak@gmail.com

Background: With improved access to pediatric antiretroviral therapy (ART), HIV infection has become a chronic illness. Preliminary data suggest that HIV- infected children have a higher risk of disabilities such as hearing impairment. This study aimed to estimate the prevalence and types of hearing loss in HIV-infected children in Lilongwe, Malawi.
Methods: This was a cross-sectional survey of 380 HIV-infected children aged 4-14 years attending ART clinic in Lilongwe, December 2013-March 2014. Data was collected through pediatric quality of life (PedsQL™) and sociodemographic questionnaires that were translated into Chichewa and reviewed with a research assistant, review of the electronic medical record, and audiologic testing for all participants. Hearing loss was defined as hearing loss >20 dB in either ear. Predictors of hearing loss were explored by multiple regression analysis generating age- and sex- adjusted odds ratios. Children with significant hearing impairment were fitted with hearing aids.
Results: Of the 380 recruited patients, 24% of patients had hearing loss in either ear. 82% of the hearing loss was conductive, 14% was sensorineural, and 3% was mixed. Twenty-one patients (23% of those with hearing loss) were referred by audiologists for hearing aid fitting. There was a higher prevalence of hearing loss in children with history of frequent ear infections (OR 7.4, 4.2-13.0) and ear drainage (OR 6.4, 3.6-11.6). Hearing loss was linked to history of WHO Stage 3 (OR 2.4, 1.2-4.5) or Stage 4 (OR 6.4, 2.7-15.2) and history of malnutrition (OR 2.1, 1.3-3.5), but not to duration of ART or measures of CD4. Only 40% of caregivers accurately perceived that their child had hearing loss. Children with hearing loss were less likely to attend school and had poorer emotional (p= 0.02) and school functioning (p = 0.04).
Conclusions: Hearing loss was common among children with HIV, and can affect school functioning and quality of life. Many children with hearing loss qualified for hearing aids. Caregivers were not reliable at identifying hearing loss. There is therefore an urgent need for improved screening and identification of hearing problems in HIV-infected children to treat this disability, especially in resource-limited settings.

TUPEB259

Serious non-AIDS events and biomarker changes in HIV-1-infected individuals

M. Sunil[1], N. Utay[2], R. Arduino[1,3], M. Martinez[1], X. Yu[3], A. Somasundaram[2], M. Nigalye[2], T. Bell[1]
[1]University of Texas Health Science Center, Houston, United States, [2]University of Texas Medical Branch, Galveston, United States, [3]Baylor College of Medicine-UT-Houston Center for AIDS Research, Houston, United States
Presenting author email: tanvir.k.bell@uth.tmc.edu

Background: HIV-1-infected individuals may experience serious non-AIDS events (SNAEs) despite suppressive antiretroviral therapy (ART), possibly from ongoing immune activation. Increased circulating levels of soluble CD14 (sCD14), soluble CD163 (sCD163) and interleukin-6 (IL-6) at a single time point have been associated with SNAEs. However, it is unknown if trends in these biomarker levels can predict the SNAEs.
Methods: We retrospectively reviewed 284 HIV-1-infected individuals with prospectively collected plasma samples from a single center. We identified 39 SNAEs (14 major cardiovascular events, 4 end stage renal disease, 3 decompensated cirrhosis, 12 non-AIDS-defining malignancies and 6 death of unknown cause) and 39 age- and gender-matched controls. sCD14, sCD163 and IL-6 were analyzed at baseline (T1) and proximal (T2) to the event (or equivalent duration in matched controls). Biomarker changes between T1 and T2 within each group and the differences in changes between two groups were tested using Wilcoxon signed rank test.
Results: Median age of cases and controls were 58 and 57 years, respectively; 79% were male. Median time between T1 and T2 of cases and controls were 34 and 35 months, respectively. 74% and 67% of cases and controls were respectively co-infected with HCV. At T2, 87% and 97% of cases and controls were on ART, and 59% and 72% of cases and controls had undetectable plasma HIV RNA levels, respectively. Table 1 shows median sCD14, sCD163 and IL-6 levels, median change between T1 and T2 in cases and controls; and the median difference in change from T1 to T2 for each case-control pair (change in case minus change in control). Similar results were obtained when evaluating the changes normalized for the time between T1 and T2. HCV co-infection status had no significant association with biomarker levels.

Marker	Cases			Controls			Median (range) difference in change case-control
	T1 Median (range)	T2 Median (range)	Change from T1 Median (range)	T1 Median (range)	T2 Median (range)	Change from T1 Median (range)	
sCD14 (µg/mL)	2.06 (1.20-3.18)	1.79 (0.64-3.29)	-0.12 (-1.82-0.78) *P*=0.14	1.93 (1.13-3.50)	1.52 (0.52-2.61)	-0.47 (-2.32-0.91) *P*<0.0001	0.15 (-2.17-1.87) *P*=0.01
sCD163 (ng/mL)	1978 (538-5655)	1671 (239-4466)	-286 (-2951-3192) *P*=0.02	1763 (554-5338)	1157 (397-4014)	-359 (-2639-1540) *P*=0.002	428 (-3032-2843) *P*=0.26
IL-6 (pg/mL)	2.83 (0.47-7.78)	3.84 (0.97-12.19)	-0.19 (-5.99-9.81) *P*=0.68	2.59 (0.54-12.81)	1.92 (0.82-7.59)	-0.15 (-10.89-3.34) *P*=0.04	1.08 (-6.55-14.64) *P*=0.02

[Table 1]

Conclusions: Overall, the biomarkers significantly decreased in both cases and controls during follow up, likely from ongoing ART. The decreases in sCD14, sCD163 and IL-6 were attenuated in the cases compared to controls and were statistically significant for sCD14 and IL-6 but not sCD163. Thus, both the absolute levels of inflammatory biomarkers and their rate of change over time may be relevant for predicting SNAE.

TUPEB260

Heterogeneity of preferences for antiretroviral drug regimens from the perspective of people living with HIV

A. Bayoumi[1,2], S. Miles[2], T. Lin[3], D. Regier[4], T. Antoniou[1,2], L. Park-Wyllie[5], C. Strike[6], J. Hoch[2,7], J. Raboud[6,8]
[1]University of Toronto, Toronto, Canada, [2]St. Michael's Hospital, Centre for Research on Inner City Health, Toronto, Canada, [3]Western University, London, Canada, [4]British Columbia Cancer Research Centre, Vancouver, Canada, [5]Toronto Central Local Health Integration Network, Toronto, Canada, [6]University of Toronto, Dalla Lana School of Public Health, Toronto, Canada, [7]University of Toronto, Institute of Health Policy, Management and Evaluation, Toronto, Canada, [8]University Health Network, Toronto, Canada
Presenting author email: ahmed.bayoumi@utoronto.ca

Background: Antiretroviral drug regimens vary in terms of efficacy, toxicity, and the potential for future cross-resistance. We conducted a discrete choice experiment and elicited preferences from people living with HIV to determine the relative importance of attributes of antiretroviral drug regimens and the degree of heterogeneity in participants' responses.
Methods: Participants completed a survey consisting of 16 choices sets; for each set, participants selected 1 of 3 hypothetical regimens, each characterized by one of four levels of the following six attributes: efficacy in suppressing viral load, cardiovascular risk, fracture risk, mood effects, pill burden, and the potential for future resistance. Participants also completed a consistency test and demographic and clinical questionnaires. We recruited a convenience sample from clinics and AIDS service organizations, with oversampling of women and black participants. We used generalized multinomial (random parameter) logit analysis and focused on two results. First, we analyzed whether participants have heterogeneous variance (scale sensitivity) in their responses and whether gender and ethnicity explained this variation. Second, we report the random parameters (regimen attribute levels) with the greatest standard deviations as an indication of preference heterogeneity.
Results: We analyzed data from 123 of 135 participants. Participants were willing to accept some inefficacy (risk of virologic failure) to avoid less convenient dosing, viral resistance, and all toxicities except wrist fracture. Participants exhibited significantly heterogeneous variance in their responses (scale parameter p-value < 0.001). Neither ethnicity nor gender explained this variance. The greatest preference heterogeneity of responses was for the attributes "greatly increase my chances of having a heart attack" and the potential for "resistance to other similar drugs is very high." The least preference heterogeneity was for the attributes related to moderately increased risks of hip and wrist fractures and for taking two pills once daily.
Conclusions: People living with HIV have heterogeneous preferences about antiretroviral therapy, particularly concerning severe cardiovascular toxicity and the potential for future resistance. In contrast, preferences for avoiding severe fractures and about pill burden are more homogeneous. Our results underscore the need to address a range of toxicities while maintaining convenient dosing regimens to meet patient-centered preferences for antiretroviral medications.

Clinical trials: phase III

TUPEB261

Safety and efficacy of DTG by age, race and gender: subgroup analysis of 96-week results from treatment-naïve patients in phase III trials [SPRING-2 (ING113086), SINGLE (ING114467) and FLAMINGO (ING114915)]

J. Koteff[1], R. Cuffe[2], C. Ganier[3], A. Zolopa[1], A. Murungi[2], B. Wynne[4], M. Aboud[2]
[1]ViiV Healthcare, Durham, United States, [2]ViiV Healthcare, London, United Kingdom, [3]GlaxoSmithKline, London, United Kingdom, [4]GlaxoSmithKline, Durham, United States
Presenting author email: justin.a.koteff@viivhealthcare.com

Background: DTG once-daily (QD) was well tolerated in ART-naïve studies and has shown comparable efficacy versus RAL (SPRING-2), favorable efficacy versus DRV (FLAMINGO) and as a regimen with abacavir/lamivudine (ABC/3TC) QD versus Atripla (EFV/FTC/TDF) QD (SINGLE). Analyses of 96-week safety and efficacy data by age, race and gender subgroups were evaluated.
Methods: SPRING-2 randomized subjects to DTG 50mg QD or RAL 400 mg BID, FLAMINGO randomized subjects to DTG 50mg or DRV/r QD. In both studies, investigator selected NRTIs (TDF/FTC or ABC/3TC). SINGLE randomized subjects to DTG 50 mg + ABC/3TC QD or EFV/FTC/TDF QD. Adverse event (AE) and response rates (by FDA Snapshot) at 96 weeks were summarized in subgroups: age (< vs ≥ 50 years), race (white vs non-white) and gender (male vs female).
Results: There were 1067 patients treated with DTG in the three clinical studies. Efficacy rates at 96 weeks remained high across subgroups and are described in Table 1. Additionally, safety summaries showed comparable grade 2-4 drug related AE's across subgroups. The rates of AEs leading to withdrawals were low across all DTG subgroups. There was some numerical variability in treatment differences in the smaller subgroups evaluated which was inconsistent across studies.

Proportion of Subjects with Plasma HIV-1 RNA <50 c/mL at Week 96 In Snapshot (Primay) Analysis; n/N (%)						
	SPRING-2		SINGLE		FLAMINGO	
	DTG	RAL	DTG	EFV/FTC/TDF	DTG	DRV/r
Overall	332/411 (81)	314/411 (76)	332/414 (80)	303/419 (72)	194/242 (80)	164/242 (68)
Age <50yr	295/370 (80)	277/365 (76)	290/361 (80)	271/375 (72)	174/214 (81)	134/206 (65)
Age ≥50yr	37/41 (90)	37/46 (80)	42/53 (79)	32/44 (73)	20/28 (71)	30/36 (83)
White	282/346 (82)	270/352 (77)	224/284 (79)	220/285 (77)	145/173 (84)	122/176 (69)
Non-White	50/65 (77)	44/59 (76)	108/130 (83)	82/133 (62)	49/69 (71)	42/66 (64)
Male	293/348 (84)	278/355 (78)	281/347 (81)	268/356 (75)	170/211 (81)	144/201 (72)
Female	39/63 (62)	36/56 (64)	51/67 (76)	35/63 (56)	24/31 (77)	20/41 (49)

[Table 1: Results by Demographic Subgroup]

Conclusions: In the three treatment naïve clinical trials DTG once daily was seen to be an effective and well tolerated treatment option across age, race and gender subgroups evaluated.

Timing of therapy initiation

TUPEB262

Short course versus deferred therapy for the treatment of HIV primary infection: a meta-analysis

J. Amin, PHIT, M Study Group
University of New South Wales, Kirby Institute, Sydney, Australia
Presenting author email: jamin@kirby.unsw.edu.au

Background: In recent years three randomised trials have been undertaken to ascertain whether short course antiretroviral therapy (ART) has benefit for persons with primary HIV infection. Each trial used varying definitions of "benefit" relating to CD4+T-cell counts (CD4+), viral load (VL) and long term ART initiation (ltART). We determined common estimates of effect across the three trials.
Methods: Available line listing data on participant follow up, CD4, VL and ART use were extracted from the Primo-SHM, SETPOINT (ACTG5217), and SPARTAC trials in 2013. We summarised CD4+ decline and ltART initiation using a common methodology across trials. The primary endpoint was time from randomisation to first of two consecutive CD4+ < 350 cells/mm^3 or ltART summarised as a between arm hazard ratio. Participants in the immediate treatment arm who did not interrupt therapy as mandated by protocol were assigned to have reached endpoint at the scheduled end of the immediate phase. Results were meta-analysed for comparisons between the deferred arm and the longest immediate treatment arm in each trial (weeks 60, 36 and 48 respectively). Data were combined using fixed effects methods.
Results: Time to primary endpoint was significantly increased in the immediate treatment arm (Table) compared to deferred ART. Of the 395 participants across all trial arms with CD4+ >350 cells/mm^3 at trial entry, 100 (18.8%) commenced ltART prior to CD4 decline < 350 cells/mm^3.

Trial	Arm	N	Events	Rate/ 1000 person weeks	95% CI	Median time to event/ weeks	Hazard Ratio	95% CI	
Primo-SHM	Deferred	36	31	12.8	9.0, 18.2	60.4			
	60 weeks	39	23	4.6	3.1, 6.9	110.5	0.3	0.2, 0.6	<0.01
SETPOINT	Deferred	64	24	7.2	4.9, 10.8	38.6			
	36 weeks	63	21	4.2	2.8, 6.5	72.0	0.6	0.3, 1.0	0.06
SPARTAC	Deferred	123	75	4.4	3.5, 5.5	135.3			
	48 weeks	118	61	3.3	2.5, 4.2	179.0	0.7	0.5, 1.0	0.08
Combined (fixed effects meta-analysis)							**0.6**	**0.3, 0.9**	**<0.01**
Q=6.4, df=2, p=0.041,I^2%=68.									

[Table. Time to first of two consecutive CD4+ <350 cells/mm^3 or commencement of long term ART]

Conclusions: Across all three trials immediate short term ART delayed disease progression or commencement of ItART. However the duration of immediate therapy accounted for much of the delay in this analysis. The high proportion of participants continuing or commencing ItART without reaching CD4 criteria likely reflects the current setting of guidelines promoting early treatment and at higher CD4 thresholds. As such an ART treatment strategy that requires interruption may be untenable.

TUPEB263

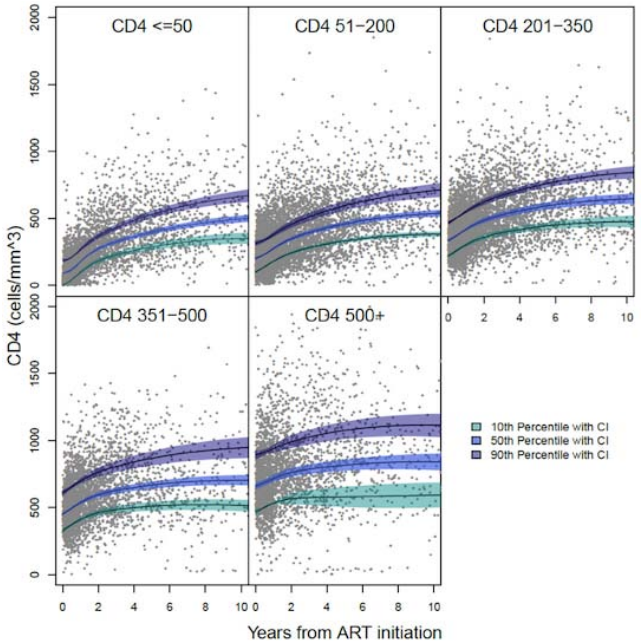
CD4 reconstitution is related to CD4 at effective antiretroviral treatment initiation

K. Calkins[1], J. Eron[2], A. Abraham[1], K. Buchacz[3], M. Horberg[4], J. Tate[5], S. Napravnik[2], R. Moore[1], R. Bosch[6], B. Lau[1]
[1]Johns Hopkins School of Public Health, Epidemiology, Baltimore, United States, [2]University of North Carolina, Chapel Hill, United States, [3]US Centers for Disease Control and Prevention (CDC), Division of HIV/AIDS Prevention, Atlanta, United States, [4]Kaiser Permanente Mid-Atlantic States, Rockville, United States, [5]Yale University School of Medicine, New Haven, United States, [6]Harvard School of Public Health, Boston, United States
Presenting author email: kcalkins@jhu.edu

Background: Despite almost 20 years of effective antiretroviral therapy (ART), the CD4 cell count (CD4) asymptote (i.e. maximum level of CD4 reconstitution) after treatment remains poorly characterized. Prior analyses examined the CD4 treatment response curve but not typical range of response or asymptote. We sought to better characterize CD4 reconstitution among individuals with optimal response to treatment.
Methods: HIV-infected individuals starting ART between 1996 and 2012 in NA-ACCORD were analyzed. Individuals that did not achieve viral suppression (< 500 copies/mL) within 1 year were censored. Those achieving initial viral suppression were censored at virologic failure (>500 copies/mL) or ART discontinuation. A natural cubic splines linear quantile mixed model was used to predict the typical CD4 response to ART (10th, 50th, and 90th percentiles) stratified by CD4 prior to treatment (≤50, 51-200, 201-350, 351- 500, and >500 cells/mm^3). Negative exponential mixed effects models with three random effects were used to identify the relationship between CD4 at ART initiation and CD4 asymptote, accounting for age, sex, race, hepatitis C coinfection at baseline, use of ART prior to start of an effective ART regimen, use of a protease inhibitor (PI) in initial ART regimen, and calendar period of ART initiation.
Results:

	Total Population (N=75,218)
Age median(IQR)	42.3 (35.6-49.3)
Female N(%)	13,423 (17.8%)
Non-Hispanic White N(%)	30,632 (40.7%)
PI in Initial ART N(%)	26,664 (35.4%)
Hepatitis C at ART initiation N(%)	8,905 (11.8%)
Prior ART use N(%)	19,768 (26.3%)
ART initiation pre-2000	27,087 (36.0%)

[Population Characteristics]



[Figure 1. Typical CD4 response to treatment (by strata of CD4 at ART initiation]

Baseline information on the 75,281 HIV-infected adults in the population is included in the table. The estimated individual level intercept and asymptote from the negative exponential model were strongly correlated (0.60 [0.59-0.62]) providing evidence that the maximum level of CD4 reconstitution is tied to an individual's CD4 at initiation of ART. The typical CD4 response (80% of individuals fall within curves) for each strata of CD4 prior to treatment was better with higher CD4 at ART initiation (Figure 1). However, the asymptote random effects suggest that a large proportion of individuals in each stratum reached CD4>500 cells/mm^3 (45%, 58%, 69%, and 76% for CD4 strata below 500).
Conclusions: The maximum level of CD4 reconstitution was determined in part by the CD4 level at ART initiation. CD4 counts above 500 cells/mm^3 were achievable even when initial CD4 was low; however likelihood of reaching this threshold decreased with lower CD4 at ART initiation.

First-line therapy

TUPEB264

Comparison of the effectiveness, tolerability and efficiency (cost-effectiveness) of an antiretroviral regimen administered as a single tablet regimen (STR) vs. multiple tablet regimens (MTR) in antiretroviral naïve HIV patients

J.M. Gatell[1], E. de Lazzari[1], J.M. Molina[2], S. Gallien[2], J. Gonzalez-Garcia[3], A. Imaz[4], D. Podzamczer[4], B. Clotet[5], J.M. Llibre[5], P. Domingo[6]
[1]Hospital Clinic, University Barcelona, Medicine, Barcelona, Spain, [2]Paris Diderot, St. Louis Hospital, Medicine, Paris, France, [3]Hospital La Paz, Medicine, Madrid, Spain, [4]Hospital Universitario de Bellvitge, Medicine, Barcelona, Spain, [5]Hospital Germans Trias i Pujol, Medicine, Badalona, Spain, [6]Hospital Sant Pau, Medicine, Barcelona, Spain
Presenting author email: gatell0@attglobal.net

Background: STR are generally recommended by guidelines. Despite higher direct cost, efficiency may be better when compared with MTR with same or different components.
Methods: All HIV antiretroviral naïve patients of 6 centers who initiated STR-Atripla®, with their components (Tenofovir+Lamivudine/Emtricitabine+Efavirenz or with Truvada® + Efavirenz; MTR-Atripla®-Components) or with a different multiple tablet regimen (MTR-Other) after June-2008 and before December-2011 were eligible. Effectiveness was measured as percentage of patients < 50 copies/ml. at 48 weeks by ITT (Missing or NC=Failure). Costs included the direct cost of antiretrovirals plus those related with outpatient visits, hospital admissions and resistance tests. Efficiency was the ratio between costs and effectiveness for the base case scenario and for the most and less favorable scenarios as a sensitivity analysis.
Results: 3736 patients (933 STR-Atripla®, 796 MTR-Atripla®-Components and 2007 MTR-Other) were included. Median age was 37 years, 82% were males, 14% were co-infected with HCV, 23% had a CD4+ cell count < 200 and 23% had viral load >100,000copies/ml. Median duration of assigned regimen was 2.2, 0.9 and 1.6 years for the STR-Atripla®, MTR-Atripla®-Components and MTR-Other respectively. Percentage of patients completing at least one year of follow-up was 95%, 94% and 91% in the STR-Atripla®, MTR-Atripla®-Components and MTR-Other respectively.Response rate (adjusted for baseline CD4+ count, viral load and hospital) at 48 weeks were 78%, 70% and 63% for STR-Atripla®, MTR-Atripla®-Components and MTR-Other respectively ($p < 0.0001$ for comparison of STR-Atripla® with the other two arms). Virological failure and interruptions for tolerance problems were 8% and 9% in the STR-Atripla®, 9% and 5% in the MDR-Atripla®-Components and 13% and 16% in the MDR-Other respectively. Cost per responder at 48 weeks (effectiveness) was 11,703 Euros in the STR-Atripla®, 11,210 Euros (0.95 times higher) in the MTR-Atripla®-Components and 17,484 Euros (1.49 times higher) in the MTR-Other . Similar trends were observed in the less and most favorable scenarios.
Conclusions: The efficiency of the STR-Atripla® and MTR-Atripla®-Components was similar but STR-Atripla® had a higher response rate. Both had a significantly better efficiency than the MTR-Other. Our data supports the recommendation of STR-Atripla® as opposed to MTR-Atripla®-Components (similar efficiency but lower effectiveness) o MTR-Other (worse efficiency).

TUPEB265

Treatment outcomes among older HIV-infected adults in Jos, Nigeria

P. Agaba[1], S. Meloni[2], H. Sule[1], R. Ojoh[3], O. Agbaji[4], S. Sagay[5], P. Okonkwo[6], J. Idoko[7], P. Kanki[2]
[1]University of Jos, Department of Family Medicine, Jos, Nigeria, [2]Harvard School of Public Health, Department of Immunology and Infectious Diseases, Boston, United States, [3]Jos University Teaching Hospital, AIDS Prevention Initiative in Nigeria, Jos, Nigeria, [4]University of Jos, Department of Medicine, Jos, Nigeria, [5]University of Jos, Department of Obstetrics and Gynaecology, Jos, Nigeria, [6]AIDS Prevention Initiative in Nigeria Lte, Abuja, Nigeria, [7]National Agency for the Control of AIDS, Abuja, Nigeria

Background: The proportion of older patients living with HIV in sub-Saharan Africa is increasing, despite inadequate prevention interventions targeted at this group. Our objectives were to compare baseline characteristics and outcomes to cART between older and younger patients in our clinical cohort in Jos, Nigeria.
Methods: Treatment-naive patients aged 15 years and above enrolled in care between 2004-2012 and commencing first-line cART were included in this analysis. We used descriptive statistics to compare baseline and treatment differences between older (50 years or older) and younger (15-49years) and Cox proportional hazard models to determine factors associated with all-cause mortality and loss to follow-up (LTFU) at 24 months.
Results: There were 10 991 patients with 860 (7.8%) aged 50 years or older. Older patients were more likely to be male (p< 0.001), married (p< 0.001), have no formal education (p< 0.001), and be unemployed (p=0.001) with a mean age of 55±5 years. Older patients had higher rates of viral suppression (< 400copies/ml) at 6 (p< 0.001), 18 (p=0.007) and 24 (p=0.006) months with comparable suppression at 12 (p=0.14) months. Older patients had significantly lower median CD4+ cell counts at most time points on cART except at 18 months (p=0.09) despite having higher counts at baseline.
In Cox proportional models stratified by age and adjusting for baseline and treatment variables, older age (aHR=1.81, CI; 1.02-3.21) and advanced clinical disease (aHR=1.63, CI; 1.28-2.07) were associated with mortality. Similarly, only advanced clinical disease (aHR=1.09, CI; 1.01-1.18) and male sex (aHR=1.12, CI; 1.03-1.22) were associated with LTFU.
Conclusions: Older patients in our cohort have poorer immunologic response and higher risk of mortality compared to younger patients despite having better viral suppression over 24 months. Age-appropriate interventions are encouraged to optimize outcomes among older patients in our setting.

TUPEB266

ANRS 12168 - DynaM-O: a 48 weeks-prospective study to compare the immuno-virological and clinical responses to HAART between HIV-1 group O and group M-infected patients

C. Kouanfack[1,2], M. Vray[3], A. Kfutwah[4], A. Aghokeng[2,5], R. Mougnutou[6], G. Unal[6], L. Le Fouler[3], L. Schaeffer[3], N. Noumsi[1], E. Alessandri-Gradt[7], E. Delaporte[2], F. Simon[8], J.-C. Plantier[7]
[1]Hôpital Central, Yaoundé, Cameroon, [2]Institut de Recherche pour le Développement, Montpellier, France, [3]Institut Pasteur de Paris, Paris, France, [4]Centre Pasteur du Cameroun, Yaoundé, Cameroon, [5]Institut de Recherches Medicales et d'Études des Plantes Medicinales, Yaoundé, Cameroon, [6]Site ANRS, Hôpital Central, Yaoundé, Cameroon, [7]CHU et Université de Rouen, Rouen, France, [8]Hôpital Saint Louis et Université Paris-Diderot, Paris, France
Presenting author email: charleskouanfack@yahoo.fr

Background: The divergent HIV-1 group O strains (HIV-1/O) are endemic in Cameroon and naturally resistant to NNRTI, largely used as first-line therapy in this country. Alternative therapeutic strategies are thus needed. DynaM-O is a prospective open-label study comparing the immuno-virological response to HAART, including two NRTI and one PI in HIV-1/O and HIV-1 group M (HIV-1/M) infected-naïve patients. Secondary objectives are to compare the kinetic of viral load responses, the CD4 restoration and the clinical events.
Methods: HAART was initiated in naïve patients with CD4 < 350/mm^3; HIV-1/O and HIV-1/M patients were matched on sex, age, CD4, Hb level and HBV status with ratio of 1:2. The primary endpoint was the percentage of patients having an undetectable viral load (VL < 60 cp/mL) at W48.
Results: 47 Cameroonian patients HIV-1/O and 94 HIV-1/M were included; results were available for 128 patients (13 died or were lost-to follow-up). At baseline, VL was significantly lower (p< 0.0001) in HIV-1/O with a median at 4.3 log cp/mL versus 5.1 in HIV-1/M. At W48, 86% of HIV-1/O samples were < 60 cp/mL vs 84% of HIV-1/M in per protocol analysis (p=0.62). In ITT analysis (missing=failure), the result was similar (79% vs 76% for HIV-1/O and HIV-1/M respectively, p=0.65). At baseline, median CD4 counts were well balanced between the two groups (227 vs 215, in HIV-1/O and HIV-1/M respectively, p=0.68); at W48, a +50% CD4 gain compared to baseline was observed for 60% vs 78% of the HIV-1/O and HIV-1/M patients respectively (p=0.03).
Conclusions: DynaM-O is the first and unique study analyzing the HAART responses in HIV-1/O infected patients compared to HIV-1/M patients. Data at W48 showed good efficacy of the regimens in both groups, but viral load was significantly lower at baseline in HIV-1/O. In contrast, the CD4 restoration was lower in HIV-1/O than that observed for HIV-1/M patients. Studying the mechanisms underlying these differences in response to HAART between these highly divergent HIV-1 strains are of importance in our understanding of the HIV natural history and to provide recommendations for HIV-1/O treatment and monitoring.

TUPEB267

"CD4 exploders" and "CD4 peak achievers" under ART in a large Italian cohort of HIV-infected subjects

M. Lichtner[1], A. Cozzi Lepri[2], S. Vita[3], G. Marchetti[4], A. Sarracino[5], A. Gori[6], C. Mussini[7], G. Madeddu[8], A. d'Arminio Monforte[9], Icona Foundation Study Group.
[1]Sapienza University of Rome, Dipartimento di Sanità Pubblica e Malattie Infettive, Rome, Italy, [2]UCL Medical School, Royal Free Campus, London, United Kingdom, [3]Sapienza University of Rome, Rome, Italy, [4]University of Milan, Department of Health Sciences, Clinic of Infectious Dis, Milan, Italy, [5]Bari University, Bari, Italy, [6]Unità Operativa di Malattie Infettive, Azienda Ospedaliera S. Gerardo-Università Milano Bicocca, Monza, Italy, [7]Clinic of Infectious Diseases, University of Modena and Reggio Emilia, Modena, Italy, [8]Clinic of Infectious Diseases, University of Modena and Reggio Emilia, Sassari, Italy, [9]San Paolo Hospital, Milan, Italy
Presenting author email: giulia.marchetti@unimi.it

Background: cART treated PLHIV gaining a large amount of CD4+ T-cells over a short time ('CD4-exploders'; *CD4e*) or reaching a very high absolute CD4 count ('CD4 peak achievers'; *CD4pa*) have been recently described. We aimed to characterize these subjects and investigate whether the rate of morbidity/mortality of CD4e or CD4pa may differ from patients who have not present this peculiar CD4 cART responses.
Methods: We included naïve patients from Icona cohort who have undetectable viral load upon starting cART-. Individuals who gained CD4 >600 cells/mm3 above pre-ART and maintained it for ≥2 consecutive analysis were defined as *CD4e*; those who achieved a CD4 >1000 cells/mm3 were defined as *CD4pa*. We estimated the frequency of CD4e and CD4pa by 3 years of suppressive cART and identified factors independently associated with the chance of CD4e/CD4pa using standard survival analysis (Kaplan-Meier curves, Cox model). Participants were further classified according to whether by 3 years of cART they belonged to CD4e or CD4pa and survival analysis was used to compare their risk of sNAE/death.
Results: 5,795 subjects were included: by 3 years, the cumulative incidence of CD4e and CD4a was 12% [95% CI (10.8-13.1)] and 10% (8.9-1.9). In multivariable analysis, older age (HR=0.79 per 10 years, 95% CI: 0.71-0.86) and HCV (HR=0.73, 95% CI: 0.54-1.00) were associated with lower chance of CD4e profile. Initiation with PI-based therapy increased the probability of an exploding CD4 response (HR=1.52, 95% CI: 1.28- 1.82). Factors independently associated with greater chance of CD4pa were younger age, without HCV, having started a PI-based regime and a higher CD4 nadir (HR=1.53 per 100 cells/mm3, 95% CI: 1.47-1.59,). Compared to others, subjects with CD4e had a reduced risk of sNAE/deaths (p=0.03) while little difference was observed for CD4pa (p=0.15).
Conclusions: By 3 years of effective cART approximately 10% of patients present an extreme CD4 count recovery. Such a CD4 count response is more likely in younger, without HCV and who started a PI-based therapy. People CD4e tended to have a subsequent lower risk of sNAE/death, suggesting that a fast kinetic of immune recovery might be more important than the absolute number achieved.

	Hazard Ratio (95% CI) p-value			
	Unadjusted		Adjusted*	
Characteristics				
CD4 exploder	1.00		1.00	
No	0.41 (0.18, 0.95)	0.038	0.40 (0.14, 1.16)	0.093
Yes				
CD4 peak achiever				
No	1.00		1.00	
Yes	1.38 (0.47, 4.04)	0.563	1.39 (0.46, 4.21)	0.565
*Adjusted for gender, age, mode of HIV transmission, time since HIV diagnosis, type of cART started (PI- vs. NNRTI-based), HCV co-infection, CD4 nadir, HBV and CMV co-infection and CD4/CD8 ratio				

[Table 1. Hazard ratios of SNAE/death from fitting a Cox regression model]

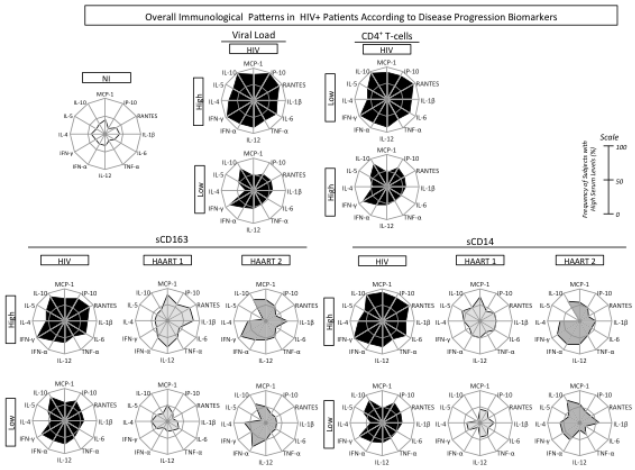
Second-line therapy

TUPEB268

HIV-1+ patients submitted to second line therapy display a comparable immunological biosignature to HIV+ untreated patients while first line therapy partially recovers immune response to a non-infected status

M.S. Espindola[1], L.J.G. Lima[1], L.S. Soares[1], M.C. Cacemiro[1], F.A. Zambuzi[1], V.S. Brauer[1], V.R. Bollela[1], M.S. Gomes[2], O.A. Martins-Filho[3], F.G. Frantz[1]
[1]University of Sao Paulo, Ribeirão Preto, Brazil, [2]Federal University of Uberlandia, Patos de Minas, Brazil, [3]René Rachou Research Center, FIOCRUZ, Belo Horizonte, Brazil
Presenting author email: frantz@usp.br

Background: Successful highly active antiretroviral therapy (HAART) has changed the outcome of AIDS worldwide. The complete suppression of viremia improves health and prolongs life expectancy of HIV-1+ patients. Few highlights are given to immunological profile of patients under distinct HAART regimens. This work aims to clarify the differences in the immune pattern of HIV-1+ patients under the first or second line HAART.
Methods: A systems biology approach was used to compare brazilian Non-infected (NI) (n=66), HIV-1+ untreated (HIV-1+)(n=46), HIV-1+ treated with NRTIs+NNRTIs (HAART1)(n=15) or NRTIs+IP patients (HAART2)(n=15). Plasma biomarkers levels of MCP-1,RANTES,IP-10,IL-1β,IL-6,TNF-α,IL-12,IFN-α,IFN-γ,IL-4,IL-5 and IL-10 were measured using a multiplex platform and sCD14 and sCD163 by ELISA. To correlate disease progression with immunological profile, HIV-1+ patients were classified into slow or rapid progressors and radar charts were constructed using the frequency (%) of high producers. Changes above 50% were considered relevant. Spearman correlation was used to define the biomarkers networks. A heatmap showing the Z-score of each biomarker was produced to verify the distance between the four groups.
Results: Considering disease progression, we found that the immunological biosignature of HIV-1+ patients is characterized by exacerbated inflammation among rapid progressors, as seen by increased frequency (above 75%) of biomarkers high producers, and moderate among slow progressors. HAART reduces exacerbated inflammation even in rapid progressors, however, biosignature of HAART1 is closer to NI individuals especially in slow progressors, while the use of HAART2 induces a moderate inflammation in rapid progressors that remains in the slow progressors, which approximates HAART2 pattern to HIV-1+.



[Immunological Patterns of HAART Regimens]

Network correlations showed that differences in IP-10, TNF-α, IL-6, IFN-α and IL-10 interactions were primordial in HIV disease and treatment. Use of HAART2 induced a completely different network profile, with the loss of most NI interactions. Heatmap showed that the best segregation biomarkers were IP-10>TNF-α>IFN-α, respectively. Additionally, most HAART1 patients were inserted into NI pattern, while most of HAART2 patients presented similar biomarkers patterns to HIV-1+.
Conclusions: By using a systems biology approach, we concluded that patients in different HAART regimens develop distinct immunological biosignature, giving rise to a novel perspective into disease outcome and scientific analysis, considering HAART patients as a heterogeneous group.

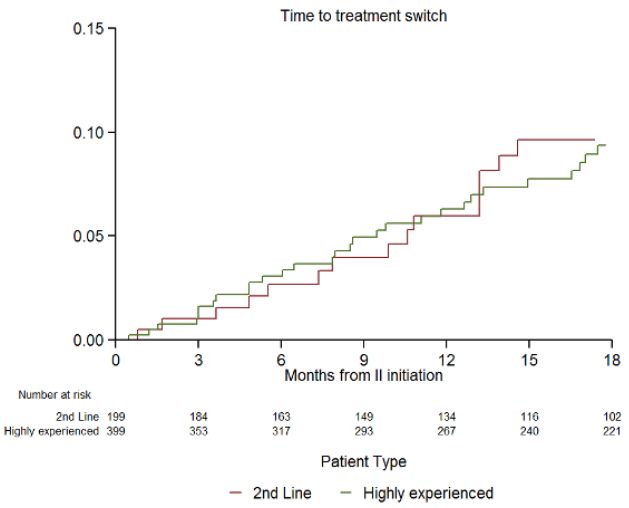
Therapy in highly treatment-experienced persons

TUPEB269

Regimen switching and virological response in treatment experienced HIV+ patients receiving an integrase inhibitor based regimen: an Australian cohort study

N. De La Mata[1], D. Cooper[1], D. Russell[2,3,4], D. Smith[5,6], I. Woolley[7,8,9], M. O-Sullivan[10], S. Wright[1], M. Law[1]
[1]Kirby Institute, UNSW, Sydney, Australia, [2]James Cook University, Townsville, Australia, [3]University of Melbourne, Parkville, Australia, [4]Cairns Sexual Health Service, Cairns, Australia, [5]The Albion Centre, Sydney, Australia, [6]School of Public Health and Community Medicine, UNSW, Sydney, Australia, [7]Monash Health, Infectious Diseases, Melbourne, Australia, [8]Monash Health, Australia Department of Medicine, Melbourne, Australia, [9]Monash University, Australian Department of Infectious Diseases, Melbourne, Australia, [10]Gold Coast Sexual Health Clinic, Miami, Australia
Presenting author email: ndelamata@kirby.unsw.edu.au

Background: Integrase inhibitors (II) offer a new option for treatment experienced patients as they reduce viral replication more rapidly than other drug classes. The aim of this study is to describe treatment durability and virological outcomes using II regimens in treatment experienced HIV+ patients receiving care outside of clinical trials.
Methods: We included patients from the Australian HIV Observational Database who have been on an II regimen for longer than 14 days and had previous treatment regimens (n=598). Patient follow-up was to March 2014. There were two groups of patient treatment experience: 2nd line patients and highly experienced patients. Highly experienced patients were those who had experienced all 3 main ARV classes (NRTI, NNRTI and PI) while all other patients were considered 2nd line patients. Survival methods were used to determine time to viral suppression and time to regimen switching, stratified by patient treatment experience. Factors evaluated as associated with regimen switching included age, gender, hepatitis B co-infection, hepatitis C co-infection, previous time on ART, patient treatment experience and baseline viral load.
Results: Time to viral suppression from II initiation was similar for 2nd line and highly experienced patients, with a probability of achieving viral suppression by 6 months of 80% for 2nd line patients and 70% for highly experienced patients. There were 60 occurrences of regimen switches observed over 1056.0 person-years of follow up, a crude rate of 5.68 (4.41, 7.32) per 100 person-years. Time to regimen switching was similar for 2nd line and highly experienced patients during the 18 months follow up, with a 6% probability of regimen switching after 12 months for 2nd line patients and highly experienced patients. Patient treatment experience was not a significant factor for regimen switching in the multivariate analysis, adjusting for relevant covariates.



[Time to treatment switch from II initiation]

Conclusions: We found that II regimens were potent and durable in experienced HIV+ patients receiving treatment outside clinical trials. These results confirm the role of II regimens as a robust treatment option.

Simplification (with one- or two-agent regimens) and switch studies

TUPEB270

Switch from PI/rtv +2 nucleos(t)ides to RPV+DRV/rtv maintains HIV suppression and is well tolerated

F. Maggiolo[1], D. Valenti[1], A. Callegaro[2], E. Di Filippo[1], G. Gregis[1], M. Rizzi[1]
[1]AO Papa Giovanni XXIII, Infectious Diseases, Bergamo, Italy, [2]AO Papa Giovanni XXIII, Microbiology and Virology Lab, Bergamo, Italy
Presenting author email: franco31556@hotmail.com

Background: A nucleos(t)ides (NRTI) free regimen may be useful in selected patients who developed NRTI related toxicity. We report the week (W) 24 results of a pilot, prospective, randomized, ongoing trial of switch to a dual regimen rilpivirine + ritonavir-boosted darunavir (RPV+DRV/r).
Methods: Virologically suppressed subjects on PI/r + FTC/TDF or 3TC/ABC for > 6 months were randomized (1:1) to switch to RPV+DRV/r or remain on their baseline 3 drugs regimen (control). Eligibility criteria included no documented resistance to RPV and no HBV co-infection. The primary endpoint was the proportion of subjects who maintained HIV-RNA < 50 copies/ml at W24 by FDA snapshot algorithm (12% noninferiority margin).
Results: Sixty subjects (80% male, 22% with a previous diagnosis of AIDS, mean age 48 years) were randomized and treated (30 RPV+DRV/r; 30 controls). At randomization FTC/TDF was used in 83% of subjects and the most commonly used PIs were ritonavir-boosted atazanavir (57%) and ritonavir-boosted darunavir (35%). Median years since first ARV use was 6.2 and median number of regimens 3. The mean CD4 count was 623 cells/mcL and baseline characteristics were similar between the groups. At W24 100% of subjects who switched to RPV+DRV/r maintained HIV-RNA < 50 copies/ml compared to 86.7% of controls (difference 13.3%, 95% CI -1.1% to +25.4%). There was no confirmed virologic failure and, at W24, HIV-RNA was < 3 copies/ml in 66.7% of subjects in either group. Compared to controls, subjects on RPV+DRV/r experienced a greater CD4+ increment (mean +24 vs -13 cells/mcL), CD8+ decrement (mean -4 vs +17 cells/mcL) and CD8+CD38+HLA*DR+ decrement (mean -3.3 vs +1.2%). There was no AE leading to drug discontinuation. At W24 there was a lower increment in fasting triglycerides for RPV+DRV/r (+10 mg/dl vs +23mg/dl) and a larger increment in both total (+14 mg/dl vs -0.7 mg/dl) and HDL cholesterol (+0.6 mg/dl vs -4.2 mg/dl).
Conclusions: Switching to RPV+DRV/r compared to continuing a PI/r + FTC/TDF or 3TC/ABC demonstrated virologic non inferiority. RPV+DRV/r presented slight immunologic advantages and was well tolerated with a favorable safety profile. Switching to this NRTI free regimen may be an option for patients experiencing NRTI related toxicity.

Pharmacology / pharmacokinetics / pharmacogenomics / role of therapeutic drug monitoring

TUPEB271

Renal safety of tenofovir and amphotericin co-administration in treatment of cryptococcal meningitis

R. Kiggundu[1], B.M. Morawski[2], N.C. Bahr[2], A. Musubire[1], D. Williams[2], K. Huppler Hullsiek[2], M. Abassi[2], J.R. Rhein[2], D.B. Meya[1], D. R Boulware[2]
[1]Infectious Disease Institute, Makerere University, Kampala, Uganda, [2]University of Minnesota, Minneapolis, MN, USA, Minneapolis, MN, USA, United States
Presenting author email: reubenkaaja@yahoo.com

Background: Tenofovir (TDF) and Amphotericin B deoxycholate (Amphotericin) are associated with kidney impairment, but the effect of TDF and Amphotericin co-administration on renal function is poorly characterized. We assessed kidney function during cryptococcal meningitis treatment and at 4-weeks post-diagnosis in patients receiving concomitant Amphotericin and TDF.
Methods: Serum creatinine was measured in 160 participants enrolled in a clinical trial investigating the survival benefit of adjunctive sertraline compared with standard antifungal therapy for the treatment of cryptococcal meningitis in Uganda. At diagnosis, participants were classified as not receiving antiretroviral therapy (ART), receiving non-TDF ART, or receiving ART including TDF. Creatinine concentrations were measured on days 1, 3, 7, 10, 14, and 28 of follow-up, and kidney function was classified per the DAIDS Adverse Events grading system. Non-parametric tests and competing-risks regression evaluated differences across ART groups.

Results:

	No ART (n=91)		ART no TDF (n=27)		ART with TDF (n=42)		P-value
Median [IQR] Creatinine Concentrations, mg/dL [1]							
Diagnosis	73	0.68 [0.58-0.81]	25	0.60 [0.48-0.71]	36	0.64 [0.53-0.79]	0.08
14 Days	60	1.11 [0.87-1.34]	18	0.83 [0.80-1.51]	27	0.97 [0.78-1.50]	0.63
28 Days	43	0.89 [0.69-1.10]	14	0.92 [0.70-1.11]	26	1.02 [0.84-1.15]	0.67
Creatinine Adverse Event Incidence [2]							
No AE	74 (81.3%)		22 (81.5%)		34 (81.0%)		0.94
Grade 2	13 (14.3%)		3 (11.1%)		6 (14.3%)		
Grade 3	3 (3.3%)		2 (7.4%)		2 (4.8%)		
Grade 4	1 (1.1%)		0 (0%)		0 (0%)		
Cumulative Incidence of Grade 2-4 Renal Adverse Event through 1 month [3]							
Incidence (95% CI)	0.18 (0.12-0.24)		0.19 (0.13-0.25)		0.16 (0.11-0.22)		0.85

[1]Kruskal Wallis rank test; [2]Fisher's Exact test; [3]Competing-risks regression

[Table 1. Incidence of grade 2, 3 and 4 creatine advrse events by baseline ART use]

At meningitis diagnosis, 17% (27/160) of patients were receiving non-TDF ART, 26% (42/160) were receiving ART with TDF, and 57% (91/160) were not receiving ART. Renal-related adverse event incidence was similar across ART groups (Table 1). After 14 days of amphotericin therapy, median creatinine concentrations (mg/dL) were also similar across groups: 1.11 (IQR: 0.87-1.34) among no ART, 0.83 (IQR: 0.80-1.51) among ART without TDF, and 0.97 (IQR: 0.78-1.50) among ART with TDF (p=0.63). At 4 weeks post-diagnosis, creatinine concentrations were approximately 0.3 mg/dL higher than at diagnosis but similar across groups, with medians of 0.89 (IQR: 0.69-1.10) without ART, 0.92 (IQR: 0.70-1.11) among ART without TDF, 1.02 (IQR: 0.84-1.15) among ART with TDF (p=0.67). During induction amphotericin therapy, ART was discontinued in 4.7% (2/42) of patients receiving TDF at diagnosis, and no patients receiving ART without TDF.
Conclusions: In persons with cryptococcal meningitis receiving amphotericin-based therapy, no differences in kidney-related adverse events or median serum creatinine were observed up to 4 weeks after amphotericin initiation, based on receipt of ART with or without TDF. TDF and Amphotericin co-administration did not substantially increase the risk of renal dysfunction. Among persons on ART presenting with cryptococcal meningitis, further study of patient management and their outcomes is necessary.

TUPEB272

The pharmacokinetic profiles of dolutegravir in Japanese HIV-1-infected patients

M. Takahashi[1], M. Mizutani[2], M. Kato[2], H. Togami[2], S. Matsumoto[2], Y. Yokomaku[3]
[1]National Hospital Organization Suzuka National Hospital, Pharmacy, Suzuka, Japan, [2]National Hospital Organization Nagoya Medical Center, Pharmacy, Nagoya, Japan, [3]National Hospital Organization Nagoya Medical Center, Clinical Research Center, Nagoya, Japan
Presenting author email: masaakit@hosp.go.jp

Background: Dolutegravir is a second-generation HIV-1 integrase inhibitor that is high potent against both wild-type and drug-resistant HIV-1 strains. The quantification of dolutegravir in human plasma is important to support clinical studies. Dolutegravir was just approved at April 2014 in Japan. Therefore, pharmacokinetic study of dolutegravir for Japanese is still not clear. We intended to develop a conventional method for determining plasma dolutegravir concentrations and compare plasma dolutegravir concentrations of Japanese HIV-1 infected patients with that of foreign patients.
Methods: We used a Waters Alliance 2695 HPLC and a Micromass ZQ-2000 MS, controlled with MassLynx version 4.0 software. Our method involves rapid liquid-liquid drug extraction from plasma and use of gradient elution on a reversed-phase C18 column. We recruited 31 Japanese HIV-1-infected patients who were treated with dolutegravir containing regimen in Japan. All patients had been administered with 50mg dolutegravir once daily in combination with other antiretrovirals.
Results: The established LC-MS method was validated by estimating the precision and accuracy for inter- and intra-day analysis in the concentration range of 79-4012 ng/ml. The calibration curve was linear in this range. Relative standard deviations of both inter- and intraday assays were less than 4.3 %. In this study, mean dolutegravir plasma concentration for Japanese patients at trough was 0.54±0.38 μg/ml. Mean dolutegravir concentration at peak was 3.32±0.62 μg/ml. A calculated elimination half-life was 12 hours and AUC was 40.7 μg·h/ml. These values were similar with dolutegravir concentrations seen in foreign HIV-1-infected patients' trials.
Conclusions: Our LC-MS method can be used conveniently in clinical routine application and enables the study on the pharmacokinetics of dolutegravir in conventional hospital laboratories. In this study, the pharmacokinetic profile of dolutegravir in Japanese were similar with that of foreigner. In general, body build of Japanese is poor in comparison with Caucasian. As a result, high plasma dolutegravir concentrations may result in dose reduction for Japanese. However, our data showed that the dose adjustment of dolutegravir is not also required for Japanese HIV-1-infected patients.

TUPEB273

Composite *CYP2B6*/*CYP2A6* genotype and risk for suicidality among HIV-infected individuals randomly assigned to initiate efavirenz-containing regimens in AIDS Clinical Trials Group studies

K.R. Mollan[1], C. Tierney[2], J.J. Eron[3], M. Hudgens[1], R.M. Gulick[4], R. Haubrich[5], P.E. Sax[6], T.B. Campbell[7], E.S. Daar[8], K.R. Robertson[9], Q. Ma[10], D.W. Haas[11], AIDS Clinical Trials Group
[1]University of North Carolina at Chapel Hill, Center for AIDS Research, Chapel Hill, United States, [2]Harvard T.H. Chan School of Public Health, Center for Biostatistics in AIDS Research, Boston, United States, [3]University of North Carolina at Chapel Hill, Department of Medicine, Chapel Hill, United States, [4]Weill Cornell Medical College, Department of Medicine, New York, United States, [5]University of California, Department of Medicine, San Diego, United States, [6]Brigham and Women's Hospital and Harvard Medical School, Department of Medicine, Boston, United States, [7]University of Colorado School of Medicine, Department of Medicine, Denver, United States, [8]Harbor-UCLA Medical Center, David Geffen School of Medicine at UCLA, Los Angeles, United States, [9]University of North Carolina at Chapel Hill, Department of Neurology, Chapel Hill, United States, [10]University at Buffalo, Department of Pharmacy Practice, Buffalo, United States, [11]Vanderbilt University School of Medicine, Department of Medicine, Nashville, United States

Background: Efavirenz (EFV)-containing regimens were associated with increased hazard of suicidality in a pooled analysis of four AIDS Clinical Trials Group (ACTG) studies wherein antiretroviral-naive individuals were randomly assigned to initial antiretroviral regimens. Here we examined relationships between composite *CYP2B6*/*CYP2A6* genotypes, which predict higher plasma EFV levels, and suicidality among individuals who initiated EFV-containing regimens.
Methods: Analyses included White, Black, and Hispanic participants in the United States from ACTG studies A5095, A5142, A5175, and A5202. Suicidality was defined as reported suicidal ideation, attempted, or completed suicide. Composite genotypes that predict 12 increasing plasma EFV exposure levels were defined by *CYP2B6* (15582C→T, 516G→T, 983T→C) and *CYP2A6* (-48T→G). Levels were also collapsed into extensive (levels 1-2), intermediate (3-7), and slow (8-12) metabolizer groups. Association between genotype and time to suicidality was evaluated with a Cox proportional hazards model stratified by race/ethnicity. Separate analyses were performed for EFV exposed (all follow-up after initiation) and EFV on-treatment (OT, follow-up from initiation to permanent discontinuation +28 days) groups.
Results: Genotypes were available for 1656 (74%) of 2239 EFV recipients, including 41 (87%) of 47 with suicidality. Of the 1656 participants, 43%, 36%, and 21% were White, Black, and Hispanic, respectively. Ordinal genotype (12 levels) was not significantly associated with suicidality by exposed analysis (hazard ratio (HR)=1.10 per level, 95% CI: 0.96, 1.24, p=0.16), but was by OT analysis (HR=1.15 per level, 95% CI: 1.00, 1.31, p=0.044). Results were similar after covariate-adjustment for sex, age, body weight, injection drug use history, and documented psychiatric history or psychoactive medication within 30 days before study entry. Estimated HRs for genotype by OT analysis in White, Black, and Hispanic participants were 1.38 (95% CI: 1.14, 1.68), 0.93 (95% CI: 0.74, 1.17), and 1.20 (95% CI: 0.86, 1.69), respectively (interaction p=0.036). Compared to extensive metabolizers, estimated HRs for suicidality by OT analysis were 1.65 (95% CI: 0.74, 3.68) in intermediate metabolizers and 3.09 (95% CI: 1.11, 8.59) in slow metabolizers (p=0.097).
Conclusions: Composite *CYP2B6*/*CYP2A6* genotype that predicts increased plasma EFV exposure may have been associated with increased risk for suicidality among individuals who initiated randomly assigned EFV-containing regimens. This association may differ by race/ethnicity.

TUPEB274

Frequency of tablet remnants of nevirapine extended-release in stools and its impact on virological outcome in HIV-infected Taiwanese: a prospective cohort study

S.-Y. Chang[1], P.-Y. Wu[1], S.-P. Yang[1], J.-Y. Zhang[1], Y.-Z. Luo[1], W.-C. Liu[2], Y.-C. Su[3], M.-J. Wu[3], S.-Y. Chang[3], S.-W. Lin[4], C.-C. Hung[2]
[1]National Taiwan University Hospital, Center for Infection Control, Taipei City, Taiwan, Province of China, [2]National Taiwan University Hospital, Internal Medicine, Taipei City, Taiwan, Province of China, [3]National Taiwan University Hospital, Laboratory Medicine, Taipei City, Taiwan, Province of China, [4]National Taiwan University Hospital, Pharmacy, Taipei City, Taiwan, Province of China

Background: Presence of tablet remnants of nevirapine extended-release (NVP XR) in stools has been reported to occur in 1-3% of the subjects enrolled in clinical trials. The incidence may have been underestimated due to the information obtained by self-reporting.
Methods: Using a face-to-face questionnaire interview of the HIV-infected patients with switch to NVP XR plus 2 NRTIs between April to December 2014, we inquired about the frequency of noticing tablet remnants of NVP XR in stools. Clinical information was collected using a computerized data collection form. Patients were invited to participate in therapeutic drug monitoring (TDM) of plasma concentrations of NVP with the use of high-performance liquid chromatography (HPLC) 12 or 24 hours after the previous dose.
Results: During the 9-month study period, 244 patients switched to NVP XR plus 2 NRTIs and 49 patients (20.0%) noticed tablet remnants of NVP XR in stools. Compared with patients who did not notice tablet remnants, those who noticed tablet remnants in stools had a similar exposure duration to NVP XR before study was conducted (162 vs 155 days), were younger (34.4 vs 38.0 years), and had a higher mean CD4 count before switch to NVP XR (612 vs 495 cells/mm^3), but a similar plasma HIV RNA load (PVL) (1.55 vs 1.66 $\log_{10}$ copies/ml). After switch to NVP XR, the patients noticing tablet remnants tended to have a lower plasma HIV RNA load (1.39 vs 1.52 $\log_{10}$ copies/ml, *P*=0.07) and higher CD4 count (626 vs 547 cells/mm^3, *P*=0.05) than those without noticing tablet remnants within a mean interval of 3 months, despite the finding that the 20 patients in the former group who underwent TDM had a lower median NVP plasma concentration at 12 hours of dosing than the 17 patients in the latter group (3.55 vs 5.7 ng/ml).
Conclusions: We found that presence of tablet remnants of NVP XR is not infrequent in HIV-infected Taiwanese and was associated with a lower NVP plasma concentrations, which did not have an adverse impact on the virological and immunological responses.

TUPEB275

Bioequivalence of two dosage strength fixed-dose combination formulations of F/TAF

J. Zack, S. West, M. Rhee, R. Yu, A. Vu, B. Kearney
Gilead, Foster City, United States
Presenting author email: julia.zack@gilead.com

Background: Tenofovir alafenamide (TAF) is a novel prodrug of tenofovir (TFV) being developed as a 'backbone' fixed-dose combination (FDC) with emtricitabine (FTC, F) for the treatment of HIV-1 infection in combination with 3rd agents. Co-administration of TAF within a regimen containing ritonavir (RTV) or cobicistat (COBI,C) as a 'booster' results in a ~2.5-fold increase in TAF exposure via Pgp inhibition; TAF dosage strengths 10 mg and 25 mg target equivalent exposures in the boosted and unboosted states, respectively. Studies were conducted to determine the bioequivalence (BE) of the 2 dosage strengths of F/TAF FDC (200/10 mg and 200/25 mg) to the elvitegravir (EVG,E), COBI, FTC, TAF (E/C/F/TAF 150/150/200/10 mg) FDC, which established the safety and efficacy of TAF in Phase 3 studies.
Methods: Two randomized, open-label, single-dose, 2-way, crossover studies were conducted in healthy adult subjects. Single-dose PK of TAF and FTC were compared between F/TAF FDC (F/TAF 200/25 mg in Study 1 and F/TAF 200/10 mg + EVG + COBI in Study 2) and E/C/F/TAF 150/150/200/10 mg FDC in the fed state. The studies were powered based on TAF C_{max}, the PK parameter with the greatest observed variability. BE of TAF and FTC was assessed using geometric least-squares mean (GLSM) ratios and associated 90% confidence interval (CI) compared to bounds of 80% to 125%. Safety was assessed throughout the studies.
Results: TAF and FTC exposures from F/TAF 200/25 mg (Study 1; N=116) and F/TAF 200/10 mg (Study 2; N=100) were comparable vs E/C/F/TAF, and in both studies, the 90% CI for GLSM of AUC_{last}, AUC_{inf}, and C_{max} for TAF and FTC were contained within the pre-specified BE bounds. (Table 1)In both studies, F/TAF and E/C/F/TAF were generally well tolerated. There were no deaths or adverse events (AEs) leading to study drug discontinuation; one subject in Study 2 experienced a serious AE following F/TAF administration, which was not related to study drug.

	TAF		FTC			
TREATMENT	F/TAF 200/25 mg N=116	E/C/F/TAF N=116	F/TAF 200/25 mg N=116	E/C/F/TAF N=116	TAF GLSMR % (90% CI)	FTC GLSMR % (90% CI)
AUClast (h*ng/mL) Mean (%CV)	347 (43)	369 (41)	9420 (19)	10500 (20)	100 (96.5, 104)	90 (88.0, 91.2)
AUCinf (h*ng/mL) Mean (%CV)	396 (43)	390 (39)	9650 (19)	10700 (20)	98.5 (94.6, 103)	90.2 (89.1, 91.4)
Cmax (ng/mL) Mean (%CV)	281 (63)	268 (60)	1580 (27)	1600 (20)	104 (95.5, 112)	97.3 (94.6, 100)
TREATMENT	F/TAF 200/10 mg N=97	E/C/F/TAF N=99	F/TAF 200/10 mg N=97	E/C/F/TAF N=99	TAF GLSMR %(90% CI)	FTC GLSMR %(90% CI)
AUClast (h*ng/mL) Mean (%CV)	337 (34)	340 (34)	10200 (17)	10100 (16)	98.0 (94.7, 101)	99.8 (98.4, 101)
AUCinf (h*ng/mL) Mean (%CV)	352 (31)	354 (33)	10300 (16)	10300 (16)	98.3 (94.8, 102)	101 (98.2, 103)
Cmax (ng/mL) Mean (%CV)	302 (49)	310 (49)	1660 (19)	1660 (19)	96.9 (89.4, 105)	99.6 (96.8, 102)

[Tabe 1]

Conclusions: The two dosage strengths of F/TAF FDC are both bioequivalent to E/C/F/TAF FDC.

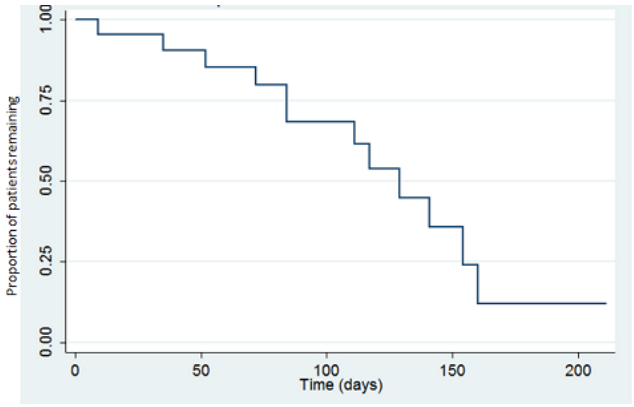
Drug interactions

TUPEB276

Rifabutin for treating tuberculosis in HIV-infected adult patients receiving boosted protease inhibitor containing ART regimen: experiences of neutropenia from an urban clinic

T. Mudzviti[1,2], T. Shamu[2], C. Chimbetete[2], C.C. Maponga[1,3], G.D. Morse[3]
[1]University of Zimbabwe, School of Pharmacy, Harare, Zimbabwe, [2]Newlands Clinic, Harare, Zimbabwe, [3]University at Buffalo, SUNY, Center of Excellence in Bioinformatics and Life Sciences, Buffalo, United States
Presenting author email: tmudzviti@yahoo.co.uk

Background: Rifabutin dosing during ritonavir co-administration remains a matter of debate due to the drug interaction between these medicines. While some studies have demonstrated that rifabutin 150 mg thrice weekly is inadequate, other studies in healthy subjects suggest that rifabutin 150 mg on alternate days, thrice weekly or every 4 days is adequate when administered with ritonavir. Several international guidelines now recommend administration of rifabutin 150mg once daily when co-administered with a ritonavir boosted protease inhibitor (PI). However there is still limited safety data with this combination for rifabutin-related toxicities. We evaluate the effect of once daily rifabutin dosing when co-administered with a ritonavir boosted PI on neutropenia.
Methods: This was a retrospective cohort study in 22 patients on an antiretroviral regimen containing a boosted PI and rifabutin 150mg once daily from Newlands Clinic in Harare, Zimbabwe. Patients had an absolute neutrophil count test prior to commencement of rifabutin 150mg and post commencement of rifabutin. Participants were also receiving either lopinavir/ritonavir or atazanavir/ritonavir as part of their antiretroviral regimen. Data was analyzed with Stata version 12 to determine survival of patients and to identify the impact of co-administration on absolute neutrophil counts.
Results: Twenty-two participants with a median age of 24.3 (range = 15.8 - 45.1) years participated, with 68% being female. Seventeen (77.3%) participants had reductions in absolute neutrophil counts after commencing rifabutin. The median decline in neutrophil count for all participants was 650 cells/μL (IQR = 100 - 1,500). Twelve (54.5%) had neutropenia (absolute neutrophil count less than 1,500) whilst on rifabutin therapy. Median baseline neutrophil count was 1,850 cells/μL (IQR = 1,300 - 2,600 cells/μL) and after a median duration of 87 days (IQR = 58 - 129 days) on rifabutin therapy, median absolute neutrophil count of the participants was 1,150 cells/μL (IQR = 700 - 2,000 cells/μL). A Kaplan-Meier survival estimate of the time to neutropenia is shown below.



[Kaplan-Meier survival estimate of neutropenia]

Conclusions: Co-administration of a ritonavir-PI containing antiretroviral regimen with rifabutin led to a decline in absolute neutrophil counts in the majority of patients. More than half the participants were neutropenic when co-administered once daily rifabutin with a ritonavir-PI antiretroviral containing regimen.

TUPEB277

HIV-1 attachment inhibitor prodrug BMS-663068: interactions with rifabutin, with or without ritonavir, in healthy subjects

R. Adamczyk[1], A. Griffies[1], P. Ravindran[1], C. Smith[2], J. Anderson[1], M. Stonier[1], D.W. Boulton[1], I. Savant Landry[1]
[1]Bristol-Myers Squibb, Princeton, United States, [2]PPD, Richmond, United States
Presenting author email: ishani.landry@bms.com

Background: BMS-663068 is a prodrug of BMS-626529, a first-in-class attachment inhibitor that binds directly to HIV-1 gp120, preventing initial viral attachment and entry into host CD4+ T cells. BMS-626529 is metabolized in part by CYP3A4. Rifabutin, a CYP3A4 inducer, is used to treat mycobacterium infections in HIV-1-infected patients and decreases BMS-626529 exposures. Ritonavir (RTV), a CYP3A4 inhibitor, is used as a protease inhibitor-boosting agent and increases BMS-626529 exposure. This study assessed the effects of combining rifabutin±RTV on BMS-626529 systemic exposures.
Methods: In this open-label, single-sequence, multiple-dose, two-cohort study, 46 healthy subjects received BMS-663068 600mg BID on Days 1-4. On Day 5, subjects were randomized 1:1 to receive BMS-663068 600mg BID+rifabutin 300mg QD (Cohort 1) or BMS-663068 600mg BID+rifabutin 150mg QD+RTV 100mg QD (Cohort 2) on Days 5-15. Pharmacokinetic parameters for BMS-626529 on Days 4 and 15 were derived using non-compartmental methods. Geometric mean ratios and 90% confidence intervals were calculated from log-transformed C_{max}, AUC_{tau}, and C_{12} using a linear, mixed-effect model.
Results: Forty-five subjects (Cohorts 1 [n=22] and 2 [n=23]) had evaluable pharmacokinetic data (Table). Compared to BMS-663068 administration alone, coadministration with rifabutin (Cohort 1) decreased BMS-626529 C_{max}, AUC_{tau} and C_{12} by 27%, 30% and 41%, respectively; coadministration with rifabutin+RTV increased BMS-626259 C_{max}, AUC_{tau} and C_{12} by 50%, 66% and 158%, respectively. Systemic exposure changes in BMS-626529 in both cohorts were not considered as clinically meaningful based on efficacy results from a wide range of BMS-663068 doses in a Phase 2b study. All adverse events (AEs) were mild or moderate; the most frequent were headache (34.8%), chromaturia (26.1%), influenza-like illness (23.9%), and nausea (21.7%). Three (13.6%) and six (26.1%) subjects discontinued due to treatment-emergent AEs in Cohorts 1 and 2, respectively. One subject requested discontinuation before randomization. No deaths or serious AEs were reported.
Conclusions: Dose modification is not required when coadministering BMS-663068 600mg BID with rifabutin±RTV, and the combination was safe with acceptable tolerability.

	Treatment and comparison [n]	Pharmacokinetic parameter, adjusted geometric means		
		C_{max} ng/mL (90% CI)	AUC_{tua}ng.h/mL (90% CI)	C_{12}, ng/mL (90% CI)
Cohort 1	BMS-663068 600mg BID [22]	2398 (2199, 2614)	14736 (13271, 16363)	387 (289, 518)
	BMS-663068 600mg BID + RIF 300mg QD [18]	1756 (1496, 2061)	10292 (9108, 11630)	230 (177, 299)
		C_{max} GMR	AUC_{tua}GMR	C_{12} GMR
	BMS-663068 600mg BID + RIF 300mg QD vs. BMS-663068 600mg BID	0.732 (0.647, 0.829)	0.698 (0.642, 0.760)	0.594 (0.461, 0.766)
Cohort 2		C_{max} ng/mL (90% CI)	AUC_{tua}ng.h/mL (90% CI)	C_{12}, ng/mL (90% CI)
	BMS-663068 600mg BID [23]	2419 (2155, 2767)	14097 (12266, 16201)	328 (257, 418)
	BMS-663068 600mg BID + RIF 150mg QD + RTV 100mg QD [16]	3631 (3166, 4164)	23406 (19868, 27574)	846 (665, 1077)
		C_{max} GMR	AUC_{tua}GMR	C_{12} GMR
	BMS-663068 600mg + RIF 150mg QD + RTV 100mg QD vs. BMS-663068 600mg BID	1.501 (1.378, 1.635)	1.660 (1.521, 1.813)	2.584 (1.954, 3.417)

[Table]

CI, confidence interval; BID, twice daily; QD, once daily; GMR, geometric means ratio; RIF, rifabutin; RTV, ritonavir

TUPEB278

Drug interactions between psychiatric drugs and antiretroviral therapy, adherence and clinical outcomes

H. Knobel[1], E. Molas[1], A. Retamero[2], D. Echeverría[2], A. Guelar[1], M. Florit[2], S. Luque[2]
[1]Hospital del Mar, Dept. Infectious Diseases., Barcelona, Spain, [2]Hospital del Mar, Pharmacy, Barcelona, Spain
Presenting author email: hknobel@telefonica.net

Background: Patients infected with HIV have a high prevalence of mental illnesses. Drug interactions (DI) between antiretroviral therapies (ART) and psychiatric drugs (PD) should be considered. The aim of the study was to describe the frequency and severity of DI between ART and PD; another objective was to compare adherence and the clinical outcomes between patients with or without PD.
Methods: A cross-sectional study in HIV-infected patients was carried out during 2014. A structured interview was conducted to detect any type of drug, frequency and grade of DI. Data collected: demographics, current ART, adherence measured by patients' self-report, last viral load (VL). DI was evaluated by using the University of Liverpool database. Chi-square test was used to compare adherence and outcomes between patients with or without PD.
Results: Patients included 761; 179 (22.6%) with PD; 135 (75.4%) men, 48 (±10) years; 158 (88.2%) Caucasian: 126 (70.4%) smokers; 26 (14.5%) alcoholics; 47 (26.3%) drug users. Total PD prescriptions: 380 (2.1 PD/patient). Type of PD: 63 (16.6%) methadone and opioid drugs; 100 (26.3%) antidepressants; 148 (38.9%) anxiolytics; 69 (18.2%) antipsychotics. At least one relevant interaction was detected in 156 (87.2%) patients. Seventeen (9.5%) interactions were considered contraindicated: quetiapine (15), trazodone (1) and midazolam (1), in these cases a switch in ART or PD was recommended. In addition, it was recommended to change the dose, switch PD or ART in 26 (14.5%) patients.
Relevant interactions were found in 156 (87.2%) and in 178 (30.6%) of patients with and without PD respectively. Table 1 shows the comparison of type of ART, adherence, interruption of ART and HIV-RNA< 20 copies/mL between patients with or without PD.

	Patients with Psychatric drugs N: 179	Patients without Psychiatric drugs N: 582	P
Protease inhibitors use	110 (61.5%)	224 (38.5%)	<0.001
Non-nucleoside use	63 (35.2%)	319 (54.8%)	0.001
Raltegravir use	23 (12.8%)	56 (9.6%)	0.6
Adherence >90%	154 (86%)	525 (90.2%	0.1
Interruption of ART	22 (12.3%)	15 (2.6%)	<0.001
HIV-RNA <20 copies/ mL	150 (83.8%)	509 (89.8%)	0.2

[Table 1]

Conclusions: A fifth of HIV patients are taking psychiatric drugs. Among them, 87% had at least one drug interaction. Contraindicated interactions were detected in almost 10% of psychiatric patients. In the group of patients taking psychiatric drugs, protease inhibitors were more frequently prescribed, interruption of antiretroviral treatment was more common and the effectiveness of antiretroviral treatment was slightly lower.

TUPEB279

Pharmacokinetics and drug interaction potential of multiple-dose tenofovir alafenamide and rilpivirine

R. Begley, F. Cheng, E. Lawson, H. Graham, H. Cao, A. Vesterdahl, J. Zack
Gilead Sciences, Foster City, United States

Background: Tenofovir alafenamide (TAF), a novel tenofovir (TFV) prodrug, coformulated in a fixed-dose combination (FDC) tablet with rilpivirine (RPV,R) and emtricitabine (FTC,F) as R/F/TAF (25/200/25 mg), is under development for treatment of HIV-1 infection. This pilot study was conducted in support of the F/R/TAF development program to evaluate whether TAF and RPV exhibit a drug interaction upon multiple-dose co-administration.
Methods: In this fixed-sequence, open-label, 2-cohort, 2-period study, healthy subjects (N=34) were randomized to receive either: TAF alone, followed by TAF + RPV, each for 14 days (Cohort 1) or RPV alone, followed by TAF + RPV, each for 14 days (Cohort 2). Intensive pharmacokinetic assessments were performed on the final day of each treatment. Primary pharmacokinetic parameters of TAF and RPV, alone or in combination, were compared via geometric least-squares mean (GLSM) ratios and associated 90% confidence intervals (CI). Safety was assessed throughout the study.
Results: Thirty-two subjects completed the study. Following co-administration of TAF + RPV, exposures of TAF, TFV and RPV were comparable to administration of TAF or RPV alone: AUC_{last} and C_{max} GLSM(90% CI) for TAF were 101(93.8,109) and 101(84.2,122), respectively, AUC_{tau}, C_{max} and C_{tau} GLSM(90% CI) for TFV were 111(107,114), 112(102,123), and 118(113,123) respectively and for RPV were 101(96.4,106), 92.9(87.4,98.7) and 113(104,123) respectively.
All treatments were well tolerated; no deaths, serious adverse events (AE), or Grade 3 or 4 AEs occurred. One subject discontinued the study due to a drug-related Grade 2 AE of increased hepatic enzymes.
Conclusions: There are no changes in TAF, TFV, or RPV exposure upon coadministration of TAF and RPV, supporting development of an F/R/TAF FDC.

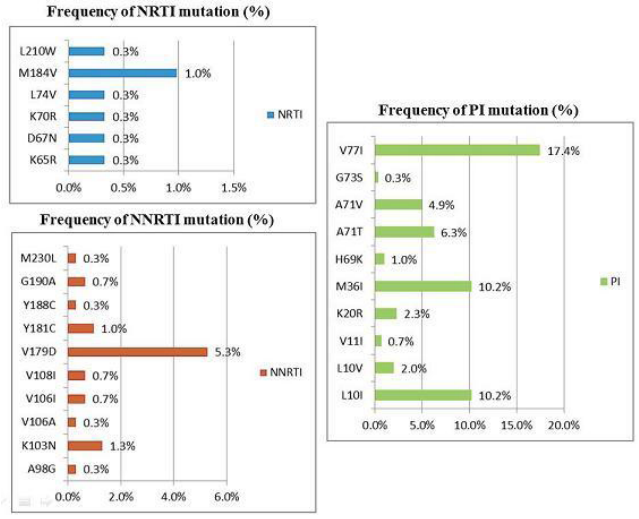
Antiretroviral drug resistance

TUPEB280

High rate of transmitted drug resistance in treatment-naïve HIV-infected VCT clients in southern Taiwan, 2007-2014

I.T. Chen, P.Y. Chou, Y.H. Chen, H.C. Tsai, S.S.J. Lee
Kaohsiung Veterans General Hospital, Infectious Diseases, Kaohsiung City, Taiwan, Province of China
Presenting author email: evaforever68@gmail.com

Background: The transmission of drug-resistant HIV-1 strains might compromise the efficacy of antiretroviral treatment. Rate of transmitted drug resistance (TDR) strains was influenced by duration of infection, selection of study populations and government policy of treatment. The aim of this study was to monitor the prevalence of TDR in Taiwan, where free highly active antiretroviral therapy (HAART) was provided since 1997.
Methods: A prospective study on TDR was conducted in antiretroviral therapy -naïve HIV-1 -infected voluntary counseling and testing (VCT) clients from 2007 to 2014 in Southern Taiwan. Genotypic drug resistance mutations were determined by ViroSeq™ system.
Results: From 2007 to 2014, a total of 20119 clients received a VCT. The positive rate for HIV-1 infection was ranged from 2.9% to 5.4% in every year. Sequences were obtained from 301 individuals, of whom 88% were infected by MSM, and 12% were infected by heterosexually. Subtype B HIV-1strains were found in 98% of the individuals, subtype CRF01_AE in 1.7% and subtype C in 0.3%. Thirty-two (10.6 %) patients were found to harbor drug resistance strains. The rates of resistance to any three classes of antiretroviral drugs (NRTI, NNRTI and PI) were 6% in 2007, 9% in 2008, 8% in 2009, 6% in 2010, 6% in 2011, 7% in 2012, 13% in 2013 and 19% in 2014. The most common NRTI resistance associated mutation was M184V. The most common NNRTI resistance associated mutation was K103N and V179D. No any PI resistance associated mutation was found in these 8 years.



[Frequency]

Conclusions: The rate of TDR was increased dramatically in these 2 years. This could be caused by the universal NNRTI based HAART treatment policy from July 2012. Further study was needed to clarify this phenomenon.

TUPEB281

Ten year prevalence of HIV-1 drug resistance mutations in New South Wales, Australia

A. Pinto[1], A. Carrera[2], H. Salem[3], K. Thapa[4], A. Shaik[1], P. Cunningham[5], R. Garsia[3], D. Dwyer[4], D. Cooper[1], A. Kelleher[1]
[1]UNSW Australia, The Kirby Institute, Randwick, Australia, [2]St Vincent's Hospital, SydPath, Sydney, Australia, [3]Royal Prince Alfred Hospital, Sydney, Australia, [4]Pathology West, Institute for Clinical Pathology and Medical Research, Sydney, Australia, [5]St Vincent's Centre for Applied Medical Research, Sydney, Australia
Presenting author email: apinto@kirby.unsw.edu.au

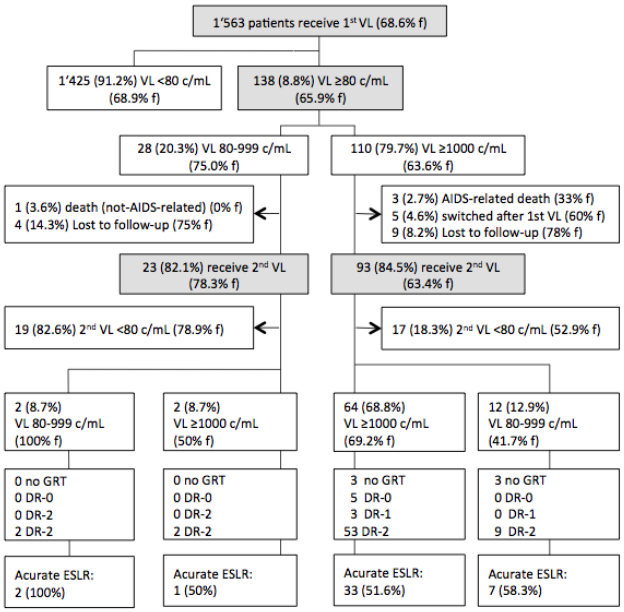
Background: New South Wales (NSW) has the greatest burden of HIV in Australia with an estimated 46% (12360/26800) of all people living with HIV. Despite universal access to antiretrovirals from early in the epidemic and recommendation in 2008 of baseline genotypic antiretroviral testing (GART), rates of prevalent drug resistance in this state are not known. A statewide analysis of prevalent drug resistance was performed to determine changes in resistance mutations.
Methods: A retrospective study of protease (PR) and reverse transcriptase (RT) genes was performed at three reference laboratories covering all genotypic drug resistance tests in NSW from 2004-2013. Duplicates within calendar year were excluded. Treatment data was available for 20% (1546/7687), allowing estimates of prevalence in treatment naïve and experienced sub groups. Genotyping was performed with Trugene, Viroseq and in house sequencing based assays. WHO 2009 Surveillance drug resistance mutations (SDRMs) were determined using Stanford Calibrated Population Resistance tool and overall frequency calculated per year.
Results: 7687 drug resistance tests were performed. Over ten years, we observed decrease in overall frequency of SDRMs from 61.6% (321/521) to 22.2% (166/747). Similarly, decreases were observed in PR mutations from 26.5% (138/521) to 4.7% (35/747), NRTI 56.3% (293/521) to 12.2% (91/747) and NNRTI 39.8% (207/521) to 12.9% (96/747). Similar declines were observed in dual class NRTI and NNRTI resistance (35% to 5.8%) and triple class resistance (17.3% to 1.2%). In treatment experienced subgroup, most frequent NRTI mutations M184VI and T215YFISCDVE and PR mutation I54VTALMV were unchanged for the last five years, whereas G190AES has replaced Y181CIV as the second most frequent NNRTI mutation after K103NS. In treatment naïve subgroup, there was no clear pattern of SDRMs, and protease mutations remain uncommon (< 6.0%). The overall rate of transmitted drug resistance (TDR) was stable at 10.3%.
Conclusions: There has been an apparent decrease in rate of prevalent SDRMs which is associated with the introduction of baseline routine genotypic testing. In a setting with universal access to antiretroviral therapy, rates of transmitted drug resistance have remained stable over time. This study provides baseline data before the implementation of statewide treatment strategies that target 90% coverage.

TUPEB282

Accuracy of WHO guidelines on management of adult patients on ART with unsuppressed viral load: a prospective multicenter study in rural Lesotho

N.D. Labhardt[1], D. Puga[2], T.I. Lejone[2], J. Bader[3], J. Ehmer[4], I. Ringera[2], M. Hobbins[4], B. Cerutti[5], T. Klimkait[3]
[1]Swiss Tropical and Public Health Institute, University of Basel, Clinical Research Unit, Medical Services and Diagnostic, Basel, Switzerland, [2]SolidarMed, Swiss Organization for Health in Africa, Maseru, Lesotho, [3]University of Basel, Molecular Virology, Department of Biomedicine - Petersplatz, Basel, Switzerland, [4]SolidarMed, Swiss Organization for Health in Africa, Lucerne, Switzerland, [5]University of Geneva, Faculty of Medicine, Geneva, Switzerland
Presenting author email: n.labhardt@unibas.ch

Background: The World Health Organization (WHO) 2013 Guidelines on antiretroviral therapy (ART) recommend routine viral load (VL) monitoring for all patients on ART. After a single VL ≥1000 copies/mL (c/mL), enhanced adherence support is offered for 3-6 months and a second VL is obtained. In cases of sustained VL ≥1000 c/mL, an empiric switch to second-line ART consisting of a protease inhibitor (PI), lamivudine, and a new nucleoside reverse transcriptase inhibitor (NRTI) is recommended.
Methods: Adults on first-line ART ≥ 6 months attending routine care in 10 rural clinics in Lesotho received VL testing. Those with detectable VL (≥80c/mL) underwent adherence support and a second VL was obtained after 3 months. Those with a second detectable VL received genotype resistance testing (GRT). Accuracy of WHO-recommendations was assessed at three levels: VL cut-off < 1000c/mL to exclude failure due to resistance (1); two subsequent VL ≥1000c/mL to confirm failure due to resistance (2); accuracy of the empiric second-line regimen (3).
GRT were classified as DR-0, DR-1, DR-2 - corresponding to the detection of genotypic mutations conferring resistance to none (DR-0), one (DR-1), or ≥2 drugs (DR-2) of the patients' first-line regimen. A report of "low-level resistance" or higher according to the Stanford HIV Drug Resistance Database was used as cut-off for this classification. Empiric second-line regimen (ESLR) where defined as "accurate" when GRT revealed full susceptibility to PI *and* at least one NRTI in the ESLR. (study-registration: NCT02126696)
Results: Figure 1 displays results stratified by the level of viremia, indicating distribution by gender.



VL = viral load; f = female; GRT = genotypic resistance testing; ESLR: Empiric Second-Line Regimen

[Figure 1]

Accuracy of VL< 1000c/mL to exclude drug-resistance was 82.6% (95%CI: 65.2%-95.7%). Two subsequent VL of ≥1000 c/mL confirmed drug-resistance with an accuracy of 88.9% (81.0%-95.2%). Overall ESLR were accurate for 58.1% (47.3%-68.9%), 6.8% (1.4%-13.5%) were inaccurate because GRT was DR-0 for first-line and in 35.1% (24.3%-45.9%) GRT revealed at least "low-level resistance" against both NRTIs of the ESLR.
Conclusions: Application of 2013 WHO-guidelines accurately identified failure due to drug-resistance in most cases. However, switching to ESLR according to guidelines would have resulted in nearly one third being switched to a regimen where HIV is at least partially resistant against ≥ 2 drugs.

TUPEB283

Projecting the epidemiological effect, cost-effectiveness and transmission of HIV drug resistance in Vietnam associated with viral load monitoring strategies

Q.D. Pham[1,2], D.P. Wilson[1], T.V. Nguyen[3], N.T. Do[4], L.X. Truong[3], L.T. Nguyen[5], L. Zhang[1]
[1]Kirby Institute, University of New South Wales, Kensington, Sydney, Australia, [2]Pasteur Institute, Department for Disease Control and Prevention, Ho Chi Minh City, Vietnam, [3]Pasteur Institute, Ho Chi Minh City, Vietnam, [4]Vietnam Authority for HIV/AIDS Control, Hanoi, Vietnam, [5]Ministry of Health, Hanoi, Vietnam
Presenting author email: pdquang@kirby.unsw.edu.au

Background: Routine viral load (VL) monitoring is not available in Vietnam for people living with HIV (PLHIV) on antiretroviral therapy (ART). We investigated the potential epidemiological impact of VL monitoring and its cost-effectiveness in Vietnam.
Methods: We collated data on reported HIV diagnoses and HIV-related deaths, number of PLHIV on ART, clinical outcomes, HIV drug resistance, and HIV treatment-related costs in Vietnam during 2005-2013. A population-based mathematical model, calibrated to reflect the status quo of CD4+ cell count and clinical monitoring, was used to assess the impacts of viral load monitoring on transmitted drug resistance (TDR), acquired drug resistance (ADR), and HIV-related mortality. We simulated scenarios of various combinations of VL testing coverage, VL thresholds for second-line ART initiation, and availability of salvage therapies and HIV drug resistance tests. We assessed cost-effectiveness as cost per disability-adjusted life year (DALY) averted.
Results: Projecting expected ART scale-up levels, to approximately double the number of people on ART by 2030, will lead to an estimated 17,600 [95% confidence interval: 9,650-29,820] cases of TDR (prevalence, 16% [11-23%]) and 50,820 [40,150-62,830] cases of ADR (prevalence, 18% [15-20%]) in the absence of VL monitoring. VL monitoring with 30% coverage is expected to lead to a reduction of 13-32% of TDR (2,420-6,050 cases), 26-59% of ADR (9,500-22,140 cases), 2-6% of HIV-related deaths (370-940 cases), and 19,660-51,000 fewer DALYs during 2015-2030. VL monitoring is estimated to cost US$5,054-5,385 per DALY averted. Maintaining a 30% VL testing coverage and providing HIV resistance testing for PLHIV with a VL>1,000 copies/ml every two years was the most cost-effective strategy for the ART programme in Vietnam. Sensitivity analysis revealed that the cost of second-line ART is the most influential factor of the cost-effectiveness ratios.

Conclusions: VL monitoring in Vietnam can have considerable benefits for individuals and lead to population health benefits. It may be marginally cost-effective according to common willingness-to-pay thresholds.

TUPEB284

HIV-1 attachment inhibitor prodrug BMS-663068 in antiretroviral-experienced subjects: analysis of emergent viral drug resistance through 48 weeks of follow-up

M. Lataillade[1], N. Zhou[1], S.R. Joshi[1], S. Lee[1], D.A. Stock[1], G.J. Hanna[2], M. Krystal[1], for the AI438011 Study Team
[1]Bristol-Myers Squibb, Wallingford, United States, [2]Bristol-Myers Squibb, Princeton, United States
Presenting author email: max.lataillade@bms.com

Background: BMS-663068 is a prodrug of BMS-626529, a first-in-class attachment inhibitor that binds to HIV-1 gp120, preventing initial viral attachment to host CD4+ T-cells. AI438011 is an ongoing, Phase IIb, randomized, active-controlled, dose-blinded trial investigating the safety, efficacy and dose-response of BMS-663068 versus atazanavir/ritonavir (ATV/r) in treatment-experienced, HIV-1-infected subjects. We report emergent drug resistance through the Week 48 database lock.
Methods: 251 treatment-experienced (≥1 week exposure to ≥1 antiretroviral) subjects with baseline susceptibility to all study drugs (including a conservative BMS-626529 IC_{50} cutoff of < 100 nM, determined by Phenosense® Entry assay) were randomized 1:1:1:1:1 to receive BMS-663068 (400 or 800 mg, twice-daily; 600 or 1200 mg, once-daily) or ATV/r (300/100 mg once-daily) with tenofovir disoproxil fumarate (TDF) + raltegravir (RAL). Emergent viral drug resistance was assessed in subjects meeting resistance testing criteria through Week 48. A conservative cutoff (>3-fold increase) was used to assess changes in BMS-626529 IC_{50} from baseline.
Results: Through Week 48, 46/200 and 9/51 subjects across the BMS-663068 and ATV/r arms, respectively, met resistance-testing criteria. Of these, 44/46 and 9/9 were successfully tested using the PhenoSense® GT and Integrase assays. No subjects had emergent TDF resistance. Six subjects across the BMS-663068 arms developed emergent RAL resistance. No subjects developed ATV resistance. 41/46 subjects across the BMS-663068 arms had an evaluable phenotype using the PhenoSense® Entry assay. Of those, 15/41 exhibited a >3-fold increase in BMS-626529 IC_{50} from baseline. Population sequencing of gp120 was successful in 14/15 subjects, and 10/14 had emergent substitutions in gp120 at positions associated with reduced susceptibility to BMS-626529 (S375, M426 or M434). Of the 15 BMS-663068-treated subjects with an emergent >3-fold increase in BMS-626529 IC_{50} from baseline, 5 achieved subsequent viral suppression to < 50 c/mL whilst on study, prior to the Week 48 database lock.
Conclusions: The rate of emergent changes in viral susceptibility to BMS-626529, and known lack of *in vitro* cross-resistance with approved antiretrovirals support the upcoming Phase III trial evaluating BMS-663068 for use in heavily treatment-experienced adults. Further evaluation of the conservative >3-fold increase cutoff in BMS-626529 IC_{50} will be required in larger clinical trials to determine its relevance in this population.

TUPEB285

Analysis of HIV drug resistance in adults receiving early antiretroviral treatment for HIV prevention: results from the HIV prevention trials network (HPTN) 052 trial

D. Sabin[1], S.E. Hudelson[1], S.S. Ou[2], S. Hart[3], C. Wallis[4], M.G. Morgado[5], S. Saravanan[6], S. Tripathy[7], E. Piwowar-Manning[1], Y.Q. Chen[2], M. McCauley[8], L. Hovind[3], J. Eron[9], J. Gallant[10], T. Gamble[11], M.C. Hosseinipour[9,12], J. Kumwenda[13], J. Makhema[14], R. Panchia[15], J.G. Hakim[16], V. Akelo[17,18], S. Faesen[19], S. Chariyalertsak[20], S.V. Godbole[21], N. Kumarasamy[6], B. Grinsztejn[22], J.H. Pilotto[23], M. Melo[24], K.H. Mayer[25,26], M.S. Cohen[9], S.H. Eshleman[1], for the HPTN 052 Study Team
[1]Johns Hopkins Univ. School of Medicine, Dept. of Pathology, Baltimore, United States, [2]Fred Hutchinson Cancer Research Center, Vaccine and Infectious Disease Division, Seattle, United States, [3]Frontier Science & Technology Research Foundation, Amherst, United States, [4]Lancet Laboratories, Johannesburg, South Africa, [5]Oswaldo Cruz Institute, Laboratory of AIDS and Molecular Immunology, Rio de Janeiro, Brazil, [6]Y. R. Gaitonade Center for AIDS Research and Education, VHS, Chennai, India, [7]National JALMA Institute of Leprosy and Other Mycobacterial Diseases, Uttar Pradesh, India, [8]FHI 360, Washington, DC, United States, [9]Univ. of North Carolina School of Medicine, Dept. of Medicine, Chapel Hill, United States, [10]Southwest CARE Center, Sante Fe, United States, [11]FHI 360, Durham, United States, [12]UNC Project, Lilongwe, Malawi, [13]College of Medicine-Johns Hopkins Project, Blantyre, Malawi, [14]Botswana Harvard AIDS Institute, Gaborone, Botswana, [15]Univ. of Witwatersrand, Perinatal HIV Research Unit, Johannesburg, South Africa, [16]Univ. of Zimbabwe, Harare, Zimbabwe, [17]Kenya Medical Research Institute, Kisumu, Kenya, [18]Center for Disease Control, Kisumu, Kenya, [19]Univ. of Witwatersrand, Clinical HIV Research Unit, Johannesburg, South Africa, [20]Chiang Mai University, Research Institute for Health Sciences, Chiang Mai, Thailand, [21]National AIDS Research Institute, Indian Council of Medical Research, Pune, India, [22]Instituto de Pesquisa Clinica Evandro Chagas, Fiocruz, Rio de Janeiro, Brazil, [23]Hospital Geral de Nova Iguacu and Laboratorio de AIDS e Imunologia Molecular-IOC/Fiocruz, Rio de Janeiro, Brazil, [24]Hospital Nossa Senhora da Conceição, Porto Alegre RS, Brazil, [25]Fenway Health, Boston, United States, [26]Harvard Medical School, Boston, United States
Presenting author email: dsabin1@jhu.edu

Background: HPTN 052 demonstrated that early antiretroviral therapy (ART) prevented 96% of linked HIV infections in serodiscordant couples. Antiretroviral (ARV) drug resistance could potentially compromise the efficacy of ART for HIV prevention. Furthermore, factors associated with emergence of resistance may be different when ART is initiated at higher CD4 counts. We evaluated resistance in participants in the early ART arm of HPTN 052 who failed ART before May 2011 (trial unblinding).
Methods: Early ART arm participants reported no prior ART and initiated ART at CD4 counts of 350-550 cells/mm^3; 72% received zidovudine/lamivudine/efavirenz (ZDV/3TC/EFV). ART failure was defined as two consecutive viral loads (VLs) >1,000 copies/mL >24 weeks after ART initiation. Resistance testing was performed using the ViroSeq system and Stanford algorithm version 6.3. HIV subtype was determined by phylogenetic analysis. Factors analyzed (data from the time of ART initiation) included age, gender, CD4 count, VL, region (Americas/Asia/Africa), regimen (ZDV/3TC/EFV vs. other), education level, marital status, number of sex partners, and time to viral suppression.
Results: By May 2011, 93 (10.7%) of 832 participants failed ART (1,647 person-years follow-up). Paired baseline/failure resistance results were obtained for 85 (89.5%) of those participants (42 from Africa; 29 from Asia; 14 from Americas; 69 subtype C, 16 other subtypes). Seven (8.2%) had baseline resistance: 1 had nucleoside/nucleotide reverse transcriptase inhibitor (NRTI) resistance; 3 had non-nucleoside reverse transcriptase inhibitor (NNRTI) resistance; 3 had NRTI+NNRTI resistance. Thirty (35.3%) had resistance at failure, including 27 (31.8%) with new resistance to ≥1 drug: 4 had new NRTI resistance; 4 had new NNRTI resistance; 19 had new NRTI+NNRTI resistance. Protease inhibitor resistance was not detected. None of the factors analyzed was associated with baseline resistance. Higher VL at ART initiation was associated with new resistance at failure (odds ratio=1.62 [1.16, 2.25], p=0.005).
Conclusions: HIV drug resistance frequently emerged in individuals who initiated ART at higher CD4 counts and failed treatment. This could potentially compromise the long-term efficacy of ART for prevention. Higher baseline VL was associated with resistance at ART failure. Further studies are planned to evaluate the relationship between baseline VL and resistance in early and delayed ART.

TUPEB286

Viral blips were infrequent and similar in treatment-naïve adults treated with rilpivirine/emtricitabine/tenofovir DF or efavirenz/emtricitabine/tenofovir DF in the STaR study

D. Porter, R. Kulkarni, W. Garner, M. Miller, K. White
Gilead Sciences, Inc., Foster City, United States
Presenting author email: danielle.porter@gilead.com

Background: The clinical impact of transient episodes of viremia (viral blips) on virologic failure and resistance development is not fully understood. Here we investigate the association of blips with clinical outcome for treatment-naïve subjects initiating therapy on rilpivirine/emtricitabine/tenofovir DF (RPV/FTC/TDF) or efavirenz/emtricitabine/tenofovir DF (EFV/FTC/TDF) through Week 96 in the STaR Study (GS-US-264-0110).
Methods: Subjects treated with ≥1 dose of study drug and with ≥1 post-baseline HIV-1 RNA value were included in this analysis. All on-drug HIV-1 RNA data points and FDA snapshot outcome data through Week 96 were utilized. Plasma HIV-1 RNA was measured using the Roche COBAS Amplicor Monitor v1.5 test. A viral blip was defined as after achieving confirmed suppression (2 consecutive HIV-1 RNA values < 50 copies/mL), any HIV-1 RNA value ≥50 copies/mL preceded and followed by HIV-1 RNA < 50 copies/mL.
Results: Of the 767 subjects included in the analysis, 67 (8.7%) experienced ≥1 blip through Week 96. Of those, 62 had single blips (62/767, 8.1%) and were distributed similarly between treatment groups (36/392, 9.2% RPV/FTC/TDF; 26/375, 6.9% EFV/FTC/TDF). A greater proportion of subjects with baseline HIV-1 RNA >100,000 copies/mL experienced blips compared to subjects with baseline HIV-1 RNA ≤100,000 copies/mL in both groups (19/133, 14.3% vs. 20/259, 7.7% RPV/FTC/TDF; 15/137, 10.9% vs. 13/238, 5.5%, EFV/FTC/TDF). Five subjects experienced two blips each (3 RPV/FTC/TDF, 2 EFV/FTC/TDF). Of 72 total blip events, 61 (85%) were low-level at 50-199 copies/mL, including all events experienced by subjects with multiple blips. Among subjects with blips, 53/67 (79%) were virologic successes at Week 96 (30/39, 77% RPV/FTC/TDF; 23/28, 82% EFV/FTC/TDF), similar to those subjects without blips (533/631, 84% overall; 275/315, 87% RPV/FTC/TDF; 258/316, 82% EFV/FTC/TDF). All 5 subjects with multiple blips were virologic successes. Among subjects with ≥1 blip through Week 96, 2/39 in the RPV/FTC/TDF group and 2/28 in the EFV/FTC/TDF group experienced virologic failure with resistance development.
Conclusions: Viral blips were infrequent and similar among subjects treated with RPV/FTC/TDF or EFV/FTC/TDF through Week 96 of the STaR study. Most blips were low-level (<200 copies/mL) and most subjects with blips remained suppressed through Week 96 without experiencing virologic failure or resistance development.

TUPEB287

Virological response and HIV drug resistance patterns in individuals on first line therapy for at least 4 years without routine viral load measurements: implications for second line regimens

F. Lyagoba[1], A. Kapaata[2], Z. Cui[3], P. Kaleebu[2], C. Mukajjanga[4], M. Nanfuka[4], M. Nyonyintono[4], J. Kim[5], J. Zhu[3], P. Munderi[2], S. Okoboi[4], J. Birungi[6], D.M. Moore[3,5]
[1]MRC/UVRI Uganda Research Unit on AIDS, Basic Sciences, Entebbe, Uganda, [2]MRC/UVRI Uganda Research Unit on AIDS, Entebbe, Uganda, [3]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada, [4]The AIDS Support Organisation (TASO), Jinja, Uganda, [5]University of British Columbia, Vancouver, Canada, [6]The AIDS Support Organisation (TASO), Research, Kampala, Uganda
Presenting author email: birungijophine@yahoo.com

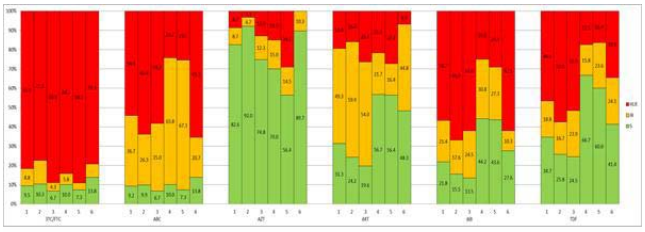
Background: Public health approach to the provision of ART in resource-limited settings is characterized by standardized drug regimens, using simplified formularies and standardized treatment monitoring, which does not insist on viral load (VL) testing. However, many patients monitored without VL testing in resource-limited settings will continue on failing regimens for long periods of time before failure is detected and will likely accumulate large numbers of drug resistance mutations (DRMs). How these accumulated DRMs affect response to the second-line ART regimens used in these settings needs to be investigated.
Methods: We enrolled patients from TASO clinic, Jinja, who had been on first-line ART regimens for >4years. We collected plasma at study enrolment and assayed for HIV-1 VL. Those with a VL ≥1000 c/ml were sequenced in the pol region, a 1257bp fragment spanning protease and reverse transcriptase genes.
Results: A total of 1091 participants enrolled in the study, of whom 74.7 % were female with median age of 44years (Q1-Q3=39-50 years). The median CD_4 cell count was 493 cells/ µL (Q1-Q3=351-687) and the median time on ART at enrolment was 6.8 years (Q1-Q3= 5.3 - 7.6). Of the 1091 patients identified, 113(10.4%) had HIV VL≥1000 c/ml and we successfully genotyped 105 (93%) of these samples.. Frequencies of mutations were highest within NRTIs 95.2% (n=100), NNRTIs 93.3% (n=98) and PI 1.0% (n=1). Mutation M184V 90.5% (n=95) followed by Y181C 40.0% (n=42) were most frequent. Mutation K65R was at 11.4%. 69 patients (66.%) had at least one TAM and 53 ((50.5%) had ≥2 TAMs. Having ≥2 TAMs was more common with lower education levels (p=0.0403), previous exposure to nevirapine and lamivudine (p=0.0018) and baseline viral loads ≥5000 c/ml (p=0.0054).
Conclusions: The prevalence of virologic failure in these patients was quite low despite more than six years of ART without VL monitoring. Among those with virologic failure, the presence of two or more TAMs as well as K65R and M184V has the potential to compromise NRTI backbones in second line regimens. Low education levels, high enrolment viral loads and previous regimens with stavudine were a risk factor for having greater numbers of TAMs.

TUPEB288

HIV-1 antiretroviral resistance patterns in patients failing NNRTI-based 1st-line treatment: results from a national survey in South Africa

K. Steegen[1], M. Bronze[2], M.A. Papathanasopoulos[1], G. Van Zyl[2,3], D. Goedhals[2,4], W. Macleod[5,6], I. Sanne[7], W.S. Stevens[1,2], S. Carmona[1,2]
[1]University of the Witwatersrand, Department of Molecular Medicine and Haematology, Johannesburg, South Africa, [2]National Health Laboratory Services, Johannesburg, South Africa, [3]Tygerberg and Stellenbosh University, Department of Medical Virology, Stellenbosh, South Africa, [4]University of the Free State, Department of Medical Microbiology and Virology, Bloemfontein, South Africa, [5]Boston University School of Public Health, Center for Global Health and Development, Boston, United States, [6]University of the Witwatersrand, Health Economics and Epidemiology Research Office, Department of Internal Medicine, School of Clinical Medicine, Johannesburg, South Africa, [7]Right to Care, Johannesburg, South Africa
Presenting author email: kim.steegen@nhls.ac.za

Background: Routine HIV-1 drug resistance testing is not recommended in 1st-line failures in resource-limited settings, therefore surveys are required to monitor resistance profiles in this population and assess the suitability of currently available 2nd-line regimens.
Methods: A prospective cross-sectional survey amongst patients failing 1st-line regimens was conducted in South Africa, using probability proportional to size sampling. Samples were collected between February 2013 and October 2014 from 91 health care facilities across 37 districts in 8 provinces. Virological failure was determined as two consecutive HIVVL results >1000 RNA copies/ml. *Pol* sequences were obtained using RT-PCR and Sanger sequencing and submitted to Stanford HIVdb v7.0.1. *Pol* subtyping was performed using Rega HIV subtyping tool v2.0. Statistical analyses were performed using GraphPad Prism 6.
Results: Of 793 available sequences 98.1% were HIV-1 subtype C. The median age of study participants was 36 years (IQR: 31-42) and most were female (64.9%). The median HIVVL was 4.7 log RNA copies/ml (IQR: 4.2-5.2) and consecutive HIVVL measurements were taken after a median of 163 days (IQR: 106-300). The median time on ART was 36 months (IQR: 19-58). Most patients failed TDF-based NRTI-backbones (TDF+3TC, 52.2%; TDF+FTC, 22.1%) in combination with EFV (82.0%). Wild-type virus was only detected in 3.7% of patients. K103N (48.8%) and V106M (34.9%) were the most common NNRTI-mutations, followed by Y181C (26.2%) and G190A (21.7%). One third of patients retained full susceptibility to 2nd-generation NNRTIs (ETR, 36.3% and RPV, 27.1%). After M184V/I (82.7%), K65R was the most common NRTI-mutation (45.8%). The prevalence of this mutation increased to 57.5% in patients failing a TDF-based regimen. The presence of ≥1 TAM was observed in 27.2% of patients, but the accumulation of TAMs remained low (≥3 TAMs, 6.4%). Cross-resistance of NRTIs was often observed (Figure 1), but did not affect future AZT use as 82.6% of all patients and 92.0% of patients failing TDF-based regimens remained susceptible to AZT.



Group 1: all patients failing 1st-line regimen (n=793); group 2: patients failing TDF-based regimen (n=426); group 3: patients failing TDF-based regimen with prior exposure to d4T (n=163); group 4: patients failing d4T-based regimen (n=120); group 5: patients failing AZT-based regimen (n=55) and group 6: patients failing other regimens (n=29). Green indicates susceptibility, yellow indicates intermediate resistance, and red indicates high-level resistance.

[NRTI drug resistance profiles]

Conclusions: The introduction of TDF-based 1st-line regimens has dramatically increased the prevalence of K65R in this population. However most patients failing TDF-based regimens remained susceptible to AZT, which is a core component of 2nd-line ART in South Africa.

TUPEB289

Prevalence of protease inhibitor and triple-class resistance in patients failing 2nd-line ART: results from a national survey in South Africa

K. Steegen[1], M. Bronze[2], M.A. Papathanasopoulos[1], G. Van Zyl[2,3], D. Goedhals[2,4], W. Macleod[5,6], I. Sanne[7], W.S. Stevens[1,2], S. Carmona[1,2]
[1]University of the Witwatersrand, Department of Molecular Medicine and Haematology, Johannesburg, South Africa, [2]National Health Laboratory Services, Johannesburg, South Africa, [3]Tygerberg and Stellenbosh University, Department of Medical Virology, Stellenbosh, South Africa, [4]University of the Free State, Department of Medical Microbiology and Virology, Bloemfontein, South Africa, [5]Boston University School of Public Health, Center for Global Health and Development, Boston, United States, [6]University of the Witwatersrand, Health Economics and Epidemiology Research Office, Department of Internal Medicine, School of Clinical Medicine, Johannesburg, South Africa, [7]Right to Care, Johannesburg, South Africa
Presenting author email: kim.steegen@nhls.ac.za

Background: Limited data on HIV-1 resistance profiles in patients failing 2nd-line regimens is available in South Africa. Knowledge of the efficacy of 2nd-line regimes is critical as the repertoire of 3rd-line drugs is limited. This study assessed the resistance profiles in 2nd-line failures across South Africa.
Methods: Patients failing PI-based 2nd-line regimens were surveyed nationally using a prospective, cross-sectional probability proportional to size sampling method. Samples were collected between February 2013 and October 2014 from 72 health care facilities across 38 districts. Virological failure was determined as two consecutive HIVVL results >1000 RNA copies/ml. *Pol* sequences were obtained using Sanger sequencing and submitted to Stanford HIVdb v7.0.1. *Pol* subtyping was performed using Rega HIV subtyping tool v2.0, and statistical analyses using GraphPad Prism 6.
Results: Of 354 available sequences 99.4% were classified as HIV-1 subtype C. The median age of volunteers was 38 years (IQR: 32-45) and 69.2% were female. The median HIVVL was 4.8 log copies/ml (IQR: 4.2-5.3) and all but six patients failed a LPV/r-based regimen. The NRTI-backbone often consisted of TDF+3TC (45.2%) or AZT+3TC (34.5%). A quarter of patients (24.9%) presented with wild-type virus. More than one third of patients presented with a combination of NRTI and NNRTI-resistance; whereas 15.3% and 7.1% presented with NNRTI or NRTI-resistance only. At least one major PI-mutation was detected in 16.4% of the surveyed population and 11.3% of patients presented with triple-class resistance. Common major PI-mutations were I54V (12.7%), V82A (12.1%) and M46I (10.2%). No patients with PI resistance showed high-level resistance to DRV/r, but more than half showed intermediate resistance to DRV/r. Few patients showed high-level resistance to ETR (5.2%), whereas 32.8% had predicted intermediate resistance to ETR.
Conclusions: One in four patients presented with wild-type virus, indicating poor compliance. The prevalence of major PI-mutations has increased compared to previous South African reports, with 16.4% presenting with at least one major PI-mutation and more than one in ten patients presenting with triple-class resistance. However, the recent availability of DRV/r, ETR and RAL in the public sector will ensure most of these patients will be able to suppress on currently available 3rd-line regimens.

Adherence

TUPEB290

Influence of the adherence to antiretroviral therapy in the effectiveness of the boosted protease inhibitor dual or monotherapy

H. Knobel[1], A. Retamero[2], A. Guelar[1], M. Florit[2], E. Molas[1], M. Montero[1], D. Echeverría[2], O. Ferrandez[2], S. Luque[2]
[1]Hospital del Mar, Infectious Diseases, Barcelona, Spain, [2]Hospital del Mar, Pharmacy, Barcelona, Spain
Presenting author email: hknobel@telefonica.net

Background: Dual (DT) and monotherapy (MT) with boosted protease inhibitors (bPIs) are strategies to reduce the toxicity and costs of antiretroviral therapy (ART). However, the impact of adherence on this approach in clinical practice is limited. The aim of this study was to assess the influence of different degrees of adherence in the effectiveness of DT and MT with bPIs
Methods: Observational study performed in a cohort of 1,600 HIV patients on ART in a hospital from January 2007 until December 2014. All patients who started a regimen with MT or DT were included. All of them were virologically suppressed at the start of this strategy.
Patients' adherence to ART was measured by 3 different methods in each visit to the Pharmacy Department: patient self-report, pharmacy records and pill counts. The level of adherence was classified in 3 categories: >90%, 90-70% and < 70%.
Virologic failure (VF) was considered when a patient had a viral load >500 copies/ml in 2 consecutive determinations. A multivariate logistic regression was used to evaluate the independent risk factors related to VF.
Results: Patients included: 180; 140 in MT (77.8%) and 40 in DT (22.2%). PIs drugs used: 103 (57.2%) DRV/r, 68 (37.8%) LPV/r and 12 (6.7%) ATV/r. Baseline characteristics were: 123 (68.3%) male, mean age 49 (SD 10.4) years, 70 (38.9%) were IDUs or ex-users and 81 (45%) were coinfected with the hepatitis C virus. Nadir CD4 cell count was 160 cells/ml and previous time with undetectable viral load before the start of the MT or DT was 55 months. VF was 4.5%, 12.9% and 23.5% for adherence rates >90%, 90-70% and < 70%, respectively. The factors associated with VF are shown in the table.

Risk factor	OR (95% CI)	P
Adherence <70%	10.04 (2.14-46.96)	0.003
Adherence 70-90%	5.38 (1.26-22)	0.029
Non-use of DRV/r as boosted PI	3.49 (0.97-12.89)	0.06

[Table 1]

Conclusions: Dual and monotherapy with bPIs have a high effectiveness when adherence to ART is optimal (higher than 90%), but they can lead to virological failure when adherence is poorer.
In addition, not all the different PIs seem to have the same effectiveness. These findings suggest the need to carefully select the patient and therapy when starting this strategy.

TUPEB291

Persistent effect of early (M4) adherence to antiretroviral treatment on long-term virological response in HIV-infected patients: results from the 11-year follow-up of the ANRS CO8 APROCO-COPILOTE cohort

C. Protopopescu[1], M.P. Carrieri[1], F. Raffi[2], L. Hardel[3], A. Sobel[4], C. Perronne[5], C. Jadand[6], J. Pierret[7], B. Spire[1], C. Leport[8], the ANRS CO8 APROCO-COPILOTE Study Group
[1]INSERM, UMR 912 (SESSTIM), Aix Marseille Université, UMR_S 912, IRD, ORS PACA, Observatoire Régional de la Santé Provence-Alpes-Côte d'Azur, Marseille, France, [2]CHRU Hôtel Dieu, Nantes, France, [3]INSERM, U 897, Bordeaux, France, [4]CHU Hôtel Dieu, Paris, France, [5]Hôpital Raymond-Poincaré, Garches, France, [6]Université Paris Diderot, INSERM, IAME, UMR 1137, Paris, France, [7]CERMES (CNRS-INSERM-EHESS), Paris, France, [8]Université Paris Diderot, Sorbonne Paris Cité, INSERM, UMR 738, Paris, France
Presenting author email: bruno.spire@inserm.fr

Background: Adherence to antiretroviral treatment (ART) plays a crucial role in determining virological response. However, few studies have investigated the relationship between the patterns of adherence and virological response over the long-term. The objective of this study was to assess the effects of early and late adherence to ART on stable virological response over an 11-year follow-up period, among HIV-infected individuals in the French ANRS CO8 APROCO-COPILOTE cohort.
Methods: The APROCO-COPILOTE cohort enrolled 1,281 individuals upon initiation of a protease-inhibitor (PI)-containing regimen between 1997-1999. Clinical and laboratory data were collected every 4 months. Standardized self-administered questionnaires collected data on psycho-social and behavioral characteristics, including adherence to ART, at enrolment (M0), at M4 and every 8/12 months thereafter over an 11-year period. At each follow-up visit a validated algorithm was used to build a three-level adherence score as follows: high, moderate and low adherence, reflecting patients who reported taking, respectively, 100%, 80-99.9%, or less than 80% of their prescribed ART doses in the previous 4 days. A stable virological response (SVR) was defined at each follow-up visit as having an undetectable viral load at all three most recent visits (current visit and previous visits 4 and 8 months beforehand). Patients who completed the adherence questionnaire at M4, and had at least one measure of both adherence and SVR during the ART maintenance period (M12-M132) were selected for the analysis. The association between early (M4) adherence and SVR was evaluated using a mixed logistic model, after adjusting for time-varying maintenance (after M12) adherence to ART.
Results: Among the 751 eligible patients, at baseline (M0) median (IQR) CD4 was 291 (141-435) cells/mm^3, median (IQR) viral load was 26,000 (5,032-128,000) copies/mL, 149 (20%) patients had AIDS; at M4, 412 (55%) were highly adherent. High early adherence (OR [95% CI]=2.7 [1.8;4.2]) was significantly associated with long-term SVR, after adjusting for time-varying maintenance adherence (3.4 [2.7;4.3] and 2.4 [1.8;3.0] for high and moderate adherence versus low adherence, respectively).
Conclusions: Adherence in the first 4 months of PI-containing ART remained a significant predictor of the long-term (11 years) stable virological response, even after adjusting for time-varying maintenance adherence.

TUPEB292

HIV patient preferences for simplified treatment regimens and impact on self-rated treatment adherence

M. Orme[1], A. Miners[2], C. Sabin[3], F. Rogatto[4], G. Reilly[4], R. Perard[4]
[1]ICERA Consulting Ltd, Swindon, United Kingdom, [2]London School of Hygiene & Tropical Medicine, London, United Kingdom, [3]University College London, London, United Kingdom, [4]Gilead Sciences Europe Ltd, Uxbridge, United Kingdom

Background: The development of effective single-tablet regimens for anti-retroviral therapy has led to the prospect of simplified treatment for HIV patients. We conducted a discrete choice experiment to estimate the relative strength of patient preference for simplified treatment regimens in relation to treatment adherence.
Methods: Data were from a prospective web survey of UK HIV patients (July to October 2014). A steering committee of clinicians, nurses, pharmacists, patient group representatives and academics guided the initial survey design. HIV patient organisations provided feedback on the pilot survey. Respondents were presented with 12 hypothetical choice scenarios of two hypothetical regimens that varied by number of tablets (1 to 4), mealtime dosing, increased risk of heart attack or insomnia (yes/no), and monthly cost to the healthcare system (£500/£600/£750/£1000). For each scenario, patients used a sliding scale (0 (no preference) to 100) to rate the treatment option that they thought would maximise their adherence to treatment. The ratings were analysed in STATA v13.1 using a two-stage model to obtain an attribute weighting that indicated the likely impact on adherence.
Results: Out of 278 respondents, 72.6% were men who have sex with men (MSM) and 14.7% were female. Median age was 44 (range 21-66) years. The time since diagnosis and duration of treatment was 8 (0-30) and 5 (0-27) years respectively. 36% were on a single-tablet regimen. 57% of patients reported that they skip treatment: MSM 59.4%, women 58.5%, others 50%. An increased risk of insomnia had the largest negative impact on likely adherence weightings (-9.6 [95% CI -10.5, -8.8], p< 0.001), a single-tablet regimen had the largest positive effect (+7.0 [95% CI 5.5, 8.5], p< 0.001). Avoiding mealtime dosing also had a significant positive impact on likely adherence weightings (+6.0 [95% CI 5.1, 6.8], p< 0.001). An increased risk of heart attack had a significant negative impact on likely adherence weightings (-3.5 [95% CI -4.4, -2.6], p< 0.001).
Conclusions: The adherence weightings estimated from these hypothetical scenarios indicate that single-tablet regimens and not being tied to mealtimes may improve treatment adherence. Treatments associated with insomnia and heart attack risk may have a negative impact on adherence.

TUPEB293

Physical and sexual violence independently correlated with reduced adherence to ART among women sex workers living with HIV in Vancouver, Canada

K. Deering[1,2], S. Goldenberg[1,2], O. Amram[2], J. Chettiar[2], S. Guillemi[3], R. Nicoletti[2], J. Montaner[1,3], S. Dobrer[3], P. Nguyen[3], K. Shannon[1,2,4]
[1]University of British Columbia, Medicine, Vancouver, Canada, [2]Gender and Sexual Health Initiative, BC Centre for Excellence in HIV/AIDS, Vancouver, Canada, [3]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada, [4]University of British Columbia, School of Population and Public Health, Vancouver, Canada
Presenting author email: kdeering@cfenet.ubc.ca

Background: Limited research has explored how violence affects the HIV care continuum, particularly for women and key populations such as sex workers (SWs), who experience high burden of violence globally. Less is known about how these relationships function on a neighbourhood level. Therefore, this study investigated the independent effect of spatial physical and/or sexual violence on adherence to antiretroviral therapy (ART) among SWs living with HIV in Metro Vancouver, Canada.
Methods: Baseline and bi-annual questionnaire data were drawn from a community prospective cohort (An Evaluation of Sex Workers' Health Access, 'AESHA', 2010-2013) of SWs and administrative data on ART dispensation (BC Centre for Excellence in HIV/AIDS Drug Treatment Program). Using geographic information systems and generalized estimating equations (GEE) logistic regression, we examined the independent effects of density of spatial client-perpetrated physical/sexual violence and having < 95% adherence (based on proportion of days of ART dispensation within 6-month follow-up periods), stratified according to residing within vs. outside the inner city epicentre of poverty, drug use and sex work scenes. For each participant, density of spatial violence was measured as the number of events of violence reported by the entire sample at each follow-up within a 250-meter buffer of participants' residential locations.
Results: Among 66 SWs living with HIV who previously used ART, over a 3.5-year period (208 observations), there were 74 events of < 95% adherence, with 29% experiencing any physical/sexual violence. In bivariate GEE analysis, spatial density of violence was independently correlated with reduced ART adherence within (p=0.01) but not outside (p=0.23) the inner city epicentre. In the multivariable GEE model adjusted for key confounders, increased density of physical/sexual violence by clients was statistically significantly correlated with <95% adherence (AOR:1.01, 95%CI:1.00-1.02) within, but not outside, the inner city epicentre.
Conclusions: This research supports global calls to address violence against SWs as part of HIV programs, tailored for neighbourhoods, and structural policy reforms including decriminalization of sex work to improve access to safer working conditions. Findings suggest that efforts to criminalize sex work, including new Canadian laws, could have major negative public health and human rights implications on engagement in the HIV care continuum.

Complementary and traditional medicines

TUPEB294

Thalidomide lead to an increase in T cell activation and inflammation on antiretroviral naive HIV-infected individuals

T.R.C. Vergara[1,2], A.M. Da-Cruz[3], J.R. Santos-Oliveira[3], N.C. Martos[1], L.B. Giron[1], M.L. Silva-Freitas[3], L.A. Cherman[4], M.S. Treitsman[2], A. Chebabo[2,5], M.C.A. Sucupira[1], R.S. Diaz[1]
[1]Federal University of Sao Paulo - UNIFESP, Retrovirology Laboratory, Sao Paulo, Brazil, [2]Oncohiv, Rio de Janeiro, Brazil, [3]Instituto Oswaldo Cruz/FIOCRUZ, Laboratório Interdisciplinar de Pesquisas Médicas, Rio de Janeiro, Brazil, [4]SMS Antonio Ribeiro Neto, Rio de Janeiro, Brazil, [5]Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil

Background: Micro-inflammation is a characteristic of HIV infection that relates to organs/tissues deterioration and cell apoptosis over time. Efforts to mitigate inflammation are necessary as coadjutant to antiretroviral therapy (ART). We hypothesize that thalidomide, a potent anti TNF agent, would lead to a decrease in HIV related micro-inflammation.
Methods: Open label controlled randomized pilot proof of concept clinical trial.
30 HIV+ ART naïve male adults with TCD4 ≥ 350 cell/mm³ were randomized to receive 100 mg of thalidomide BID for 3 weeks (Group-1, 16 patients) or not (Group-2, 14 patients) and to be followed by 48 week. Blood samples were collected at weeks 1, 2, 3, 4, 8, 12, 16, 20, and 24 weeks for viral loads, $CD4^+CD8^+$ T-cell counts, ultra-sensitivity C-reactive protein (US-CRP), CD38 and/or HLADR on $CD4^+$ and $CD8^+$ T-cells, IL-1β, IL-6, IL-8, IL-10, IFN-γ, TNF, LPS were determined.
Results: Baseline characteristics were similar and viral loads remained stable in both groups. During thalidomide no class 3 or 4 adverse events have been detected. At the end of treatment, a decline of CD4/CD8 ratio (p=0.08) and $CD4^+$ T- cell counts (p=0.04) were observed. Group 1 also presented increased activation status inferred by % $CD38^+$/$HLA\text{-}DR^+$ on $CD8^+$ (p< 0.05) or US-CRP (p< 0.01). All altered lab values detected in group 1 returned to baseline levels after thalidomide withdrawal. No differences on cytokines levels were detected. All these parameters remaining stable in group 2.
Conclusions: Although safe, short-term use of thalidomide among antiretroviral naïve individuals lead to an intense transitory increase in T cell activation and inflammation, with decrease of $CD4^+$ T-cells without detectable change in viral replication, although it might be difficult to detect viral load changes among naturally viremic individuals. These results warrant further *in vitro/vivo* studies exploiting a potential purging activity of thalidomide.

TUPEB295

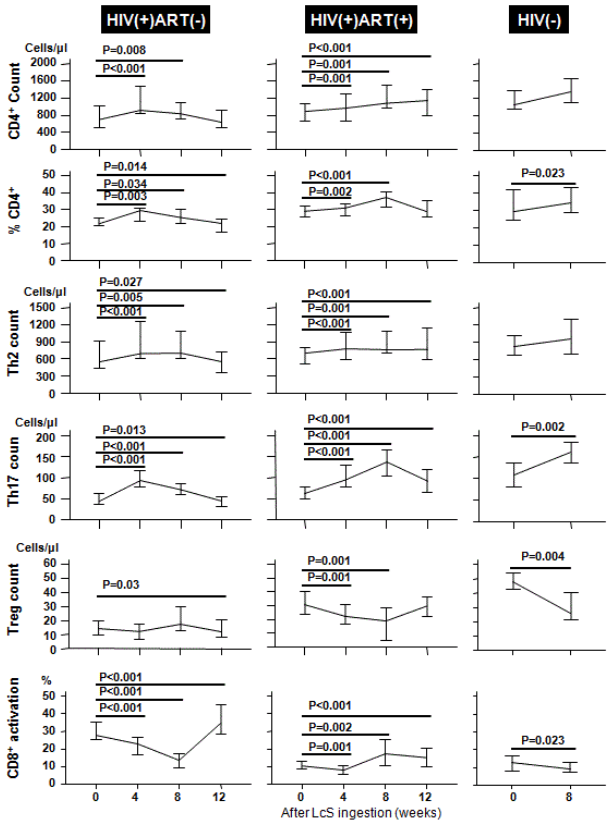
Effects of short-term probiotic ingestion in children with HIV-1 infection

H. Ichimura[1], A. Ishizaki[1], X. Bi[1], L.V. Nguyen[2], K. Matsuda[3], H.V. Pham[2], C.T.T. Phan[2], K. Ogata[3], T.T.T. Giang[2], T.T.B. Phung[2], T.T. Nguyen[2], A.N. Pham[2], D.T.K. Khu[2]
[1]Kanazawa University, Department of Viral Infection and International Health, Graduate School of Medical Sciences, Kanazawa, Japan, [2]National Hospital of Pediatrics, Hanoi, Vietnam, [3]Yakult Central Institute for Microbiological Research, Tokyo, Japan
Presenting author email: ichimura@med.kanazawa-u.ac.jp

Background: The destruction of $CD4^+$ T cells, particularly the Th17 subset, in the gut-associated lymphoid tissue, intestinal microbial translocation, and chronic systemic immune activation are the main pathogenic characteristics of HIV-1 infection. Several probiotics have been reported to have functions modulating intestinal microbiota, enhancing the barrier function of gut mucosa, and intensifying the gut innate immunity. The aim of this study was to investigate the efficacy of a probiotic, *Lactobacillus case*i strain Shirota (LcS), on the status of immune activation and the intestinal microbial translocation in children with HIV-1 infection.
Methods: This was a prospective study that was conducted at the National Hospital of Pediatrics in Hanoi, Vietnam from May to August 2012. We included 60 children with HIV infection [HIV(+)]: 31 without antiretroviral therapy (ART) [ART(-)] and 29 with ART for 3.5 years (median, range: 0.8-5.8) [ART(+)], and 20 without HIV infection [HIV(-)]. All participants were given oral LcS (6.5×10^9 cfu) daily for 8 weeks. Blood and stool samples were collected and analyzed virologically, immunologically, and bacteriologically before and after LcS ingestion.
Results: No serious adverse events were observed during LcS ingestion in both HIV(+) and HIV(-) groups. After 8-weeks of LcS ingestion, the peripheral $CD4^+$ T-cell and "Th2" sub-

set (CXCR3$^-$CCR6$^-$CD4$^+$) counts increased significantly in the HIV(+) groups. "Th17" subset (CXCR3$^-$CCR6$^+$CD4$^+$) counts and percentages of CD4$^+$ T-cells in lymphocytes increased significantly in both HIV(+) and HIV(-) groups. "Regulatory T (Treg)" cell subset (CD25^{high}CD4$^+$) decreased significantly in ART(+) and HIV(-) groups. The activation of CD8$^+$ T cells decreased dramatically in the ART(-) and slightly in HIV(-) groups. The plasma HIV-1 viral load decreased slightly but significantly in the ART(-). The detection frequencies of bacterial 16S rRNA genes in the plasma were not significantly different between before and after LcS ingestion among the three groups. *Lactobacillus* and/or *Bifidobacterium* were significantly increased in the stools of the three groups during the LcS ingestion period.

Conclusions: The 8-week-LcS ingestion was safe clinically, and would be beneficial immunologically, virologically, and bacteriologically for children with HIV-1 infection.



[Change of immunologic markers after LcS ingestion]

Curative interventions (including those aimed at reservoir depletion)

TUPEB296

Reduction in total HIV-1 proviral DNA following re-boost immunizations using the peptide-based therapeutic vaccine candidate, Vacc-4x, during ART

J.K. Rockstroh[1], D. Asmuth[2], G. Pantaleo[3], B. Clotet[4], D. Podzamczer[5], J. van Lunzen[6], K. Arasteh[7], R. Mitsuyasu[8], B. Peters[9], A. Lazzarin[10], D. Jolliffe[11], M. Ökvist[12], K. Krogsgaard[13], A. Mørk[12], M.A. Sommerfelt[12]

[1]Universitätsklinikum Bonn, Medizinsche Klinik und Poliklinik I, Bonn, Germany, [2]University of California at Davis, Sacramento, United States, [3]University of Lausanne, Lausanne, Switzerland, [4]Irsicaixa Foundation, Hospital Universitari 'Germans Trias i Pujol', UAB, UVIC-UCC, Badalona, Spain, [5]Infectious Disease Service Hospital Universitari de Bellvitge, Barcelona, Spain, [6]University Medical Center Hamburg-Eppendorf, Hamburg, Germany, [7]EPIMED, Vivantes Auguste-Viktoria-Klinikum, Berlin, Germany, [8]UCLA Care Center, University of California at Los Angeles, Los Angeles, United States, [9]Dept. Infectious Diseases, King's College London, London, United Kingdom, [10]IRCCS San Raffaele, Dept. of Infectious Diseases, Milan, Italy, [11]S-Cubed Ltd., Abingdon, United Kingdom, [12]Bionor Pharma ASA, Oslo, Norway, [13]KLIFO, Copenhagen, Denmark
Presenting author email: ms@bionorpharma.com

Background: This study (2012/1 - NCT01712256) investigated the impact of booster immunizations on sustaining vaccine effect in a therapeutic HIV vaccine setting. The effect of two Vacc-4x booster immunizations on total proviral DNA during ART, and on viral load (VL) set-point following a new ART interruption were determined.
Methods: At weeks (w) 0 and 2, eligible study participants from the clinical study (2007/1 - NCT00659789) were given intradermal (i.d.) Vacc-4x booster immunizations (1.2mg) on ART with GM-CSF (60µg) i.d. as a local adjuvant. At w12, ART was interrupted for up to 16 weeks (w28). Study participants were thereafter followed on ART until w36. Total proviral DNA was measured at w0,4,16,28 and 36 using real-time PCR (Taqman) targeting the *gag* gene. VL set-point was defined as the mean of the last two VL values prior to ART resumption. All study participants provided signed informed consent. The per protocol population (PP) included participants with no major deviations that would challenge the validity of the data.
Results: This open, multicenter, clinical study conducted from 12.2012 to 01.2014 enrolled 33 participants from 9 clinical trial sites within the US and Europe. In the PP, a statistically significant reduction in total proviral DNA (49%) between w0 and w4 was observed (Wilcoxon signed rank p-value 0.030, n=26) which could suggest immune-based killing of infected cells while on ART.
The duration of ART prior to the first reboost immunization was mean 36 months (n=22) (min 26; max 47 months). The VL set-point in this study (2012/1) had a geometric mean (GM) value of 26279 copies/ml and was significantly lower than the pre-ART VL set-point (GM VL 74048 copies/ml) (p=0.021, n=13). The VL set-point in this 2012/1 study (GM VL 18162 copies/ml) was reduced compared to the 2007/1 study VL set-point (GM VL 22035 copies/ml), however the difference was not statistical significant, paired t-test p-value 0.453 (n=18).
Conclusions: Vacc-4x booster immunizations safely restored virus control to the VL set-point established following primary Vacc-4x therapeutic vaccination. The reduction in total proviral DNA supports the potential for Vacc-4x therapeutic vaccination to impact on HIV reservoirs during ART and to contribute to HIV cure strategies.

TUPEB297

A feasibility study of weight-based pegylated IFN-α2b immunotherapy to target persistent HIV-1 on ART

L. Azzoni[1], E. Papasavvas[1], K.M. Lynn[2], A. Kapalko[3], L. Lalley-Chareczko[3], F. Aberra[4], P. Tebas[5], K.C. Mounzer[3], J.R. Kostman[5], Q. Li[6], L.J. Montaner[1]

[1]The Wistar Institute, HIV Immunopathogenesis Laboratory, Philadelphia, United States, [2]University of Pennsylvania, Presbyterian Hospital, Philadelphia, United States, [3]Philadelphia FIGHT, Philadelphia, United States, [4]University of Pennsylvania, Gastroenterology, Philadelphia, United States, [5]University of Pennsylvania, Medicine, Philadelphia, United States, [6]University of Nebraska, School of Biological Sciences, Lincoln, United States
Presenting author email: azzoni@wistar.org

Background: In our prior study (NCT00594880), a 20-week course of pegylated (peg)-IFN-α2a resulted in a significant reduction in proviral HIV DNA in participants with chronic HIV-1 infection on suppressive antiretroviral therapy (ART), suggesting that type 1 interferon immunotherapy may reduce latent viral reservoirs.
Methods: A pilot study was started to evaluate feasibility, safety and the effects of peg-IFN-α2b on levels of integrated HIV-1 DNA in 20 HIV-1 infected subjects receiving suppressive ART. 1 µg/kg/week peg-IFN-α2b was added to current ART for 20 weeks, interrupting ART between weeks 5 and 9 of treatment.

Results: Study disposition (7-Jan-2015): 22 screened; 20 enrolled (2 not qualified); 20 exposed to treatment (17 completed ART interruption); 9 concluded treatment; 8 undergoing treatment and 3 prematurely discontinued (2 toxicities during ART interruption, 1 voluntary withdrawal). Enrollment is closed.
At baseline, participants had median 756 CD4+ T cells/µl (IQR 642-930), all had VL < 50 copies/ml. Baseline rectal biopsies showed detectable HIV-1 RNA positive cells by in situ hybridization in all individuals tested.
Safety data on 20 participants were evaluated (cumulative 202 visits, ~ 404 person/wk on treatment, 84 person/wk follow-up). 15/17 participants had complete labs for the 4-week ART interruption. Of these, 8/15 sustained VL < 400 copies/ml (with 6 VL < 50 copies/ml); 7/15 had rebounds between 421 and 101040 copies/ml. 12/15 sustained CD4+ T cell count > 350 cells/µl during the ART interruption. Of the participants with post-interruption follow-up, 10/13 achieved VL < 50 copies/ml 4 weeks after resuming ART, and 10/10 were suppressed 4 weeks later. 13/13 had CD4 > 350 4 weeks after resuming ART
6 participants experienced neutropenia: 4 grade-3 ANC at treatment weeks 2, 5, 9 and 16 (managed with Filgrastim and/or dose reduction) and 2 grade 4 ANC at weeks 5 and 12 (withdrawn from study). No grade ≥ 3 depression or reportable SUSAR were observed.
Conclusions: A 20-week course of weight-based peg-IFN-α2b, inclusive of a 4-week ART interruption, in subjects with chronic HIV infection receiving suppressive ART is feasible and tolerable, but intense safety monitoring of ANC and CD4 counts should be implemented for enhanced safety.

TUPEB298

Optimized antiretroviral therapy during allogeneic hematopoietic stem cell transplantation in HIV-infected individuals

A. Cash[1], A. Capoferri[1,2], D. Xu[1], H.L. Mchugh[1], O. Laeyendecker[1,3], S. Sakoian[4], L. Tony[4], C. Bullen[1], C. Pohlmeyer[1], P. Pham[1,5], J. Lai[1], J.E. Gallant[6], R.F. Siliciano[1,2], C. Flexner[1], K. Pratz[4], M. Levis[4], R.J. Jones[4], Y.L. Kasamon[4], R.F. Ambinder[4], C.M. Durand[1,4]
[1]Johns Hopkins University, Department of Medicine, Baltimore, United States, [2]Howard Hughes Medical Institute, Baltimore, United States, [3]National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, United States, [4]Johns Hopkins University, Sidney Kimmel Cancer Center, Baltimore, United States, [5]Johns Hopkins University, Department of Pharmacy, Baltimore, United States, [6]Southwest CARE Center, Santa Fe, United States
Presenting author email: acash4@jhu.edu

Background: A reservoir of latently infected memory CD4+ T cells is a major barrier to HIV cure. With allogeneic hematopoietic stem cell transplantation (alloHSCT), host hematopoietic cells are replaced with donor hematopoietic cells after cytotoxic therapy and graft versus host (GVH) effects. If antiretroviral therapy (ART) is continued during alloHSCT, it should protect donor hematopoietic cells from infection and result in a reduction or elimination of HIV. However, ART is often interrupted during alloHSCT due to drug interactions, mucositis and vomiting, or organ dysfunction.
Methods: We performed a pilot study on the safety and feasibility of continuing optimized ART during alloHSCT in HIV-infected individuals being treated for hematologic malignancy. Optimized ART included:
1) avoidance of ritonavir-based ART to minimize drug interactions,
2) ART changes for organ dysfunction and
3) subcutaneous enfurvirtide (ENF) during post-transplant cyclophosphamide and if oral ART was not tolerated.
Primary endpoints were incidence of adverse events (AE) from ENF and maintenance of ART through day 60. Secondary outcomes included HIV persistence measures.

Patient ID	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Cancer	Hodgkins	Non-Hodgkins	AML	AML	Burkitt lymphoma	Non-Hodgkins
Phase of Treatment	Chronic	Chronic	Chronic	Chronic	Chronic	Chronic
Pre alloHSCT CD4 Count	85 cells/ul	231 cells/ul	274 cells/ul	57 cells/ul	260 cells/ul	227 cells/ul
Pre alloHSCT Viral Load	79 c/ml	<20 c/ml	<20 c/ml	<20 c/ml	<20 c/ml	<20 c/ml
PBMC Donor Chimerism	100%	87%	100%	73%	N/A	TBD
CD3+ Donor Chimerism	100%	74%	100%	95%	N/A	TBD
Number of ART Changes	6	2	2	2	N/A	TBD
ART Maintenance	73%	95-100%	Poor	95-100%	N/A	TBD
Oncology outcomes, survival	Died at week 49, liver failure	Alive, cancer free at week 76	Alive, cancer free at week 45	Alive, cancer free at week 31	Died, prior to BMT	Received BMT on Jan 2nd 2015

[Patient Summary]

Results: Six HIV+ individuals enrolled; five received alloHSCT and one died from malignancy prior to alloHSCT. The remaining 5 patients tolerated ENF without AEs. Patients 1-4 reached day 60 without interruption of ART but required ART changes. Patient 1 achieved 100% donor chimerism by week 8, with undetectable plasma HIV and negative viral outgrowth assay (VOA). The patient died at week 49 with liver failure. Patient 2 has mixed chimerism (87% donor) at week 52 with undetectable plasma HIV, but positive VOA. Patient 3 achieved 100% donor chimerism by week 4 with undetectable plasma HIV but became non-adherent with ART, and at month 5 had viral rebound and meningoencephalitis. Patient 4 has mixed chimerism at week 24 (73% donor) with undetectable plasma HIV but positive VOA.
Conclusions: During alloHSCT, with optimized ART, it is feasible to maintain ART but regimen changes are common due to drug interactions and organ dysfunction. ENF is a well-tolerated alternative to oral ART. Interruption of ART during alloHSCT can cause a severe acute retroviral syndrome. At early time-points, with mixed chimerism, HIV persists but further studies are needed over time.

Clinical approaches to drug and alcohol dependence treatment: harm reduction

TUPEB299

Impact of opioid substitution therapy on antiretroviral therapy: a systematic review and meta-analysis

A. Low[1], G. Mburu[2], C. Davies[1], C. French[1], M. May[1], S. McLean[1], T. Rhodes[3], L. Platt[3], A. Guise[3], P. Vickerman[1]
[1]Bristol University, Bristol, United Kingdom, [2]AIDS Alliance, Brighton, United Kingdom, [3]London School of Hygiene and Tropical Medicine, London, United Kingdom
Presenting author email: andrea_low@hotmail.com

Background: Injecting drug is an important driver of HIV transmission in Eastern Europe, Central and South Asia, and some mixed- epidemics in Africa. Although current injecting can reduce the effectiveness of antiretroviral treatment (ART), emerging evidence suggests that opiate substitution therapy (OST) could alleviate this effect**.** We conducted the first systematic review to evaluate the impact of OST on ART related outcomes among people who inject drugs (PWID).
Methods: We searched Medline, PsycInfo, Embase, Cochrane and Web of Science databases and conference abstracts for primary cross-sectional, longitudinal and surveillance studies published between 1996 and November 2014 that measured the impact of OST (compared to no OST) among PWID. Outcomes of interest included: coverage of ART (the proportion of PWID with current ART use), adherence to ART above a predefined threshold (usually >95%), viral suppression after ART initiation, discontinuation of ART and mortality. Meta-analysis was conducted using random effects modelling, and heterogeneity assessed using Cochran's Q test and I^2 statistic.
Results: We identified 4691 titles and abstracts, from which 33 studies, conducted among 16 populations of PWID in North America (n=9), Europe (n=5), Indonesia (n=1) and China (n=1) were included. The most frequently reported outcomes were viral suppression and ART coverage. OST was associated with a two-fold increase in both ART coverage (OR 2.03; 95% CI: 1.68-2.37, I^2=77%, 9 studies) and adherence (OR 2.01, 95% CI: 1.41-2.60, I^2=97%, 9 studies), and a 17% decrease in the odds of ART discontinuation (OR 0.83, 95% CI:0.71-0.95, I^2 =26%, 7 studies). OST was also associated with an 78% increase in odds of viral suppression (OR=1.78, 95%CI:1.40-2.16, I^2 =91%, 13 studies), but had no impact on mortality (HR=1.01, 95% CI:0.60-1.42, I^2 =76%, 5 studies). There was considerable heterogeneity for all studies except for ART discontinuation.
Conclusions: This systematic review suggests OST could have a multi-faceted role in improving ART outcomes among PWID, adding to the considerable evidence for the beneficial effects of OST for the treatment of HIV among PWID. We note the concomitant need to synthesise qualitative and programme evidence to delineate models of ART-OST integration and delivery to maximise such potential.

Diagnosis of HIV disease in children and adolescents (including early infant diagnosis)

TUPEB300

Adolescent representation among clients accessing HIV testing at a large tertiary facility in north-central Nigeria

A. Ibrahim[1,2], S. Erekaha[1,3], C. Onuchukwu[4], M. Essen[4], V. Tepper[5], M. Charurat[6], H. Swomen[1], W. Blattner[6], N.A. Sam-Agudu[1,5,6]
[1]Institute of Human Virology Nigeria, Abuja, Nigeria, [2]University of Ibadan, Institute of Child Health, Ibadan, Nigeria, [3]University of Ibadan, Department of Health Promotion and Education, Ibadan, Nigeria, [4]Federal Medical Center Keffi, Keffi, Nigeria, [5]University of Maryland Baltimore, Department of Pediatrics, Baltimore, United States, [6]University of Maryland Baltimore, Institute of Human Virology Epidemiology and Prevention, Baltimore, United States
Presenting author email: hswomen@ihvnigeria.org

Background: Globally, HIV-related mortality has dropped by 30%; in adolescents living with HIV (ALHIV), it has increased by 50%. The WHO has cited low access to HIV Testing & Counseling (HTC)-and subsequent care-as a factor. Adolescents comprise ~22% of the general Nigerian population, and nearly 6% of Nigerian PLHIV are adolescents. In national HIV sero-prevalence surveys, adolescents comprised 16.6% of all tested, and 9.7% of pregnant women tested. This study was conducted to determine adolescent representation among clients accessing HTC at a large referral facility in North-Central Nigeria.
Methods: This retrospective study was conducted at Federal Medical Center Keffi, Nasarawa State, where ~7,000 HIV+ clients are enrolled. HTC data from Jan. to Dec. 2013 were reviewed for Adult, Pediatric and PMTCT Units. Data for adolescents aged 10 to 19 years were extracted and analyzed. Chi-square was used to compare proportions.
Results: A total of 6,336 clients including 325 adolescents accessed HTC in the review period; 81% of tested adolescents were female, of whom 49% were pregnant. Median age for all adolescents tested was 18yrs (IQR 16-18.5); for pregnant adolescents, 18yrs (IQR 17-19, range 15-19). HIV prevalence was higher in non-pregnant (14.1%) vs pregnant adolescents (2.2%), p=0.0002. Further results are presented in Table 1.

HIV Testing and Counseling Clients			Adolescent Clients (10-19 years)			P Value (HIV prevalence comparisons)	Adolescent Representation among HTC Clients (%)
Total no. tested (all tested, all ages)	Total no. tested HIV+	HIV prevalence (%)	Total no. tested	Total no. tested HIV+	HIV Prevalence (%)		
6,336	1,090	17.2	325	30	9.2	0.0002	5.1
Total no. pregnant women tested (all ages)			Total no. pregnant tested	Total no. pregnant tested HIV+			
3,264	288	8.8	134	3	2.2	0.007	4.1
Total no. non-pregnant clients tested (all ages)			Total no. non-pregnant tested	Total no. non-pregnant tested HIV+			
3,072	802	26.1	191	27	14.1	0.0002	6.2

[Table 1. Adolescent Representation amongst HTC Clients]

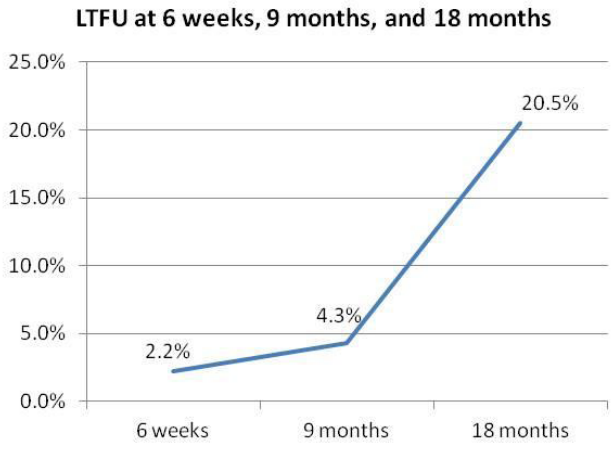
Conclusions: Adolescents' HTC access did not reflect their large representation in the Nigerian population. In this study, adolescents were underrepresented among all tested and all pregnant women tested, compared to national survey figures. Our results portray a gap in HTC access/uptake for adolescents in the real-world, non-survey setting. There is an urgent need to control transmission in this population, specifically in the non-pregnant. We propose that adolescent HTC be made more accessible beyond antenatal testing, and supported to be available for greater independent access. These strategies will facilitate timely testing, improved impact of HIV prevention, early treatment of ALHIV, and reduced mortality in this population.

TUPEB301

Loss to follow-up along the early infant diagnosis care continuum in Kenya

K. Clark[1], V. Okoth[2], B. Gautney[3], S. Khamadi[2], K. Goggin[4], R. Wafula[5], I. Mukui[5], C. Martin[6], S. Finocchario-Kessler[6]
[1]Office of the U.S. Global AIDS Coordinator and Health Diplomacy (S/GAC), Washington, D.C., United States, [2]Kenya Medical Research Institute, Nairobi, Kenya, [3]Global Health Innovations, Kansas City, United States, [4]Children's Mercy Hospital, Division of Health Services and Outcomes Research, Kansas City, United States, [5]National AIDS & STI Control Programme, Nairobi, Kenya, [6]University of Kansas Medical Center, Department of Family Medicine, Kansas City, United States
Presenting author email: cmartin8@kumc.edu

Background: Loss to follow-up (LTFU) among HIV-exposed infants continues to be a significant challenge, with estimates in Kenya ranging between 4.8 and 75% LTFU by 3 months of age (Sibanda, et al., 2013). The HIV Infant Tracking System (HITSystem©) is an e-health intervention for early infant diagnosis (EID) targeting rapid antiretroviral therapy (ART) initiation among HIV+ infants and complete retention (until confirmed HIV-uninfected at 18 months postnatal or 6 weeks after breastfeeding cessation).
Methods: We conducted a retrospective cohort analysis using de-identified data for 2483 HIV-exposed infants enrolled in EID services at 8 (3 urban/ 5 peri-urban) hospitals utilizing the HITSystem intervention between April 2011 and December 2013. LTFU status at 6 weeks, 9 months, and 18 months of age was categorized as: (1) not receiving testing when indicated; (2) not notifying infant's mother/caregiver of HIV-positive results; and (3) failure to initiate ART among HIV+ infants. We calculated the percentage of infants LTFU at each time point.
Results: Median age at EID enrollment was 8.1 weeks (x =14.3; *SD*=14.3). 254 infants, (10.2%), were discharged early: 134 (5.4%) transferred facilities, 77 (3.1%) relocated to a different catchment area, and 43 (1.7%) infants died. After excluding those discharged early, data for 2229 infants were analyzed.
Testing: All enrolled infants were age eligible for their 6 week HIV/DNA PCR test. Only 17 (0.8%) infants failed to receive an initial test. Among all infants age eligible for a 9 month antibody retest (n=1546, 69.4%) and 18 month antibody retest (n=712, 31.9%), 96 (5.6%) and 383 (53.8%), failed to receive re-testing at 9 and 18 months, respectively.
Notification: 10 HIV-positive infants were LTFU because their caregivers were never notified of their HIV-positive test results.
ART initiation: Among the 130 (5.8%) infants with HIV-positive PCR results, 25 (19.2%) failed to receive treatment. In total, 50 (2.2%) infants were LTFU at 6 weeks, 96 (4.3%) at 9 months and 383 (20.5%) at 18 months. In total, 529 (23.7%) infants were LTFU, leaving an overall retention rate of 76.3%.



[LTFU at 6 weeks, 9 months, and 18 months]

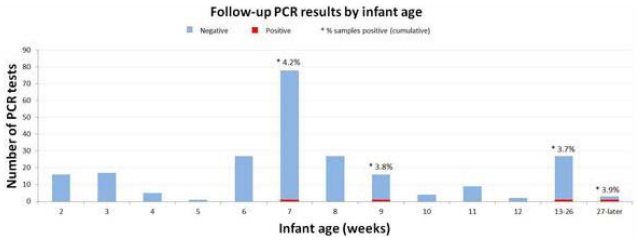
Conclusions: LTFU rates achieved with the HITSystem were much lower than those identified in previous EID research.

TUPEB302

Low birth HIV infection rate in infants from high-risk-for-transmission pregnancies in South Africa

J. Maritz[1,2], A. Nelson[3], V. Cox[3], G. van Zyl[1,2], W. Preiser[1,2], G. van Cutsem[3,4], H. Rabie[5], L. Frigati[5], J. Bernheimer[3], J. Giddy[6], M. Cotton[5]
[1]University of Stellenbosch, Medical Virology, Cape Town, South Africa, [2]National Health Laboratory Service, Medical Virology, Cape Town, South Africa, [3]Médecins Sans Frontières, Cape Town, South Africa, [4]University of Cape Town, School of Public Health and Family Medicine, Cape Town, South Africa, [5]University of Stellenbosch, Pediatric Infectious Diseases, Cape Town, South Africa, [6]Provincial Government Western Cape, Cape Town, South Africa
Presenting author email: maritzj@sun.ac.za

Background: Successful interventions to prevent mother-to-child transmission of HIV have reduced the infection rate in 6 week old infants in the Western Cape province, South Africa to 0.99% (2014 data).
It is well established that early diagnosis and treatment of HIV-infected infants improve health outcomes. Universal PCR testing at birth is desirable but unaffordable for resource-limited settings. As pregnancies at high risk for transmission may contribute disproportionately, targeted testing early after birth may expedite identifying infected infants.
Here we report preliminary findings of an ongoing study of targeted early HIV diagnosis for infants at high risk of intra-uterine infection in Cape Town, South Africa.
Methods: High-risk-for-transmission pregnancies are identified by reviewing labour ward records at a primary care midwife obstetric unit and at an academic referral hospital. Screening is performed by research nurses using predefined criteria, namely insufficient or interrupted exposure to antiretroviral therapy or prophylaxis, a maternal viral load of greater than 1000 copies/ml (where available) or premature or low birth weight infants. Samples for molecular HIV testing are taken as early as possible after birth, with subsequent early therapy initiation in infected infants.
Results: Of 286 birth PCRs from high risk pregnancies, 5 were positive (1.75%). Within this at-risk population, none of the predefined potential risk factors increased the relative risk of transmission.
Follow-up PCR tests on 233 (81%) infants found an additional 4 positive patients at weeks 7, 9, 19 and 27 of age respectively (total positivity rate 3.9%). No differences in risk factors were identified between positivity at birth and at follow-up. In only 131 (56%) of cases was follow-up testing done between 5 and 8 weeks of age.



[Figure 1]

Conclusions: A relatively low rate of HIV transmission was identified from presumed high-risk-for-transmission pregnancies. Despite guidelines recommending PCR testing at 6 weeks, repeat testing was delayed in about half of patients. Late diagnosis motivates strongly for improved diagnostic algorithms with more frequent testing. Further research is required to identify factors which would influence when the mothers return for repeat testing as this might inform programmatic recommendations.

ARV management strategies: children and adolescents cohort studies

TUPEB303

High sensitivity CRP (hsCRP) levels in long-term survivors of perinatal HIV infection

K. Kancherla[1], S. Kalyanam[1], N. Desai[2]
[1]St. George's University, School of Medicine, Kings County Hospital Center, Pediatrics, Brooklyn, United States, [2]Kings County Hospital/SUNY Downstate Medical College, Pediatrics, Brooklyn, United States

Background: Perinatally HIV infected children are now young adults because of long term HAART. Long term HAART is known to be associated with side effects including insulin resistance and lipodystrophy. While hsCRP is used as a general predictor of future coronary events little information is available on hsCRP in long-term surviviors of perinatal HIV as they progress towards adulthood.
Methods: Data was collected by retrospective chart review over a 10 year period (2004-2014) for hsCRP, BMI, Viral Load, CD4% and HAART in a closely followed cohort of perinatally HIV infected youth in our clinic. Student t-test was used as a test of significance.
Results: 48 patients (25 M and 23 F; Ages 8-26 years - median age 18) had 151 hsCRP values available. 96% of patients were Black/Hispanic and 4% Caucasian. 8 patients had one hsCRP value, while others had at least two or more levels tested over 10 years. According to median age 18, hsCRP levels were significantly higher in those >= 18 years old (m=2.42, r=0.1-19.8) than those < 18 (m=1.48, r=0.2-12.6); p-value=0.06. hsCRP levels were significantly lower with CD4% < 25 (m=1.32, r=0.1-8.5) as compared to hsCRP levels with CD4% >25 (m=2.36, r=0.1-19.88); p-value=0.049. hsCRP levels were significantly higher in patients on double Protease Inhibitor (PIs) therapy (m=2.51, r=0.15-14.55) compared to those on 1 PI or none (m=1.61, r=0.1-8.5); p-value=0.079. hsCRP levels in the overweight and obese female group were (m=3.38, r=0.6-11) as compared to females with normal BMI (m=1.89, r=0.15-12.6); p-value=0.1. We also looked at hsCRP levels in relation to viral load < 1000 and >1000, undetectable versus detectable viral load, BMI in males, and CD4% < 10, which showed no significance.

	Patients <18 years old	Patients >= 18 years old	CD4% <25	CD4% >25	Patients taking <2 PIs	Patients taking 2 PIs	Female Normal BMI	Female Over-weight and Obese
n=(sample size)	70	78	53	94	88	60	36	18
hsCRP (mean, range)	1.48, 0.2-12.6	2.42, 0.1-19.8	1.32, 0.1-8.5	2.36, 0.1-19.8	1.61, 0.1-19.8	2.51, 0.15-14.55	1.89, 0.15-12.6	3.38, 0.6-11
p-value	0.06		0.049		0.0796		0.1	

[Table 1]

Conclusions: While hsCRP levels show a rising trend with age, our findings suggest that hsCRP levels may be a useful screening test for cardiovascular risk in long term surivivors of perinatal HIV infection. Overweight and obese females, patients on double PI therapy, and patients with CD4 counts >25% have higher hsCRP levels; these patients may need further studies to assess cardiovascular risk as the patients age into adulthood.

TUPEB304

Durability of first-line antiretroviral therapy (ART) in children in the European Pregnancy and Paediatric HIV Cohort Collaboration (EPPICC)

R.L. Goodall[1], I.J. Collins[1], T. Childs[1], C. Foster[2], L. Ene[3], C. Smit[4], C. Kahlert[5], A. Judd[1], D. Gibb[1], European Pregnancy and Paediatric HIV Cohort Collaboration (EPPICC) in EuroCoord
[1]MRC CTU at UCL, London, United Kingdom, [2]Paediatric Infectious Diseases, Imperial College Healthcare NHS Trust, London, United Kingdom, [3]HIV Department, 'Dr. Victor Babes' Hospital for Infectious and Tropical Disease, Bucharest, Romania, [4]Dutch HIV Monitoring Foundation, Amsterdam, Netherlands, [5]Children's Hospital of Eastern Switzerland, Saint Gallen, Switzerland
Presenting author email: r.goodall@ucl.ac.uk

Background: Global data on durability of first-line ART in children is scarce. We assessed time to switch to second-line therapy for any reason in EPPICC (Thailand and 13 European countries including Russia and Ukraine).
Methods: ART-naïve children < 18 years at initiation of combination ART (NNRTI or boosted-PI plus ≥2 NRTIs) were included. Switch to second-line was defined as:
(i) change across drug class (PI to NNRTI or vice versa) and change of ≥1 NRTI;
(ii) change within PI-class plus ≥1 NRTI;
(iii) change from single to dual PI; or
(iv) addition of a new drug class.
Documented switches for simplification, TB or pregnancy were ignored. A cause specific hazard model assessed time to switch and potential predictors, with death as a competing risk. Children were at risk from ART initiation until the earliest of: switch, death, last visit in paediatric care or 21st birthday.
Results: Of 3050 children, 47% were male and 84% perinatally infected. At ART initiation, median [IQR] age was 3.3 years [1.0-8.0], CD4% 20% [13-28] in < 5-years, CD4 count 200 cells/mm3 [55-362] in ≥5-years and 19% were CDC C. Initial regimens were 30% PI-based, 34% NVP-based, 31% EFV-based, and 4% NNRTI+3NRTI. Median duration of follow-up on ART was 5.1 years [2.4-8.0]. Overall, 86 (3%) died, 111 (4%) were lost to follow-up and 684 (22%) met the definition of switch: median time to switch was 28 months [15-57]. 5-year cumulative proportion switching was 22% (95%CI 20-24). Reasons for switch (available in 236 (34%)) were: 69% treatment failure, 14% toxicity, 17% other. 70% of patients with missing reason for switch had viral load (VL)>1000c/ml or CDC B/C event within 6-months of switch, varying by regimen (lowest for PIs (46%)). In multivariable analysis, older age and higher VL at ART start, UK/Ireland & Rest of European region, and initiation on NVP-based or NNRTI+3NRTI regimens were associated with more rapid time to switch (Table 1).

	Multivariable Model		
	SHR	95% CI	p
Age at ART initiation:			**<0.0001**
<2 years	1.00	-	
2-4	1.25	(0.88, 1.76)	
5-9	1.95	(1.40, 2.70)	
10+	2.35	(1.67, 3.32)	
Viral Load at ART initiation (per log unit increase)	1.16	(1.03, 1.31)	**0.013**
First-line regimen:			**<0.0001**
EFV	1.00	-	
NVP	1.80	(1.38, 2.34)	
NNRTI+3NRTI	1.71	(1.11, 2.63)	
PI	0.77	(0.55, 1.06)	
Region:			**<0.0001**
UK/Ireland	1.00	-	
Russia and Ukraine	0.51	(0.29, 0.90)	
Rest of Europe	0.91	(0.70, 1.19)	
Thailand	0.25	(0.18, 0.35)	
SHR = Sub hazard ratio			

[Table 1: Factors associated with time to switch]

Conclusions: Over a fifth of children met the definition of switch by 5-years of ART, with approximately two-thirds likely to be failure related. NVP-based and NNRTI+3NRTI regimens were more likely to switch than EFV or PI-based regimens.

TUPEB305

Adolescents are at higher risk of attrition from HIV care: results from a cohort study in Ethiopia

D. Jerene[1], W.A. Taye[2], K.T. Gari[3], L. Wissow[4], A.J. Ruff[4]
[1]Management Sciences for Health, Heal TB, Addis Ababa, Ethiopia, [2]Addis Ababa University, Department of Child Health and Pediatrics, Addis Ababa, Ethiopia, [3]Hawassa University, Department of Child Health and Pediatrics, Hawassa, Ethiopia, [4]Johns Hopkins University, Baltimore, United States
Presenting author email: degujerene@gmail.com

Background: Attrition from HIV care is a huge challenge in all age groups. However, studies describing attrition rates among adolescents are scarce. Since many children living with HIV are now growing to adolescence and adulthood, it is important to understand the challenges of retention in this age group in order to design appropriate interventions.The objective of this study was to compare the rate of attrition from HIV care between adolescents and younger children treated and followed at public health facilities in Ethiopia.
Methods: We conducted a retrospective cohort study in seven hospitals and one health center in two regions of Ethiopia between April-November 2014. The study population constituted adolescents (age 10-19 years) and children (0-9 years) enrolled in chronic HIV care from January 1, 2005 through December 31 2013. Trained nurses assisted by site data clerks and under supervision of pediatricians did retrospective chart review using pre-tested data abstraction form. The primary end point was attrition from care (pre or post-ART) defined as occurrence of one or more of the following: death, loss to follow up, and transfer out. We used Cox regression analysis and calculated adjusted hazard ratios (aHR) after controlling for gender, disease stage, CD4, and hemoglobin.
Results: We included 2058 patients (1072 adolescents and 986 children) in the study ,and they contributed 2422 person-years of observation (PYO) during pre-ART follow up. Their median age was 10 years and 54% were girls. Being adolescent was the only independent predictor of pre-ART attrition after controlling for covariates [aHR (95% CI)=1.62 (1.25-2.09); p< 0.001]. At the end of the pre-ART follow up, 74.4% were put on ART and they contributed 5984 PYO. Of 1531 put on ART, 93 died during follow up, making the mortality rate 15.5 per 1000 PYO (23.2 versus 8.6 in adolescents and children respectively). Adolescents were at significantly higher risk of attrition from ART follow-up [aHR (95% CI)=2.14 (1.71-2.69); p< 0.001]. Gender was not associated with attrition from care.
Conclusions: Adolescents experienced significantly higher rates of attrition from care both before and after initiation of ART in public health facilities in Ethiopia. Further studies and adolescent-specific interventions are urgently needed.

TUPEB306

12-month response to early LPV-based antiretroviral therapy in West-African children treated before the age of 2 years, the MONOD ANRS 12206 cohort

C. Amani-Bossé[1], D. Dahourou[2], K. Malateste[3], M. Coulibaly[2], M. Timité-Konan[4], N. Méda[5], A. Emième[6], R. Ouédraogo[7], C. Devaux[8], P. Van de Perre[9], S. Blanche[10], V. Leroy[3,11], MONOD ANRS 12206 Study Group
[1]Programme PACCI, Site ANRS, Projet MONOD-ANRS 12206, Abidjan, Cote D'Ivoire, [2]Centre de Recherche Internationale pour la Santé, Projet MONOD ANRS 12206, Ouagadougou, Burkina Faso, [3]University of Bordeaux, Institute of Epidemiology and Public Health, Bordeaux, France, [4]Centre Hospitalier Universitaire (CHU) de Yopougon, Service de Pédiatrie, Abidjan, Cote D'Ivoire, [5]Université de Ouagadougou, Ouagadougou, Burkina Faso, [6]Laboratoire du CeDReS, Abidjan, Cote D'Ivoire, [7]Laboratoire du CHU Charles de Gaulle, Ouagadougou, Burkina Faso, [8]Laboratoire de Rétrovirologie, CRP-Santé, Luxembourg, Luxembourg, [9]University of Montpellier, Inserm U 1058, Montpellier, France, [10]University of Paris-Descartes, EA 3620, Paris, France, [11]University of Bordeaux, Inserm U 897, Bordeaux, France
Presenting author email: valeriane.leroy@isped.-bordeaux2.fr

Background: Outcomes of early antiretroviral treatment (EART) initiation remains unknown. We described the 12-month virologic response to LPV/r based-ART in West-Africa.
Methods: All HIV-infected children <2 years of age confirmed by DNA-PCR were enrolled in a 12-month cohort based on LPV/r in Ouagadougou, Burkina Faso, and Abidjan, Côte d'Ivoire. Viral load was measured three-monthly, CD4 six-montly. Virological success (VS) at 12-month (< 500 copies/ml) and correlates of VS using a logistic regression were assessed. HIV-1 genotyping was performed when VL>1000 copies/ml.
Results: In the context of low early infant diagnosis coverage (16% in Abidjan; 29% in Ouagadougou), 226 HIV-infected children < 2 years of age were screened between 05/2011 and 01/2013; 156 (69%) children were initiated on EART. The median ages at diagnosis and at ART initiation were 8.6 months and 13.5 months, respectively. 63% were from Abidjan, 53% were girls, 48% were not exposed to a PMTCT-intervention. Mother was the main caregiver for 81%, 67% had access to tap water. At inclusion, median CD4% was 19%, median VL was 6.4 log copies/ml and 55% of the children were classified 3-4 WHO-stage. At 12-month on ART, 11 infants died (7%), 5 were lost-to-follow-up (3%), 140 were followed (90%). VS was achieved for 70% of children enrolled and 78% of those alive. When adjusting for country and sex, access to tap water and an increase of CD4%>10% between inclusion and M6 were respectively associated with a higher rate of VS (aOR:2.43 [0.97-6.12]) and (aOR:3.29 [1.33-8.11] while having a father as the main child caregiver was associated with lower rate of VS (aOR:0.33 [0.12-0.91]). At 12-month, 25/29 eligible children had a genotype, 19 (76%) had ≥1 resistance (64% to 3TC; 28% to EFV, 4% to AZT and LPV/r).
Conclusions: In 2011-2013, challenges still remain for improving EART in HIV-infected children in West Africa. Nevertheless, rate of VS on LPV-based EART is high and comparable to those observed in Europe. Lack of tap water and father as the main child caregiver, correlates of lower VS, are probably markers of a poor adherence. These risk factors could be identified at ART initiation and adherence systematically reinforced.

TUPEB307

Determinants of durability of first-line ART regimen and time from first-line failure to second-line ART initiation. The IeDEA paediatric West African Database (pWADA)

S. Desmonde[1], F. Eboua[2], K. Malateste[1], F. Dicko[3], D.K. Ekouevi[1,4], S. N'Gbeche[5], F. Koueta[6], H. Signate Sy[7], L. Renner[8], S. Koumakapi[9], V. Leroy[1]
[1]Université Bordeaux, Institut de Santé Publique, d'Epidémiologie et de Développement, Bordeaux, France, [2]CHU de Yopougon, Abidjan, Cote D'Ivoire, [3]Hopital Gabriel Toure, Bamako, Mali, [4]IeDEA Regional Centre, PACCI, CHU de Treichville, Abidjan, Cote D'Ivoire, [5]Centre Pédiatrique de Prise en Charge, de Recherche et de Formation, Abidjan, Cote D'Ivoire, [6]Hopital Pédiatrique, CHU Charles de Gaulle, Ouagadougou, Burkina Faso, [7]Hopital d'Enfants Albert Royer, Dakar, Senegal, [8]Korle Bu Hospital, Accra, Ghana, [9]Service Pédiatrie CHU National, Cotonou, Benin
Presenting author email: sophie.desmonde@isped.u-bordeaux2.fr

Background: In resource-limited settings, antiretroviral therapy (ART) options are limited in HIV-infected children. It is important to understand reasons for switching to second-line treatment and document time to switch in those failing first-line ART.
Methods: We included children aged ≤15 years enrolled in seven clinical sites participating in the IeDEA paediatric West-African collaboration. We estimated the incidence of switch (≥1 drug class change) within 24 months of first-line ART and associated factors were identified in a multinomial logistic regression. Clinical failure was defined as the (re)appearance of WHO stage 3 or 4 events after ≥24 weeks on ART in a treatment-adherent child. Immunological failure was defined as developing or returning to age-related immunological thresholds after 24 weeks on ART. Among children in treatment failure, the 24-month probability of switching to second-line ART and the associated factors were estimated using a competing risk approach;

the competing event was death. We excluded children who switched to second-line ART following the withdrawal of nelfinavir in 2007.
Results: Overall, 2820 children were included at a median age of 5 years at ART initiation. Most initiated a non-nucleoside reverse transcriptase inverse based regimen (70.9%), however 144 (5%) were on nelfinavir. At 24-month post-ART, among the remaining 2676 children not on nelfinavir, 165 (5.9%) had died, 702 (24.9%) were lost-to-follow-up and 188 (7%) had switched to second-line ART. The most frequent reasons for switch were drug stock-outs (20%), toxicity (18%), treatment failure (16%) and poor adherence (8%). By 24 months post-ART, 322 (12%) were in failure after a median delay of 7 months: 205 (64%) experienced clinical failure alone, 96 (30%) immunological failure alone and 21 (6%) had both. Of these children, 21 (6.5%) switched to second-line ART after a median time of 21 weeks in failure. This was associated with older age (sHR: 1.21, 95% Confidence Interval (CI):1.10-1.33) and longer time on ART (sHR: 1.16, 95%CI:1.07-1.25).
Conclusions: Switches after clinical /immunological failure were insufficiently covered. These gaps reveal that it is crucial to advocate for both sustainable access to first-line potent ART and alternative regimens to provide adequate roll-out of paediatric ART programmes.

Clinical issues in men who have sex with men

TUPEB308

Hospitalisation and predictors of morbidity in community-based cohorts of HIV- positive and -negative gay and bisexual men

C.L. Moore[1], A.E. Grulich[1], G. Prestage[1,2], H.F. Gidding[3], F. Jin[1], L. Mao[4], K. Petoumenos[1], I.M. Poynten[1], I.B. Zablotska[1], M.G. Law[1], J. Amin[1]
[1]The Kirby Institute, University of New South Wales, Sydney, Australia, [2]Australian Research Centre in Sex, Health and Society, La Trobe University, Melbourne, Australia, [3]School of Public Health and Community Medicine, University of New South Wales, Sydney, Australia, [4]National Centre in HIV Social Research University, University of New South Wales, Sydney, Australia
Presenting author email: cmoore@kirby.unsw.edu.au

Background: There is evidence that among HIV positive people a significant burden of morbidity is due to non-AIDS-related complications. To date it has been difficult to determine what part of this excess risk is due to the health effects of HIV, its treatment, or to lifestyle factors common to the gay and bisexual (GBM) population. We aimed to calculate overall and cause-specific hospitalization rates and risk factors for hospitalizations in HIV negative (HIV-ve) and HIV positive (HIV+ve) cohorts of GBM and compare these with rates in the general male population.
Methods: We conducted a record linkage study of two cohorts of HIV-ve (*n*=1325) and HIV+ve (*n*=557) GBM recruited in Sydney, New South Wales (NSW). Participants were probabilistically linked with their respective administrative hospital data from 01 July 2000 to 30 June 2012. Age and year adjusted relative risk (RR) for hospitalization was calculated using an Andersen-Gill model for repeated events. Age and year specific hospitalization rates for each cohort were compared with those in the NSW male population and summarized as standardized hospitalization ratios (SHRs). Incidence rate ratios with 95% confidence intervals were estimated using Poisson regression models to assess risk factors for hospitalization.
Results: The median age/follow-up was 35.3/10.1 yrs and 40.9/11.9 yrs in the HIV-ve and HIV+ve cohorts, respectively. 2,207 hospitalizations were observed in the HIV-ve cohort during 13,025 person year (PYs) [crude rate: 16.9/100 PYs (95%CI 16.3-17.7)], and 2,278 hospitalizations in the HIV+ve cohort during 5,580 PYs [crude rate: 40.8/100 PYs (95%CI 39.2-42.5)]. HIV+ve individuals had an increased risk of hospitalization compared with the HIV-ve individuals [RR: 1.98 (95%CI 1.64-2.40)]. Adjusted hospital admission rates were lower in the HIV-ve cohort [SHR: 0.72 (95%CI 0.67-0.78)] and higher in the HIV+ve cohort [SHR: 1.45 (95%CI 1.33-1.59)] compared with the general population. The primary causes of hospitalization differed between groups. Poorer socioeconomic indicators and drug use were associated with hospitalization in both cohorts.
Conclusions: HIV+ve GBM continue to experience excess morbidity compared with HIV-ve GBM men and the general population. GBM identity did not confer any excess risk. The primary risk factors for hospitalisation in the HIV+ve cohort related to HIV infection.

Clinical issues in people who use drugs

TUPEB309

Factors associated with ART adherence and plasma HIV-1 RNA suppression among crack cocaine users in Vancouver, Canada

K. Hayashi[1,2], E. Wood[1,2], P. Nguyen[1], S. Guillemi[1], R. Hogg[1,3], J. Montaner[1,2], T. Kerr[1,2], M.-J. Milloy[1,2]
[1]British Columbia Centre for Excellence in HIV/AIDS, Vancouver, Canada, [2]University of British Columbia, Department of Medicine, Vancouver, Canada, [3]Simon Fraser University, Faculty of Health Sciences, Burnaby, Canada
Presenting author email: khayashi@cfenet.ubc.ca

Background: Crack cocaine use has been shown to increase the risk of HIV infection and contribute to poor adherence to antiretroviral therapy (ART). However, little is known about facilitators of or barriers to ART adherence and viral suppression among individuals using crack cocaine. Therefore, we sought to identify correlates of ART adherence and viral suppression among crack cocaine users receiving highly active antiretroviral therapy (HAART) in Vancouver, Canada.
Methods: Data were derived from a prospective cohort of HIV-positive people who use illicit drugs in Vancouver between December 2005 and November 2013. We used multivariable mixed-effects modelling to longitudinally identify factors associated with ≥95% adherence to ART (estimated based on prescription refill compliance) and plasma HIV-1 RNA suppression (< 50 copies/mL) among HAART-exposed crack cocaine users. In a sub-analysis, we evaluated the impact of opioid substitution therapies on ART adherence and viral suppression among dual crack cocaine and opioid users.
Results: Among 438 HAART-exposed crack cocaine users, 240 (54.8%) had ≥95% adherence to ART in the previous 6 months at baseline. In multivariable analyses, older age (adjusted odds ratio [AOR]: 1.65; 95% confidence interval [CI]: 1.33-2.04) was independently and positively associated with ART adherence, while homelessness (AOR: 0.58; 95%CI: 0.44-0.77), at least daily crack cocaine smoking (AOR: 0.64; 95% CI: 0.50-0.81), and at least daily heroin use (AOR: 0.43; 95%CI: 0.29-0.65) were independently and negatively associated with ART adherence. None of the addiction treatment modalities assessed (e.g., inpatient treatment, outpatient detoxification, and drug counselling or peer-support meetings) were significantly associated with ART adherence. The results were consistent with viral suppression, except that among 293 dual crack cocaine and opioid users, participation in opioid substitution therapies was positively associated with viral suppression (AOR: 1.87; 95%CI: 1.25-2.79).
Conclusions: Among our sample of HAART-exposed crack cocaine users, homelessness, and high-intensity crack cocaine and heroin use were independently associated with suboptimal ART adherence and viral non-suppression. Except for opioid substitution therapies, the addiction treatment modalities do not appear to facilitate ART adherence or viral suppression. These findings suggest an urgent need to identify evidence-based addiction treatment options for crack cocaine use that also confer benefits to ART-related outcomes.

TUPEB310

Advanced liver fibrosis and mortality of HIV/HCV co-infected patients with alcohol use disorders

P. Zuluaga[1,2], D. Fuster[1,2], F. Bolao[3,4], A. Sanvisens[1], I. Rivas[5], M. Torrens[2,6], J. Tor[1,2], R. Muga[1,2]
[1]Hospital Universitari Germans Trias i Pujol, Badalona, Spain, [2]Universitat Autònoma de Barcelona, Barcelona, Spain, [3]Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Spain, [4]Universitat de Barcelona, Barcelona, Spain, [5]Centro Delta, Institut Municipal de Serveis Personals-IMSP, Badalona, Spain, [6]Parc de Salut Mar, Barcelona, Spain
Presenting author email: rmuga.germanstrias@gencat.cat

Background: Liver fibrosis is the main predictor of progression to end stage liver disease. HIV/HCV co-infection and alcohol use disorders (AUD) negatively impact liver fibrosis and survival. We aimed to analyze the role of HIV/HCV co-infection in mortality of patients with AUD.
Methods: Observational study in patients referred to treatment of AUD between 1999 and 2011 in Barcelona, Spain. Characteristics of patients and blood samples for HIV infection (EIA and HIV-1 RNA) and HCV infection (EIA and HCV RNA) were obtained at admission. CD4 cell count and use of HAART at admission were obtained from clinical charts. Advanced liver fibrosis (ALF) was defined by FIB-4 > 3.25 [FIB4 = (Age*AST)/(Platelet*ALT$^{1/2}$)]. Patients were followed up until December 2013 and causes of death were ascertained through ICD-10 codes and the death registry.
Results: 1.021 patients were consecutively admitted (80% M); age at admission was 44 years (IQR: 38-51 years), duration of AUD was 18 years (IQR: 11-24 years), daily alcohol consumption was 190 grams (IQR: 120-250 grams). Almost 17% had history of injection drug use. Overall, 22% of patients had ALF according to FIB-4.
Prevalence of HIV and HCV infection was 7% and 20% respectively and, 7% were HIV/HCV co-infected. Median CD4 cells among the HIV+ patients was 313 cells/mL (IQR: 140-560) and prevalence of HAART use at admission was 51%.

At the end of study (median follow-up 5.8 years (IQR 3.6-8.8), 6.434 person-years), 18% (n=184) of patients had died. Table shows the mortality rates and Relative Risk (RR) of death according to ALF and co-infection at entry:

	Patients	Deaths	Follow up (p-y)	Mortality rate (x 100 p-y) (95% CI)	Relative Risk (95% CI)
HIV-/HCV - without ALF	613	84	3942	2.1 (1.7-2.6)	1
HIV-/HCV- with ALF	157	37	910	4.1 (2.9-5.5)	1.9 (1.3-2.8)
HIV+/HCV+ without ALF	34	10	227	4.4 (2.2-7.8)	2.1 (1.0-3.8)
HIV+/HCV + with ALF	27	13	128	10 (5.6-17)	4.7 (2.5-8.3)

[Table]

HIV/HCV co-infected patients with ALF had significantly increased mortality rates (10.1 x 100 p-y) with respect to those without viral infections (4.1 x100 p-y) (RR 2.5, 95% CI 1.3- 4.6; p=0.003).

Conclusions: The reduced survival of HIV/HCV co-infected patients with AUD suggest that combined treatment of chronic hepatitis C and alcohol abuse is a priority in this population.

TUPEB311

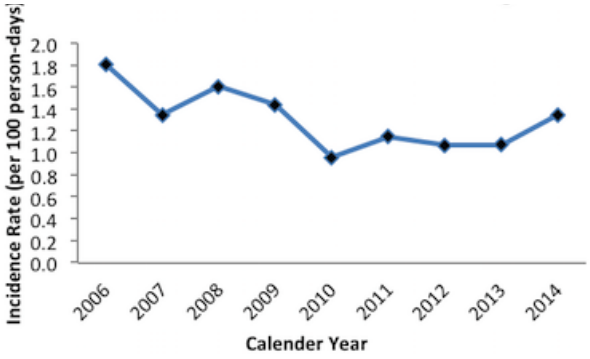
Discharge against medical advice from the HIV ward at St. Paul's Hospital, Vancouver, British Columbia, Canada from 2005-2014

J.H. Kremer[1], M. Hull[1,2], P. Phillips[1,2], D. Jaworsky[2], Z. Cui[1], N. Oliveira[1], R.S. Hogg[1,3], J. Montaner[1,2]
[1]British Columbia Centre for Excellence in HIV/AIDS, Vancouver, Canada, [2]University of British Columbia, Vancouver, Canada, [3]Simon Fraser University, Burnaby, Canada
Presenting author email: hkremer@cfenet.ubc.ca

Background: Inpatient admissions for AIDS defining illness have declined with the advent of effective antiretroviral therapy (ART), however mental health and addictions-related comorbidities continue to play a role in hospitalizations for HIV-infected individuals. Hospital discharge against medical advice (AMA) is a significant barrier to providing adequate care patients on the HIV ward at St. Paul's Hospital (SPH) in Vancouver, British Columbia (BC), Canada. This study evaluated trends in the rate of AMA discharges over time and identified factors associated with leaving AMA.

Methods: We conducted a retrospective analysis of data collected for patients discharged from the SPH HIV ward between July 1, 2005 and Dec 31, 2014. Discharge AMA was defined as leaving hospital against physician recommendations as per the discharge records for each hospital visit. Viral load, ART usage, and CD4 cell count data were obtained through linkage with the provincial Drug Treatment Program database. Rates of AMA discharges over time were summarized and factors associated with an AMA discharge were evaluated using generalized estimating equations in a multivariate model.

Results: We analyzed data from 3843 visits of which 753 (19.5%) were discharged AMA. The median age at initial visits was 46 years (39-53) and 77.8% of patients were male. The incidence rate of discharge AMA declined from 1.8/100 patient-days in 2006 to 1.3/100 patient-days in 2014 (Relative Risk [RR] 0.947, 95% Confidence Interval [CI] 0.90 - 0.98)(Figure 1). Patients discharged AMA had a significantly (p< 0.001) shorter length of stay (median (Q1-Q3) 6 (3-13) vs 9 (5-18)). AMA discharges were associated with younger age (adjusted relative risk [ARR] per year 1.041; 95% CI 1.029 - 1.053), female gender (ARR 1.358; 95% CI 1.079 - 1.708) and IDU (ARR 3.540; 95% CI 2.360 - 5.308), no ART use (ARR 1.960; 95% CI 1.336 - 2.875), no need for long-term antibiotics (ARR 1.913; 95% CI 1.354 - 2.704), and no use crystal meth (ARR 1.734, 95% CI 1.100 - 2.735).



[Figure 1. Incidence of AMA discharge]

Conclusions: Leaving the hospital AMA may lead to sub-optimal patient outcomes. IDU was strongly co-related with discharge AMA; strengthening of addictions medicine inpatient clinical services and support programs may help to reduce AMA discharges.

TUPEB312

Prescription opioid injection is strongly linked with illicit drug-related vulnerability and plasma HIV-1 RNA viral load detectability among HIV-positive illicit drug users in a Canadian setting

S. Lake[1,2], T. Kerr[1,3], R. Hogg[1], S. Guillemi[1], H. Dong[1], J. Montaner[1,3], E. Wood[1,3], M.-J. Milloy[1,3]
[1]British Columbia Centre for Excellence in HIV/AIDS, Vancouver, Canada, [2]University of British Columbia, School of Population and Public Health, Vancouver, Canada, [3]University of British Columbia, Faculty of Medicine, Vancouver, Canada
Presenting author email: stephielou.lake@gmail.com

Background: Prescription opioid analgesic (POA) use is rising across North America and is associated with unprecedented morbidity and mortality from accidental opioid overdose. Further, the diversion of POAs has led to high rates of illicit POA use among people who inject drugs (IDUs). However, we are unaware of any research characterizing POA injection among HIV-positive IDUs, including the impact of POA injection on plasma HIV-1 RNA viral load suppression. Thus, using longitudinal data, we sought to identify the prevalence and correlates of POA injection among ART-exposed IDUs in a setting of universal no-cost HIV/AIDS treatment and care.

Methods: We used data from the ACCESS study, an ongoing prospective cohort of community-recruited HIV-positive illicit drug users linked to comprehensive HIV clinical monitoring data. Generalized linear mixed-effects regression was used to model the relationships between illicit POA injection in the last six months and a range of behavioural-, social-, structural- and clinical-level factors.

Results: Between December 2005 and November 2013, the study enrolled 715 participants with median age 43.6 years. The prevalence of recent POA injection peaked at 22.6% in November 2006. At the most recent follow-up, 13.8% of participants reported injecting POAs in the previous six months. In a multivariable analysis, younger age (adjusted odds ratio [AOR]: 1.06) and later year of observation (AOR: 1.01) as well as drug-related behavioral characteristics, including drug dealing (AOR: 4.46), ≥daily crack smoking (AOR: 1.69), and ≥daily cocaine injection (AOR: 1.95) were significantly and positively associated with POA injection. Participants who recently injected POAs were also significantly less likely to exhibit non-detectable plasma HIV-1 RNA viral load (AOR: 0.70). All $p < 0.05$.

Conclusions: Among this group of HIV-positive IDU on ART, periods of illicit POA injection were significantly associated with a constellation of high-risk illicit drug using exposures as well as a lower likelihood of optimal virologic outcomes. These findings contribute to a list of significant social and structural barriers IDUs face in achieving optimal HIV outcomes, despite the setting of universal HIV treatment. Efforts to both minimize drug-related risk behaviors and support ART adherence should be inclusive of people who inject POAs.

PEP

TUPEC499

Delayed HIV seroconversions in patients receiving post-exposure prophylaxis (PEP)

L. Leal, B. Torres, A. León, A. Inciarte, C. Lucero, V. Díaz-Brito, J.M. Gatell, F. García
Hospital Clinic Barcelona, Infectious Diseases, Barcelona, Spain
Presenting author email: gatell0@attglobal.net

Background: Some patients who attend clinics to prevent HIV acquisition after a sexual exposure have a delayed seroconversion despite counseling. Our objective is to assess the rate and factors associated with a delayed HIV seroconversion, select those patients with higher risk and propose them additional preventive strategies as closer and longer follow-up or preexposure prophylaxis.

Methods: Demographics, sexual behaviour, PEP use, HIV testing and sexually transmitted infections (STI) history were compared between patients with a delayed seroconversion and non-seroconverters, matched by gender, age and date attending the clinic from a cohort of 3089 HIV uninfected patients followed-up due to a sexual exposure to HIV from 2003 to 2013.

Results: 69 out of 3089 patients (2.2%) seroconverted after a median (IQR) of 18 (9-34) months since the last visit for sexual exposure. CD4 T-cell count at HIV diagnosis was significantly higher in those patients in whom HIV was detected earlier (568 vs 441 cells/mm3 for patients with HIV diagnose before and after 18 months after last visit in the clinic, p= 0.01). HIV seroconverters were predominantly male (96%), with 36 years old, MSM (96%) and Caucasian (67%). No differences were observed between seroconverters and non-seroconverters regarding birth place (Spain 67% vs 71%, p=1), risk of exposition (high 18% vs 20%, p=0.8), current PEP prescription (77% vs 70%, p=0.4), hours from exposition to PEP prescription (18 vs 19 hours, p=0.9), good adherence to PEP (91% vs 96%, p=0.4) and presence of coinfections at baseline (hepatitis A, B and C or syphilis). Conversely, the proportion of MSM (96% vs 75%, p< 0.0001), sexual partner with known HIV infection (52% vs 33%, p=0.1), previous PEP (19%

vs 6%, p=0.05), previous STI (88% vs 48%, p=0.01), and previous HIV testing (58% vs 41%, p=0.05) was higher in seroconverters.
Conclusions: Delayed HIV seroconversions are usual between HIV exposed patients attending a clinic. Closer and longer follow-up and/or preexposure prophylasis should be considered in MSM with sexual contacts with known HIV infected patients and previous and repeated sexual exposure. These measures could prevent new infections or at least permit the diagnosis of HIV infection at earlier stages.

TUPEC500

Post-exposure prophylaxis outcomes for survivors of sexual assault in resource poor settings: evidence from rural South Africa

C.R. Carty[1,2], E. Toska[3], T. Mukaro[4], F. Nicholson[4]
[1]Relevance Network, Johannesburg, South Africa, [2]Thohoyandou Victim Empowerment Programme, Research and Advocacy, Sibasa, South Africa, [3]University of Oxford, Department of Social Policy and Intervention, Oxford, United Kingdom, [4]Thohoyandou Victim Empowerment Programme, Monitoring and Evaluation, Sibasa, South Africa
Presenting author email: tapiwa@tvep.org.za

Background: Challenges associated with the care for survivors of sexual assault at risk for HIV remains largely unstudied. Evidence from the Thohoyandou Victim Empowerment Programme's sexual and gender based violence cohort (n=19,975) in Limpopo, South Africa offers compelling arguments for the integration of longer-term, more rigorous and holistic post-exposure prophylaxis (PEP) monitoring as standard practice.
Methods: Data captured (2002 - 2014) was disaggregated according to type of assault, resulting in a cohort of 6,828 survivors of sexual abuse. This includes 5,934 (86.9%) survivors of rape and 894 (13.1%) of non-penetrative sexual abuse (Table 1). Client demographics (including sex), case information, PEP-related variables, perpetrator details, and support received were reported. Analyses included descriptive characteristics, univariate and multivariate logistic regressions using SPSS 19.

Characteristic	Rape (n=5934)		Non-penetrative (n=894)		Total (n=6828)	
	Mean (SD)	N (%)	Mean (SD)	N (%)	Mean (SD)	N (%)
Age	29.3 (12.7)		16.9 (12.1)		19.8 (12.7)	
Children (0-9)		688 (11.6)		224 (25.1)		912 (13.4)
Adolescents (10 - 19)		2958 (49.8)		424 (47.4)		3382 (49.5)
Adults (>20)		2176 (36.7)		244 (27.3)		2420 (35.4)
Sex: Female		5536 (93.3)		637 (71.3)		6173 (90.4)
Sex: Male		327 (5.5)		257 (28.7)		584 (8.6)
Previous Assault		5122 (8.6)		60 (6.7)		86 (1.3)
Pregnant		294 (5.0)		9 (1.0)		303 (4.4)

[Table 1. Client characteristics]

Results:
Nearly half of all cases were adolescents (49.5%) and the majority were females (90.4%). Factors linked to rape compared with non-penetrative sexual abuse were: adolescence or adult age (p≤0.001); female sex (p≤0.001); history of assault (p=0.007); and pregnancy (p≤0.001). 66% of the cohort (76% of rape survivors) was PEP-eligible based upon serostatus, time-to-report, and assault type. Among those who initiated, PEP completion data was recorded for 41.7%. Completion rates were 91.6%. Child and female survivors were less likely to initiate PEP (p≤0.001), as were those with a history of assault (p≤0.001). Being the breadwinner was associated with higher initiation of PEP (p=0.034). In a multivariate regression, older age and history of assault remained significant (p≤0.001). PEP completion was more likely among young children and adults when compared to adolescents (p=0.047). Data on HIV retesting at 6 months post completion of PEP was available for only 1,047 survivors. Of those, 90% retested and 84.3% of them remained HIV negative.
Conclusions: This sample represents a rare glimpse into survivor populations at risk for HIV who reside in resource poor, rural areas in South Africa. Of note, the findings suggest that adolescents are vulnerable to not initiating or completing PEP, a reflection of HIV cohort findings with regard to loss-to-care among this particularly vulnerable subpopulation.

TUPEC501

Awareness of post-exposure prophylaxis (PEP) among a cohort of gay, bisexual and other men who have sex with men (MSM) in Vancouver, Canada

A. Rich[1], M. Hull[1,2], N.J. Lachowsky[1,2], Z. Cui[1], P. Sereda[1], K. Stephenson[3], M. Thumath[2,4], E.A. Roth[5,6], R.S. Hogg[1,7], D. Moore[1,2,4]
[1]British Columbia Centre for Excellence in HIV/AIDS, Epidemiology and Population Health, Vancouver, Canada, [2]University of British Columbia, Vancouver, Canada, [3]Vancouver Coastal Health, Vancouver, Canada, [4]British Columbia Centre for Disease Control, Vancouver, Canada, [5]University of Victoria, Victoria, Canada, [6]Centre for Addiction Research BC, Victoria, Canada, [7]Simon Fraser University, Burnaby, Canada
Presenting author email: arich@cfenet.ubc.ca

Background: Post-Exposure Prophylaxis (PEP) is a strategy to reduce HIV infection in those with high-risk exposure. This study characterized PEP awareness amongst Vancouver MSM.
Methods: Momentum Health Study participants were recruited via respondent driven sampling (RDS) and completed a self-administered computer-based interview. Multivariable logistic regression identified factors associated with PEP awareness, asked between November 2012 and February 2014.
Results: Of 673 participants included in this analysis, 384 (57.1%) had heard of PEP, a proportion that did not significantly differ over time (p=0.45). Of those who had heard of PEP, 31.6% reported knowing "not much, or nothing at all" about PEP, 59.3% "a bit in general", and 9.1% "a lot"; only 29.7% reported talking about PEP with friends or sexual partners in the past 6 months. Of the 9 participants who had used PEP, 7 identified the provincial nPEP pilot program as the source. Factors associated with greater odds of PEP awareness include being a student (AOR=2.09, 95%CI:1.31-3.35), reporting ≥10 lifetime insertive anal sex partners (AOR=1.81, 95%CI:1.15-2.83), having had any condomless anal intercourse with an unknown or discordant serostatus partner in the past six months (AOR=1.56, 95%CI:1.00-2.43), having ever been diagnosed with genital warts (AOR=1.76, 95% CI: 1.04-2.98), having attended barebacking sex parties (AOR=2.20, 95%CI:1.06-4.55), assuming partner's serostatus as positive versus negative (AOR=3.29, 95%CI:1.79,6.06) and reporting use of other preventive strategies such as abstaining from anal intercourse (AOR=2.06, 95%CI:1.36-3.11) or sero-sorting for condomless anal intercourse (AOR=1.92, 95%CI:1.27-2.89). HIV-positive participants who ask their partner's serostatus were more likely to be aware of PEP than those who do not ask (AOR=3.86, 95%CI: 1.61-9.25). PEP awareness was negatively associated with self-identified Aboriginal ethnicity versus White (AOR=0.15, 95%CI:0.07-0.34), non-gay sexual orientation (AOR=0.47, 95%CI:0.28-0.81), high school education or less (AOR=0.60, 95%CI:0.38-0.94), higher Sexual Altruism-Personal sub-scale scores (AOR=0.56, 95%CI:0.39-0.79), and lesser agreement with the statement "I always have condoms when having sex" (agree versus strongly agree: AOR=0.47, 95%CI:0.29-0.76).
Conclusions: PEP awareness is high, has been rarely used (2.6%), and is positively associated with certain behaviours with greater potential for HIV transmission. Further research is needed to investigate how best to incorporate this strategy within combination HIV prevention.

PrEP

TUPEC502

Willingness to receive PrEP among HIV-uninfected Chinese MSM who are users of a popular geosocial networking application

H.T.H. Wong[1], S.S. Lee[1], D.P.C. Chan[2]
[1]Chinese University of Hong Kong, Stanley Ho Centre for Emerging Infectious Diseases, Hong Kong, Hong Kong, [2]Chinese University of Hong Kong, Stanley Ho Centre for Emerging Infectious Diseases, Shatin, Hong Kong
Presenting author email: chandenise@gmail.com

Background: Pre-exposure prophylaxis (PrEP) against HIV has recently been recommended as a prevention option for MSM who practice unprotected sex. Previous studies have revealed that MSM users of geosocial networking applications (Apps) are more inclined to engage in risky sexual behaviours. This study aimed, therefore, to investigate their willingness to receive PrEP in a Chinese population where PrEP has not been introduced.
Methods: Between November and December 2014, five waves of invitations to a web-based survey were sent to all MSM locating in Hong Kong using the geosocial networking App *Grindr*. Study domains included demographics, sexual behaviours, self-perceived HIV risk and views on PrEP. Basic information about PrEP (such as its usage and effectiveness) was provided. Telephone numbers of community-based organizations were shown to participants at the end of the survey for those wanting to know more about PrEP. The study was non-remunerated and entries of duplicated IP address were removed to uphold data quality.

Results: Among the 401 HIV-negative Chinese MSM (82.0% Hong Kong permanent residents) recruited, 47.1% had engaged in unprotected anal sex and 1.7% had sex with an HIV-infected partner in the previous year. Only three (0.7%) had received post-exposure prophylaxis. Majority (79.6%) had never come across any information about PrEP; and none had ever received PrEP. On a scale of 1 (lowest) to 10 (highest), 68.6% gave a score 7 or above for their willingness to use PrEP. Half (55.4%) considered that PrEP should be made accessible to all MSM to prevent HIV in the community. Their major concerns of PrEP included its side effects (74.3%), affordability (63.1%) and effectiveness in reducing HIV transmission (58.1%). Some 30.2% agreed that PrEP would decrease their motivation of using condom during sex. Linear regression showed that willingness to receive PrEP was positively associated with participants' self-perceived HIV risk.
Conclusions: Although many MSM who practice risky sexual behaviours are interested in using PrEP, only a few had come across information about the intervention. To maximize public health benefit, more information on PrEP should be provided to address MSM's concerns before making it accessible to the community.

TUPEC503

PrEP in real-life settings: good adherence and no increase in high-risk behavior

R. Thomas, C. Galanakis, D. Longpré, J.-P. Kerba, L. Charest, S. Lavoie, E. Huchet, D. Murphy, B. Trottier, N. Machouf
Clinique Médicale L'Actuel, Montreal, Canada

Background: Little is known about pre-exposure prophylaxis (PrEP) use and adherence in real-life settings and its impact on high-risk behaviors is unclear. We aimed to evaluate adherence to follow-up and treatment, and behavioral changes in a high-risk clinical population.
Methods: We prospectively assessed patients receiving PrEP (TDF-FTC) at our clinic from 2011-2014. After their initial visit, patients were seen at 3-month follow-up intervals (FU). Treatment adherence and behavioral data were measured by self-report at every FU visit. Adherence and behavioral changes were analyzed by chi-square and time to treatment discontinuation was estimated by Kaplan-Meier analysis.
Results: 112 patients were prescribed PrEP. The main indication for PrEP was regular unprotected anal intercourse (64%). Patients requesting PrEP were male (99%) and MSM (98%) with a mean age of 38 (Range=20-61y). The majority of patients had a history of STDs (80%) and 67% reported having more than 10 sexual partners. On average, condom use was 59% for receptive anal intercourse and 63% for insertive. Among the 87 patients with available FU data, median FU was 12 weeks. In the first 3 months after starting PrEP, 92% of patients attended a FU visit. Furthermore, 86% of patients reported taking PrEP daily, whereas 2% had adherence problems and 4% took PrEP intermittently. Overall, 18 patients (21%) stopped PrEP; 44% of which occurred in the first 3 months of FU. Five patients (5/18, 28%) discontinued due to adverse events: four patients had elevated creatinine and 1 patient suffered from nausea and vomiting. Increases in high-risk behavior following PrEP use were not observed. There was no difference among the reported number of sexual partners (p=0.557) and condom use (p=0.293).
Conclusions: Patients receiving PrEP seem adherent to treatment and to follow-up. However, one-fifth discontinued prophylaxis. PrEP does not promote an increase in high-risk behaviors.

TUPEC504

Concerns and benefits of PrEP: lessons from the national PrEP demonstration project formative study in Nigeria

Y. Nancin Dadem[1], J. Idoko[2], M. Folayan[3], O. Grace Kolawole[1], J. Anenih[2], E. Alhassan[2]
[1]Jos University Teaching Hospital, Infectious Disease Unit, APIN, Jos, Nigeria, [2]National Agency for the Control of AIDS (NACA), Abuja, Nigeria, [3]Obafemi Awolowo University, Institute of Public Health and Department of Child Dental Health, Ile-Ife, Nigeria
Presenting author email: nancindadem@yahoo.com

Background: The use of antiretrovirals (ARVs) as pre-exposure prophylaxis (PrEP) reduces the risk of HIV transmission in serodiscordant couples in Africa. The design of effective strategies for delivery and optimal uptake of this new prevention tool begins with an understanding of likely public concerns. To inform design of the national PrEP Demonstration Project in Nigeria, we conducted a formative study to identify: (a) a Demonstration target group, (b) effective approaches to public health messaging about PrEP, (c) possible community concerns and logistic challenges, and (d) options for addressing these challenges when implementing a PrEP Demonstration project in Nigeria.
Methods: The sample represented a broad spectrum of relevant stakeholder groups, including:
(1) health care professionals and policy makers concerned with HIV treatment and prevention,
(2) local communities,
(3) high-risk HIV populations, and
(4) civil rights organizations.
Qualitative data were generated in three phases. First, individual in-depth interviews (N=101), focus groups (N=12 groups; 6-12 participants per group), and telephone interviews (N=113) were conducted. Then, informative meetings with mixed stakeholder groups (N=2 meetings) were carried out to seek feedback on initial findings, and to use findings to identify specific barriers and facilitators to implementing PrEP for serodiscordant couples (the identified Demonstration target group). Lastly, an online survey to generate wider perspectives was completed by 70 voluntary participants from around the world. Qualitative data were inductively analyzed to construct categories addressing study-related objectives.
Results: Findings suggest PrEP will be widely accepted in Nigeria as an additional option for HIV prevention for heterosexual HIV serodiscordant couples. Perceived benefits included preserving serodiscordant marriages, increasing options for conception for serodiscordant couples, and reducing HIV transmission risk. Concerns include likely increase in risky sexual behavior, stigmatization of PrEP users, possible drug side effects, and non-adherence with drug regimen.
Conclusions: Despite general enthusiasm for PrEP, concerns suggest there might be barriers to PrEP uptake by beneficiaries. A robust campaign and delivery strategy to address barriers is critical. Involving communities through advocacy, providing accurate information to the public and combating stigma in communities are steps towards eliminating barriers and gaining PrEP acceptance as a HIV prevention tool in Nigeria.

TUPEC505

HIV pre-exposure prophylaxis (PrEP) product preference among women in the VOICE-D (MTN-003D) study

E. Luecke[1], H. Cheng[1], K. Woeber[2], T. Nakyanzi[3], O. Munaiwa[4], A. van der Straten[1,5]
[1]RTI International, Women's Global Health Imperative, San Francisco, United States, [2]Medical Research Council, Durban, South Africa, [3]Makerere University - Johns Hopkins University Research Collaboration, Kampala, Uganda, [4]UZ-UCSF Collaborative Research Programme, Harare, Zimbabwe, [5]University of California San Francisco, Center for AIDS Prevention Studies (CAPS), San Francisco, United States
Presenting author email: eluecke@rti.org

Background: HIV PrEP is only effective if used consistently and correctly, thus a deeper understanding of women's product preferences, and the correlates of those preferences, is valuable in guiding future research. VOICE-D (MTN-003D), a qualitative ancillary study conducted after release of the VOICE results, retrospectively explored participants' tablet and gel use, as well as their preferences for other potential PrEP products.
Methods: We conducted a mixed methods analysis of data from VOICE-D participants. During in-depth-interviews (IDIs), women were presented with pictures and descriptions of potential PrEP products including the oral tablet and vaginal gel tested in VOICE, and asked to discuss which products they would prefer to use and why. Seven of the original products displayed were combined into preferred product categories based on exploratory factor and latent class analyses. We examined demographic and behavioral correlates of these preferred product categories. IDIs with participants were conducted, coded, and analyzed for themes related to product preference.
Results: Of the 68 female participants who completed IDIs (22 South Africa, 24 Zimbabwe, 22 Uganda), median age was 28 (range 21-41), 81% were HIV-negative, and 90% were married or had a primary sex partner. Four preferred product categories were created: 1) oral tablets; 2) vaginal gel; 3) injectable, implant, or vaginal ring; and 4) film or suppository. A majority of women (55%) expressed a preference for products included in category 3. Characteristics significantly associated with each preferred product category differed (Table 1). VOICE study product assignment was only significantly associated with category 2: vaginal gel. Participants' explanations for their preferred product selections included duration of activity, ease of use, route of administration, provider- vs. self-administration, and degree of familiarity with product.

Preferred Product Category	Factors Significantly Associated with Preference for Product Category (p<0.05 Fisher's exact test)
Category 1: Tablet	HIV positive Age ≤25
Category 2: Gel	Vaginal gel VOICE study product assignment Age 26+
Category 3: Implant, Injectable, or Ring	Not from Uganda Completed secondary school
Category 4: Film or Suppository	From South Africa Does not live with primary sex partner Parity ≤1 Completed secondary school Highest socioeconomic status

[Table 1. Correlates of preferred products]

Conclusions: While there was interest in a variety of potential PrEP products, a majority of VOICE-D participants preferred long-acting methods. Preference for a particular product category was associated with varying participant characteristics. Analyses of the correlates of product preference can inform messaging and market segmentation for different products as well as research funding and resources to invest in products that target populations are most interested in using.

TUPEC506

Patient-provider communication about sexual behaviors and pre-exposure prophylaxis: results from a national online survey of men who have sex with men in the United States

D.S. Krakower[1,2], C.E. Oldenburg[3], M.J. Mimiaga[3,4,5], D. Novak[6], J.G. Rosenberger[7], S. Elsesser[5], K.H. Mayer[1,2,5]
[1]Beth Israel Deaconess Medical Center, Division of Infectious Diseases, Boston, United States, [2]Harvard Medical School, Boston, United States, [3]Harvard School of Public Health, Boston, United States, [4]Massachusetts General Hospital, Boston, United States, [5]The Fenway Institute, Boston, United States, [6]Online Buddies, Cambridge, United States, [7]George Mason University, Fairfax, United States
Presenting author email: dkrakowe@bidmc.harvard.edu

Background: Successful implementation of HIV pre-exposure prophylaxis (PrEP) will depend on whether men who have sex with men (MSM) are willing to disclose HIV risk behaviors to healthcare practitioners. A recent online study surveyed MSM to assess their comfort and experiences discussing sexual risk behaviors with primary care providers (PCPs).
Methods: In August 2013, U.S. members of a website for MSM seeking sex partners completed surveys assessing sexual behaviors, experience and interest in chemoprophylaxis, comfort disclosing same-sex behaviors, and experiences discussing sex with PCPs. Analyses were restricted to respondents identifying a PCP and indicating interest in using PrEP. Logistic regression models with robust variance estimators accounting for clustering by state identified factors associated with effective communication.
Results: Surveys were analyzed from 1,394 respondents. Their mean age was 44; 87% were white, 4% Black, 7% Latino, 69% had completed college, and 47% earned ≥ $60,000/year. In the prior 3 months, 48% had condomless anal intercourse (CAI) with ≥ 3 partners, and 29% reported serodiscordant CAI. Forty-three percent were uncomfortable discussing male-male sex with PCPs, and 61% had not discussed CAI. Lack of discussion with PCPs about PrEP (84%) and beliefs that PCPs would not be willing to prescribe PrEP (76%) were perceived as barriers to accessing chemoprophylaxis. Accordingly, 53% of respondents would prefer to obtain PrEP from sources other than their PCPs. Comfort disclosing same-sex behaviors to PCPs was associated with income ≥ $60,000/year (adjusted odds ratio (aOR) 1.89; 95% confidence interval (CI) 1.23-2.92), prior STI (aOR 1.60; CI 1.24-2.07), and depression (aOR 1.54; CI 1.11-2.13), and inversely associated with heterosexual identity (aOR 0.30; CI 0.21-0.77) and preference to obtain PrEP from non-PCP clinicians (aOR 0.06; CI 0.05-0.08). MSM who discussed CAI with PCPs more often identified as Latino (aOR 2.21; CI 1.25-3.92) and indicated awareness of post-exposure prophylaxis (aOR 1.79; CI 1.40-2.29), and less often preferred non-PCP clinicians as a source of PrEP (aOR 0.14; CI 0.10-0.18).
Conclusions: Suboptimal communication about sexual risk behaviors could prevent many MSM who are already engaged in healthcare from accessing PrEP from their PCPs. Interventions to optimize MSM-provider communication about HIV risk behaviors are needed.

TUPEC507

Absence of sexual behavioral disinhibition in a PrEP adherence trial: considerations for medical providers who prescribe PrEP for men who have sex with men (MSM)

S. Elsesser[1], K. Biello[1,2], S. Taylor[1,3], J. Tomassilli[1], S. Safren[1,4], K. Mayer[1,5]
[1]Fenway Health, The Fenway Institute, Boston, United States, [2]Harvard School of Public Health, Boston, United States, [3]Wheelock College, Boston, United States, [4]Harvard Medical School/Massachusetts General Hospital, Boston, United States, [5]Harvard Medical School/Beth Israel Deaconess Medical Center, Boston, United States

Background: Antiretroviral pre-exposure prophylaxis (PrEP) has been shown to decrease HIV incidence in MSM. Although earlier trials did not find evidence of increased condomless sex in trial participants, recent evidence suggests that some medical providers remain concerned about behavioral disinhibition after starting PrEP, which could limit access for those who need it the most. We compared sexual behavior data pre- and post-initiation of PrEP among MSM enrolled in a study designed to enhance PrEP adherence.
Methods: Between November 2012 and December 2013, 50 Boston-area MSM were randomized into either a PrEP-specific adherence intervention, which included four weekly sessions to address barriers and facilitators of PrEP use, or to a time-matched control: sessions that emphasized general health information, but also provided information about PrEP. Participants self-reported sexual behavior at baseline and six month follow-up visits via computer survey. Using SPSS, differences in sexual behavior were examined using ANOVA.
Results: Participants were primarily White (94%) and college educated (64%). Rates of condomless sex did not differ significantly between the three months prior to initiation of PrEP (baseline) and the final three months of the six month trial (post-initiation of PrEP) [$F(1, 38) = 1.90$, $p = 0.17$, $\eta_p^2 = 0.047$].
Over that same time period, change in total number of sex acts [$F(1, 38) = 1.10$, $p = .30$, $\eta_p^2 = 0.028$] and the proportion of total sex acts which were condomless [$F(1, 37) = 0.14$, $p = .71$, $\eta_p^2 = 0.004$] was not significant.
At the 6 month follow-up, Tenofovir and FTC were detected in the blood of 90% of participants, with 74% of participants having levels consistent with daily use. None of these findings differed significantly between the two randomized conditions.
Conclusions: In this open-label PrEP study of Boston MSM, behavioral disinhibition was not seen in conjunction with PrEP use. Before study entry, participants were already engaging in condomless sex, and during the study, generally adherent. Medical providers who prescribe PrEP to MSM who engage in condomless sex may want to focus on optimizing adherence in this population, rather than behavioral disinhibition.

TUPEC508

Significant increases in HIV pre-exposure prophylaxis (PrEP) uptake in Boston, a Boston Community Health Center in 2014: who are the recent users?

K. Mayer[1,2], D. Krakower[1,2], K. Levine[3], C. Grasso[3], M. Gelman[3]
[1]Fenway Health/Harvard University, The Fenway Institute, Boston, United States, [2]Beth Israel Deaconess Medical Center, Medicine, Boston, United States, [3]Fenway Health, The Fenway Institute, Boston, United States
Presenting author email: khmayer@gmail.com

Background: Although the US FDA and CDC approved the use of tenofovir/emtricitabine for PrEP in 2010, uptake was initially slow. However, in 2014, PrEP use markedly increased among Boston MSM.
Methods: Fenway Health (FH) is community-based facility in downtown Boston that has longstanding expertise in HIV primary care and prevention research. FH has used the Centricity™ electronic medical record for patient care since 1997, which was reviewed to perform the current analyses to characterize recent socio-demographic, behavioral and clinical trends in PrEP utilization.
Results: In 2011, 5 FH patients (pts) initiated PrEP, whereas 20 initiated in 2012, 102 in 2013, and 536 in 2014 (with 88.5% still using PrEP as of 12/31/14; longest duration: 3.8 years). PrEP users at FH were predominantly white (79.7%), though 8.0% were Black and 12.3% were Latino. Most (97.1%) PrEP users were male; 95.1% of 447 pts whose sexual orientation was recorded identified as gay or bisexual. Only 15 transgender people and 2 women accessed PrEP. PrEP users were geographically dispersed, living in 158 different postal codes, with the largest cluster in a nearby neighborhood with 7.8% of PrEP users. The most common reasons for PrEP initiation were: engaging in condomless anal intercourse (64.6%), being in an HIV serodiscordant relationship (14.9%), wanting an additional level of protection during sex (9.6%). The major payors for PrEP were private insurers (80.7%), Medicare (9.0%), Medicaid (8.7%). Seventy-seven pts (11.7%) subsequently terminated PrEP use. The most common reasons for discontinuation were: changes in risk behavior/relationships (38.9%), drug-related side effects or toxicities (18.2%). Only 1.2% cited cost/insurance issues. Of those who terminated PrEP, 25.9% restarted. Four pts who initiated PrEP subsequently became HIV-infected, but had either discontinued PrEP or were non-adherent at the time of infection. In 2014, 25.2% of pts with a new bacterial STD, and 33.3% of pts using PEP, subsequently initiated PrEP.
Conclusions: PrEP use has recently markedly increased among MSM accessing services at a Boston community health center. Although many high risk pts initiated PrEP, further research is needed to understand reasons why some who might benefit did not access PrEP, particularly MSM from racial and ethnic minority communities.

TUPEC509

Pre-exposure prophylaxis (PrEP) knowledge and use in a population-based sample of younger Black men who have sex with men (YBMSM) in Chicago

A. Khanna[1,2], S. Michaels[3], B. Skaathun[1,4], E. Morgan[1,4], L.E. Young[1,2], P. Schumm[4], J.A. Schneider[1,2,3], UConnect Study Group
[1]Chicago Center for HIV Elimination, University of Chicago, Chicago, United States, [2]University of Chicago, Medicine, Chicago, United States, [3]National Opinion Research Center, Chicago, United States, [4]University of Chicago, Public Health Sciences, Chicago, United States

Background: In the United States early evidence exists of racial disparities in PrEP knowledge, seeking behavior and uptake. YBMSM in particular have lower PrEP engagement when compared to other racial/ethnic groups, even in the context of increased health care access due to the Affordable Care Act. We examine factors associated with PrEP knowledge and uptake from the first population-based sample of YBMSM 16-29 years of age.
Methods: A representative sample of YBMSM was generated using Respondent Driven Sampling (RDS) in Chicago (n=623) from June 2013 to July 2014. HIV antibody/Ag/RNA testing was performed using dry blood spots. Outcomes included PrEP knowledge and previous PrEP use. Several sociodemographic, behavioral, clinical and social factors were collected to examine associations with outcomes. Bayesian Model Averaging was used to select variables into final multivariate logistic regression models.

Results: Mean age was 22 years and 28% were HIV seropositive. 40.4% of eligible participants (*n*=252) knew about PrEP, but only 9% of those (4% of overall sample) had used PrEP themselves (*n*=22), and 29.7% (*n*=75) of the PrEP-aware knew others who had used PrEP. Models did not converge for PrEP uptake due to small numbers who had used PrEP previously. Factors associated with PrEP knowledge included completing college (aOR 2.22; p=0.05), having a medical provider (aOR 1.59; p=0.04), HIV positive status (aOR 2.17; p=0.002), having previously participated in an HIV prevention program (aOR 3.18; p< 0.001), and membership in the House/Ball community (aOR 2.32; p=0.003). No significant association was found between PrEP knowledge and closeness to the Black or Gay community, socializing in Boystown, (a gay-affiliated neighborhood), or behavioral risk factors such as condomless sex with male partners and group sex.
Conclusions: Several clinical factors were associated with PrEP knowledge suggesting that accelerating access to health care and HIV prevention programming may increase PrEP knowledge. In addition some YBMSM sub-groups, such as the House/Ball community and HIV infected individuals may be exposed more to PrEP information. Engaging YBMSM not engaged with HIV prevention/clinical systems and those with sex behaviors associated with HIV risk is urgently required if PrEP uptake is to have public health impact on the US HIV epidemic.

TUPEC510

PrEP in the real world: implementation of PrEP in a medium-sized city community health clinic

R. Corales, S.-R. Chen, S. Holt, A. Zuppelli, J. Ritzler, J. Roberts, W. Schaefer, M. Mancenido, W. Valenti
Trillium Health, Rochester, United States
Presenting author email: rbcorales@aol.com

Background: Truvada (TVD) used for HIV Pre-Exposure Prophylaxis (PrEP) was approved by the FDA in July 2012 to reduce the risk of sexually acquired HIV-1 in high risk adults. PrEP was shown to be safe and efficacious in clinical trials, however, longitudinal real world data are lacking. We describe a team approach to implementation of PrEP over a two year period, and report on patient health outcomes.
Methods: From August 2012 to Jan 2015, we evaluated102 patients for PrEP. Our team approach started with high risk evaluation, HIV education, and rapid HIV Ab test. Sexual history and physical exam was completed by a medical provider. A clinical pharmacist addressed potential efficacy, adverse events, and possible financial obstacles with the patient. Patients were seen every three months by a medical provider, and comprehensive harm reduction and prevention education given at each visit.
Results: All 102 patients evaluated were high risk, defined as having unprotected sex and at least one of the following: are casual partners of people of unknown HIV status, have multiple sexual partners, are in a sero-discordant relationship, had a recent sexually transmitted infection (STI), are engaged in transactional sex. 94 of 102 (92%) patients started PrEP. 10 of 94 (11%) patients discontinued PrEP during the reported time period. All 94 individuals who started PrEP remained HIV negative while on treatment. There was no increase in the STI rates observed when compared with the historical timed data, and the overall reported adherence rate was greater than 90%. Ten patient interviews suggest that the decision to take PrEP is motivated by disease prevention, that sexual behaviors do not change, and peace of mind as well as staying HIV negative are positive outcomes for patients.
Conclusions: To date, in our medium-sized city community clinic, utilizing a team approach, all 94 patients remained HIV negative while on treatment, had an adherence rate of >90%, had no increase in STI rate, and had no change in their sexual routines.

TUPEC511

Fertility intentions, pregnancy and PrEP use in African HIV serodiscordant couples

R. Heffron[1,2], K. Thomson[2], C. Celum[1,2,3], N. Mugo[1,4], E. Katabira[5], E. Bukusi[4], S. Asiimwe[6], K. Ngure[1,7], N. Bulya[5], J. Odoyo[4], E. Tindimwebwa[6], D. Donnell[1,8], J. Baeten[1,2,3], The Partners Demonstration Project Team
[1]University of Washington, Global Health, Seattle, United States, [2]University of Washington, Epidemiology, Seattle, United States, [3]University of Washington, Medicine, Seattle, United States, [4]Kenya Medical Research Institute, Nairobi, Kenya, [5]Makerere University, Kampala, Uganda, [6]Kabwohe Clincal Research Center, Kabwohe, Uganda, [7]Jomo Kenyatta University of Agriculture and Technology, Nairobi, Kenya, [8]Fred Hutch, Seattle, United States
Presenting author email: rheffron@uw.edu

Background: Understanding fertility intentions among HIV serodiscordant couples and their use of peri-conception HIV risk reduction strategies is important for the development of safer conception programs.
Methods: We are following 1013 Kenyan and Ugandan HIV serodiscordant couples in the Partners Demonstration Project, a multi-site, pre-exposure prophylaxis (PrEP) and antiretroviral therapy (ART) delivery program. We described fertility intentions and pregnancy rates of HIV infected and uninfected women. Using multivariable generalized estimating equations, we determined the association of immediate fertility intentions with sexual behavior and PrEP use by HIV uninfected women.
Results: Two-thirds (67%) of women in the cohort are the HIV infected partner. 65% of HIV infected women and 38% of HIV uninfected women have no children with their study partner. At enrollment, 7% of women reported having an immediate fertility intention (within 1 year), and 54% reported intentions to have a child in more than 1 year. To date, overall pregnancy incidence is 18.5 and 25.8 per 100 person years among HIV infected and uninfected women and substantially greater among women with immediate fertility intention (76.1 per 100 person years). Women with an immediate fertility intention were more likely to report condomless sex for at least 80% of sex acts (adjusted odds ratio [OR] 4.46, 95% confidence interval [CI] 3.33-5.99) and consistent use of PrEP (at least 80% of doses dispensed based on MEMS, adjusted OR 1.83, 95% CI 1.21-2.76).
Conclusions: In an HIV serodiscordant couple cohort, many women express intentions to become pregnant and pregnancy rates are high. PrEP use was high among women reporting immediate fertility intentions and is an important component for safer conception programs.

TUPEC512

Differences in HIV pre-exposure prophylaxis use and intention to use between stimulant and alcohol-using men who have sex with men in Boston, United States

C. Oldenburg[1,2], J. Mitty[2,3], K. Biello[1,2], E. Closson[2], K. Mayer[2,3,4], M. Mimiaga[1,2,5]
[1]Harvard School of Public Health, Department of Epidemiology, Boston, United States, [2]Fenway Community Health, The Fenway Institute, Boston, United States, [3]Beth Israel Deaconess Medical Center, Department of Medicine, Boston, United States, [4]Harvard School of Public Health, Department of Global Health and Population, Boston, United States, [5]Massachusetts General Hospital, Department of Psychiatry, Boston, United States
Presenting author email: ceo242@mail.harvard.edu

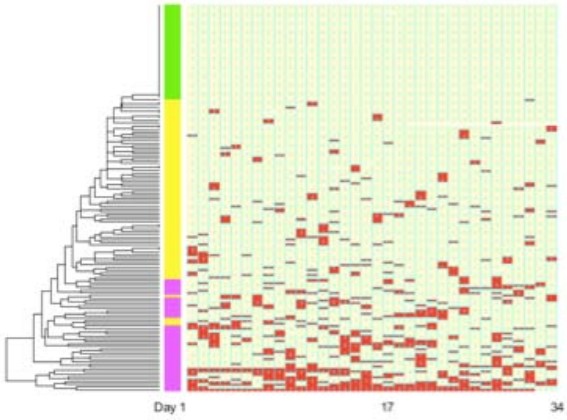
Background: Heavy alcohol and stimulant use are associated with elevated HIV risk among MSM and there is some concern that these behaviors may also be a potential barrier to uptake of HIV pre-exposure prophylaxis (PrEP).
The objective of this study was to assess acceptability and feasibility of PrEP among alcohol and non-injection drug users in Boston.
Methods: From September 2012-2013, a quantitative assessment was conducted with MSM who reported condomless sex with another man in the context of stimulant (crack/cocaine and crystal methamphetamine) and alcohol use. Participants were asked about awareness, acceptability, and use of PrEP, perceived barriers to use, and potential for changes in sexual behavior after PrEP uptake. Multivariable modified Poisson models were used to estimate risk ratios for associations between stimulant versus alcohol use and sexual behaviors and PrEP-related factors, adjusted for demographic and social factors.
Results: Of 254 participants enrolled, 132 (52.0%) were stimulant users and 48.0% were exclusively alcohol users. Median age was 31 years (stimulant users: 36; alcohol users: 27), 63.0% of the sample was white/Caucasian (stimulant users: 56.1%; alcohol users: 70.5%), 15.8% Black/African American (stimulant users: 25.0%; alcohol users: 5.7%), and 14.6% Latino (stimulant users: 12.9%; alcohol users: 16.4%). Of the stimulant users, 13 (9.9%) had previously used PrEP. No alcohol users had used PrEP. Both alcohol (73.0%) and stimulant (83.3%) users demonstrated substantial interest in using PrEP. In multivariable models, stimulant use was associated with increased risk of serodiscordant condomless anal sex with ≥3 partners (aRR=2.13, 95% CI 1.44-3.15), more frequently having heard of PrEP (aRR=1.31, 95% CI 1.04-1.65), more concern that substance use would affect PrEP use (aRR=2.28, 95% CI 1.38-3.75), and more frequently reporting that they would not need to worry about condomless sex with HIV infected partners following initiation of PrEP (aRR=3.07, 95% CI 1.39-6.82).
Conclusions: Despite potential barriers to PrEP use, interest in PrEP was high, with greater awareness and experience with PrEP among stimulant users. PrEP implementation programs with alcohol and non-injection drug users should consider differences in barriers to PrEP use and potential for differential behavioral compensation between users of different types of substances.

TUPEC513

Text messaging responses correlate with tenofovir-diphosphate dried blood spot concentrations among men who have sex with men on pre-exposure prophylaxis

J. Blumenthal[1], D. Moore[1], S. Jain[1], K. Corado[2], M. Dube[3], J. Young[1], S. Sun[1], P. Anderson[4], S. Morris[1], R. Haubrich[1], California Collaborative Treatment Group
[1]University of California San Diego, San Diego, United States, [2]Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, Infectious Diseases, Torrance, United States, [3]University of Southern California Keck School of Medicine, Los Angeles, United States, [4]University of Colorado, Denver, United States
Presenting author email: jblumenthal@ucsd.edu

Background: The effectiveness of pre-exposure prophylaxis (PrEP) is strongly linked to adherence. Methods to reliably measure adherence are needed. We sought to validate a daily texting adherence metric (individualized Texting for Adherence Building, iTAB) using a biologic marker (tenofovir diphosphate, TFV-DF, levels in dried blood spots, DBS).
Methods: CCTG 595 is an ongoing 48-week RCT testing the efficacy of iTAB to promote PrEP adherence in HIV-uninfected men who have sex with men (MSM). Analysis was performed on subjects randomized to receive iTAB with week 12 DBS TFV-DP levels and iTAB data available. TFV-DP levels were compared to proportion of messages responded to positively (Yes, I took my medication) and adherence patterns over the 34 days (two red blood cell TFV-DP half-lives) prior to week 12. Baseline risk factors and demographics were explored as covariates of adherence. Methods for statistical analysis included scatter-plot, correlation test and Wilcoxon rank sum test for association, and heatmap and Ward Hierarchical Clustering for adherence patterns.
Results: Among 152 subjects included, the mean TFV-DP concentration was 1353±558 fmol/punch. Participants reported taking a mean of 87% of doses as measured by positive iTAB responses. There was a significant correlation between TFV-DP concentrations and proportions of positive iTAB responses (r=0.26, p=0.001). Subjects with TFV-DP>891 (consistent with >5 doses/week) had a higher proportion of positive iTAB responses (89 versus 76%, p=0.003). Subjects clustered into 3 adherence groups by text responses over the 34 days (Figure): perfect (n=37), high (n=75) and moderate (n=40) adherence corresponding to mean TFV-DP levels of 1547±694, 1356±484 and 1167±495 fmol/punch, respectively. Perfect/high adherers combined had significantly higher TVF-DP concentrations than moderate adherers (p=0.037). Baseline variables associated with better adherence cluster included older age (p=0.002), non-Hispanic ethnicity (p=0.027) and less drug use (p=0.005).



[Figure. The heatmap is based on iTAB data over the 34 days (x-axis). Light green boxes indicate the days a subject reported taking the dose; red the days a subject reported missing the dose; white are the missing data. Subjects (y-axis) are clustered into 3 groups based on Ward Hierarchical Clustering representing perfect (green), high (yellow) and moderate (magenta) adherence]

Conclusions: Early adherence to PrEP was high among those assigned to text messages. Subjects with a higher proportion of positive iTAB responses had significantly higher TFV-DP levels and were more likely to have TFV-DP levels consistent with taking at least 5 doses/week. Since iTAB response data correlates with a biologically confirmed adherence marker (TFV-DP levels), iTAB might be useful to monitor MSM on PrEP.

TUPEC514

PrEP utilization estimates in Australia

I. Zablotska, G. Prestage, A.E. Grulich
University of New South Wales Australia, The Kirby Institute, Sydney, Australia
Presenting author email: izablotska@kirby.unsw.edu.au

Background: Daily pill Truvada is recommended for preexposure prophylaxis of HIV (PrEP) in people at high risk for infection. The uptake levels remain low internationally. The population-level benefit of PrEP will require much higher levels of use than is observed. In Australia, gay and other men who have sex with men (GMSM) contribute most to HIV transmission. We estimated how many GMSM are likely to request PrEP as it becomes available for prescription.
Methods: We used data from the Australian Bureau of Statistics (2013) and the second Australian Study of Health and Relationships (ASHR2, 2013) to estimate the size of the population of GMSM. PrEP eligibility for GMSM was defined by the national PrEP guidelines. Input indicators from a series of studies, including the national behavioural surveillance (Gay Community Periodic Surveys, GCPS) and other studies conducted in Australia in recent years, were applied to estimate the numbers of men eligible for PrEP based on each individual and any behavioural eligibility criteria as per the national PrEP guidelines. We also estimated how many eligible GMSM are likely to request Truvada for primary HIV prophylaxis.
Results: The estimated 143,000 Australian men would identify as gay/homosexual plus 95,000 as bisexual or other GMSM. In GCPS, 15.7% of the HIV non-positive GMSM reported sustained risk behaviour (6 or more sex partners in the last 6 months). Having at least one episode of receptive condomless anal intercourse (CLAI) with any casual HIV-infected or status-unknown male partner in the last 6 months appeared the most common behavioural eligibility criterion for PrEP (5% of HIV non-positive GMSM). 5.7% would satisfy any of the behavioural eligibility criteria. In the recent Australian study of current and likely PrEP use, 44.9% of gay/homosexual GMSM reported interest and being likely to uptake PrEP.
Conclusions: We estimated the size of the group of GMSM eligible for and most likely to request PrEP in the near future. This estimation helps to predict services and medication needs for PrEP provision. We discuss the methods, assumptions and finding of this estimation in light of the integration of PrEP into the HIV prevention strategy.

TUPEC515

HPTN 067 ADAPT: 'PrEP Ubuntu' and experiences with open-label PrEP among South African women

M. Wallace[1], L.-G. Bekker[1], S. Roux[1], M. Atujuna[1], E. Sebastian[1], B. Dye[2], V. Elharrar[3], R. Grant[4], R. Amico[5]
[1]Desmond Tutu HIV Centre, Medicine, Cape Town, South Africa, [2]FHI 360, Durham, United States, [3]Clinical Prevention Research Branch/PSP/DAIDS/NIAID/NIH, Bethesda, United States, [4]Gladstone Institutes, University of California, San Francisco, United States, [5]University of Michigan, Department of Health Behavior and Health Education, Brighton, United States
Presenting author email: ramico@umich.edu

Background: Uptake and adherence to oral FTC/TDF PrEP among African women has been highly variable between studies. There has been no published experience with open-label access to PrEP in women after the concept was proven effective. Qualitative research performed at the Cape Town site of the HPTN 067 ADAPT trial focused on women's experiences with PrEP and randomly assigned dosing regimens (daily, twice weekly with a post-sex dose, and pre/post-sex dosing).
Methods: Convenience sampling from trial participants (N=179) identified focus group (FG) participants, while combined convenience and targeted sampling to include participants who indicated poor adherence/discontinued product use was used for in-depth interview (IDI) participants. Six FGs (n=42) and 18 IDIs were conducted using a semi-structured interview guide. Data was transcribed and double-coded using framework analysis.
Results: Adherence facilitators included keeping tablets on-hand, support from others, and PrEP efficacy beliefs, with daily PrEP users also noting use of cell-phone reminders or linking doses to recurring events. Barriers included forgetting, fear of disclosure of study participation and side-effects. The post-sex dose in the non-daily arms was noted as a poor fit to the typical post-sex situation (away from home, resting with partner). The main advantage of daily PrEP over non-daily was routine. Across arms, a theme of participant struggle with community and personal trust in PrEP emerged. Trust issues related to drug safety and the motivations of the PrEP study. While some women responded to this struggle by disengaging from PrEP-use, an alternative response, defined here as 'PrEP Ubuntu', was to intentionally disclose PrEP use and study participation in order to promote community acceptance of and trust in PrEP.
Conclusions: Daily dosing was deemed to have multiple advantages, with post-sex dosing poorly 'matched' to the common post-sex experience. In a struggle between community and research, women's responses ranged from disengagement from PrEP to 'PrEP Ubuntu'- where Ubuntu highlights the social intricacies of PrEP use and the potential influence of PrEP users who seek to tip community perceptions in an effort to improve community-wide HIV-prevention. Successful PrEP roll-out will undoubtedly rely heavily on these PrEP champions.

TUPEC516

HIV evolution in breakthrough infections in a human trial of oral PrEP with FTC/TDF

S. Ruone[1], L. Paxton[2], T. Mclaurin[3], A. Taylor[1], W. Heneine[1], J.T. Brooks[1], J.G. Garcia-Lerma[1]
[1]CDC, Atlanta, United States, [2]CDC, Dar es Salaam, Tanzania, United Republic of, [3]UNC Charlotte, Charlotte, United States
Presenting author email: jng5@cdc.gov

Background: Daily PrEP with FTC/TDF is a novel HIV prevention strategy. Since current PrEP regimens are not 100% protective, it is essential to understand the characteristics of acute infections that occur during PrEP. We investigated viral evolution dynamics in participants infected with HIV who were assigned to daily FTC/TDF or placebo during the CDC-sponsored TDF-2 PrEP trial.
Methods: HIV dynamics were investigated in the 4 participants who seroconverted in the FTC/TDF arm and in 3 viral load-matched seroconverters assigned to placebo. Two of the 4 infections in the FTC/TDF arm had no detectable FTC or TFV in plasma. HIV env (V1-V5) was amplified from plasma HIV RNA by single genome amplification at the seroconversion visit and 8-12 months later. Time since infection and number of transmitted/founder (T/F) viruses was estimated by exploring env diversity at seroconversion. Viral diversity was inferred by analysis of neighbor-joining trees and by the Poisson-Fitter and Highlighter tools.
Results: At seroconversion, the average virus diversity in the seroconverters assigned to placebo or who were non-adherent was 0.69% (0.11%-2.0%) compared with 0.05% and 0.07% in the two adherent PrEP participants. HIV infections in adherent participants followed a star phylogeny and were initiated by a single T/F virus. In contrast, infections in the 2 non-adherent PrEP participants and 2 of the 3 placebo controls were heterogeneous (mean= 3 T/F viruses) and did not follow a star phylogeny. Virus diversity 8-12 months after infection remained higher in seroconverters assigned to placebo or who were non-adherent to PrEP (1.6% [range 1.1%-2.3%]) compared with the 2 adherent participants (0.3% and 0.9%). At 1 year, mean nucleotide divergence from the most common T/F viruses was also lower in the adherent seroconverters compared with the placebo and non-adherent seroconverters ($9.5x10^{-3}$ vs $1.9x10^{-2}$ nt substit/site/year, p< 0.0001).
Conclusions: HIV sequences from PrEP-adherent seroconverters were more homogeneous and evolved more slowly than those from placebo or non-adherent seroconverters. If confirmed in other PrEP trials, these findings suggest that transient PrEP exposure during acute infection may have a long-lasting effect on virus evolution. Our observations underscore the need to better understand the potential impact of PrEP on HIV control.

TUPEC517

HIV-negative male couples' attitudes about pre-exposure prophylaxis (PrEP), and PrEP use within the context of their relationships and sexual agreements

J. Mitchell[1], J.-Y. Lee[1], J. Bauermeister[2], C. Woodyatt[3], S. Patrick[2], S. Lim[2], P. Sullivan[3], R. Stephenson[4]
[1]University of Miami Miller School of Medicine, Department of Public Health Sciences, Miami, United States, [2]University of Michigan, School of Public Health, Ann Arbor, United States, [3]Emory University, School of Public Health, Atlanta, United States, [4]University of Michigan, School of Nursing, Ann Arbor, United States
Presenting author email: jwm35@med.miami.edu

Background: Between one- and two-thirds of US MSM acquire HIV from their primary relationship partner (male couple). One promising biomedical approach to preventing new HIV infections is PrEP - a daily regimen of HIV treatment (i.e., Truvada™) taken by those who are HIV-negative to prevent HIV acquisition. The US CDC has provided guidelines for who may benefit from taking PrEP, including MSM in relationships. Although studies note that HIV-negative MSM support PrEP use, their knowledge about PrEP varies. Moreover, *little is known about male couples' attitudes about PrEP and whether PrEP could be integrated into their sexual agreements.*
Methods: The present study is part of a larger intervention project aimed to help male couples form and adhere to a sexual agreement via an online interactive HIV prevention toolkit. Active and passive recruitment strategies were used to enroll 29 consented HIV-negative male couples from Detroit, MI and Atlanta, GA to participate in semi-structured individual- and couple-level interviews about couples' sexual agreements and attitudes toward other preventive methods. All couples had an agreement; none were on PrEP. Interviews were digitally recorded, transcribed verbatim, and anonymized. Grounded theory was used to identify themes from the codes developed.
Results: Themes about PrEP uptake were *general and relationship support (vs. not).* Themes for integrating PrEP into an agreement included *condom use and adherence.* Our findings were data rich. Some couples were supportive of PrEP, but conditionally and/or believed PrEP should be used with condoms. PrEP support for relationships included enhancing sexual needs and/or to protecting them from potential "slip-ups". Less PrEP support centered on riskier behaviors and medication side effects. Couples had mixed attitudes about using PrEP in agreements: some thought PrEP should only occur with condom use while others said it could help reduce risk while enhancing pleasure by forgoing condoms and/or increase comfort and communication about sex and reduce worry about HIV.
Conclusions: Our findings highlight the need to use examples and scenarios of how PrEP use may benefit male couples' relationships and risk for HIV when developing content and activities for our online prevention 'toolkit'.

TUPEC518

Risk compensation among men who have sex with men (MSM) in Southern California following the initiation of pre-exposure prophylaxis (PrEP)

J. Milam[1], S. Jain[2], D. Moore[2], E. Daar[3], M. Dube[4], J. Young[2], J. Blumenthal[2], S. Sun[2], R. Haubrich[2], S. Morris[2], CCTG 595 and 597 Study Teams
[1]University of Southern California, Preventive Medicine, Los Angeles, United States, [2]University of California, San Diego, United States, [3]Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, Torrance, United States, [4]University of Southern California, Los Angeles, United States
Presenting author email: milam@usc.edu

Background: A concern of using pre-exposure prophylaxis **(**PrEP) for HIV prevention is risk compensation, where PrEP users may take more sexual risks.
Methods: We examined sexual risk behaviors following TDF/FTC PrEP initiation among men who have sex with men (MSM) enrolled in CCTG 595, a PrEP adherence study. Self-reported number of sexual partners by HIV status and unprotected receptive and insertive anal sex acts (over the previous month) were compared at study weeks 0 and 24 using the Wilcoxon signed-rank test. Analyses were limited to participants who completed the week-24 survey.
Results: The 268 MSM were: 36 years old; 30% Hispanic; 85% White and 5% Black. The number of HIV-positive partners in the prior month increased from week 0 to 24 (p< 0.05). The number of HIV unknown status partners in the prior month declined from week 0 to 24 (p< 0.05). The number of unprotected receptive anal sex acts in the prior month marginally increased from week 0 to 24 (p=0.056). The number of unprotected insertive sex acts in the prior month did not significantly change (p=0.58).

Behavior (past month)	Study Week 0	Study Week 24
Mean number of HIV+ partners (SD, median, range)	0.89 (1.51, 1, 0-15)	1.13 (2.02, 1, 0-20)*
Mean number of HIV unknown partners (SD, median, range)	1.26 (2.39, 1, 0-15)	1.01 (2.42, 1, 0-20)*
Mean unprotected receptive anal sex acts (SD, median, range)	1.79 (3.74, 0, 0-25)	2.58 (7.40, 0, 0-100)+
Mean unprotected insertive anal sex acts past month (SD, median, range)	2.47 (5.07, 1, 0-30)	2.52 (4.85, 0.5, 0-36)
Comparisons by Wilcoxon signed rank test; +p=.056, *p<0.05, vs. week 0.		

[Table 1: Sexual Risk Behavior among Men who have S]

Conclusions: These preliminary analyses in MSM suggest an increase in the number of HIV positive partners in the first 24 weeks following PrEP initiation. However, because there was only a marginal increase in unprotected sex and a reduction in partners of HIV unknown status, the evidence for risk compensation among this population of PrEP initiating MSM is limited. Future analyses will include data up to one year to determine if these trends change over time.

TUPEC519

Reasons for accepting or declining HIV pre-exposure prophylaxis in a diverse black US population

H. Kwakwa[1], R. Wahome[2], D. Sturgis[1], N. Mvula[1], S. Bessias[1]
[1]Ambulatory Health Services, Department of Public Health, Philadelphia, United States, [2]AIDS Care Group, Sharon Hill, United States
Presenting author email: hkwakwa@aol.com

Background: Studies on HIV pre-exposure prophylaxis (PrEP) show clear efficacy associated with adherence, and previously unpredicted patterns of non-adherence for which fully adequate explanations remain elusive. In an attempt to better understand perceptions of PrEP as potential reasons for adherence or lack thereof, we examine reasons for the acceptance or refusal of PrEP in a large diverse black population in Philadelphia.
Methods: Between July 2012 and December 2014, African Americans of lower socio-economic strata in a large HIV testing program in Philadelphia's city health centers, and African and Caribbean immigrants in a large community-based HIV testing program were administered an anonymous survey. Included among survey questions were questions about acceptance or refusal of PrEP, and reasons for acceptance or refusal. Responses for each were categorized and analyzed using the Epitools package.

Results: During the study period 8869 individuals met criteria for this analysis. Of these 6114 were African American and 2755 African or Caribbean. Overall, 49.7% were female. PrEP acceptance rates were similar for American men (62.3%) and women (59.2%), but lower and different for immigrant blacks (49.3% for men, 34.2% for women, p< 0.0001). Main reasons for acceptance of PrEP were fear of HIV, a familiarity with the concept of prevention, and recognition of one's HIV risk. Reasons for refusal of PrEP were a lack of recognition of risk, a dislike of medicine/pills, a desire to use alternative prevention methods, and a distrust of the medical establishment. Among immigrants only, trust of clinicians' recommendations was cited as an additional reason for acceptance.
Conclusions: Understanding the reasons for accepting or declining PrEP among at-risk communities are key to partnering effectively with such communities to make PrEP available. Addressing risk perception and barriers to medication use are two important ways of improving acceptance of PrEP.

TUPEC520

Individual and sexual network characteristics are associated with HIV serodisclosure in the global iPrEx study

J.C. Hojilla[1], M. Mehrotra[2], V. Mcmahan[2], L.-G. Bekker[3], J.V. Guanira[4], B. Hoagland[5], S. Hosek[6], K.R. Amico[7], D. Glidden[1], R. Grant[2], iPrEx Study Team
[1]University of California, San Francisco, United States, [2]Gladstone Institutes, Institute of Immunology and Virology, San Francisco, United States, [3]Desmond Tutu Health Foundation, Cape Town, South Africa, [4]Investigaciones Medicas en Salud, Lima, Peru, [5]Fundação Oswaldo Cruz, Rio de Janeiro, Brazil, [6]Stroger Hospital of Cook County/CORE Center, Chicago, United States, [7]University of Michigan, Ann Arbor, United States
Presenting author email: carlo.hojilla@ucsf.edu

Background: Accurate HIV serodisclosure is an important sexual risk-reduction strategy because it enables seroadaptive behaviors. Pre-exposure prophylaxis (PrEP) is a viable HIV prevention strategy but there are concerns that PrEP may cause individuals to forego other risk-reduction efforts, like serodisclosure. We are unaware of any study that has examined serodisclosure before and after PrEP use. This study analyzes serodisclosure patterns among HIV-negative men and transwomen who have sex with men (MSM and TGW) in the iPrEX Open Label Extension (OLE).
Methods: Baseline sexual network data were assessed in participants in iPrEx OLE by computer-assisted self-interview (CASI). All participants were previously involved in a PrEP randomized clinical trial. Logistic regression using generalized estimating equations modeled predictors of serodisclosure to sexual partners in the last three months.
Results: A total of 1593 HIV seronegative participants and 2643 partnerships were analyzed. Among those with available data from CASI, the median age of participants was 28 years (range 18-70); 89% (n=1419) were MSM and 11% (n=174) TGW; 66% (n=1059) were Hispanic/Latino; 42% (n=662) were married or partnered; and 70% (n=1119) received PrEP at enrollment. Overall, 60% reported disclosing HIV status to their last sexual partners. In bivariate analysis, participants in the USA; greater age; persons whose most recent sexual partner involved both a sexual and emotional connection; and higher education were associated with higher odds of serodisclosure. Participants in Thailand and those who identified as Hispanic/Latino had lower odds of serodisclosure. Controlling for all other variables, participants in the USA, relationships involving a sexual and emotional connection, and education were independently associated with HIV serodisclosure. No differences were observed between participants who received PrEP and those who did not.
Conclusions: This study suggests that serodisclosure in MSM and TGW may be associated with individual and sexual network characteristics, and may have no relationship with PrEP use. Serodisclosure between persons on and off PrEP did not significantly differ at baseline despite prior participation in PrEP trials. These findings provide an early assessment to address concerns that PrEP might lead individuals to forego risk reduction strategies like serodisclosure and can help inform future interventions to promote communication of HIV status.

TUPEC521

Validation of a Truvada for PrEP algorithm using an electronic medical record

T. MacCannell[1], S. Bush[2], S. Verma[1], V. Shvachko[1], K. Rawlings[2], R. Mera[1]
[1]Gilead Sciences, Epidemiology, Foster City, United States, [2]Gilead Sciences, Medical Affairs, Foster City, United States
Presenting author email: robertino.mera@gilead.com

Background: Tenofovir/Emtricitabine (TVD) combination was approved for a Pre-exposure Prophylaxis (PrEP) indication in the US in July 2012. There are no ICD9 or procedure codes that reliably predict subjects who take TVD monotherapy for PrEP from those subjects who receive TVD for HIV or Chronic Hepatitis B (CHB) treatment, or Post-Exposure Prophylaxis (PEP).
An algorithm was developed to identify presumptive TVD for PrEP subjects from large-scale administrative databases based on excluding subjects with diagnostic codes and prescriptions documenting HIV, CHB, or PEP.
Methods: The present study validated the algorithm with a focused chart review using an Electronic Medical Record (EMR). Two blinded investigators independently reviewed each electronic chart for subjects who were prescribed TVD and assigned them as a) PrEP, b) HIV+, c) CHB, or d) PEP. Non-parametric models were used in the computation of AUC statistics.
Results: 10,645 subjects from the EMR started TVD therapy after January 1st 2012, and the algorithm classified 6.3% (671) as PrEP, 0.24% (26) as CHB, 0.12% (13) as PEP and 93.3% (9,935) as HIV+. 70.9% of the subjects were male and 29.1% female. A random 1% of HIV+ subjects and all charts from other groups were reviewed (810 charts). The chart review results were considered the gold standard and the algorithm the classifier, which had an area under the curve (AUC) of 99.1 (95% CI 98.9 - 99.2), with a sensitivity of 100% (95% CI 99.2 - 100) and a specificity of 98.2% (95% CI 97.9 - 98.4). Among those categorized by the algorithm as PrEP, 9.9% (95% CI 7.9-12.5) were identified by the chart review as TVD monotherapy for high risk sexual PEP, while 4.0% (95% CI 2.8 - 5.8) were CHB subjects. The positive predictive value of the algorithm, or those assigned by the chart review and the algorithm as PrEP was 72.4% (95% CI 68.9 - 75.8).
Conclusions: A PrEP algorithm of exclusion demonstrated high sensitivity and specificity, and accurately categorized other TVD indications. The chart review suggests that 1 out of 10 subjects on TVD monotherapy are taking it for short periods after episodes of high risk sexual exposure.

Microbicides (including vaginal and rectal microbicides)

TUPEC522

Safety of cervical and vaginal biopsies in microbicide and contraceptive research

A. Thurman[1], T. Kimble[1], A. Nel[2], B. Chen[3], S. Achilles[3], M. Keller[4], I. McGowan[3], T. Hirbod[5], R. Kaul[6], K. Linton[7], J. Schwartz[7], G. Doncel[7], C. Mauck[7]
[1]CONRAD, Obstetrics and Gynecology, Norfolk, United States, [2]International Partnership for Microbicides, Paarl, South Africa, [3]University of Pittsburgh, Obstetrics and Gynecology, Pittsburgh, United States, [4]Albert Einstein College of Medicine, New York, United States, [5]Karolinska Institutet, Stockholm, Sweden, [6]University of Toronto, Toronto, Canada, [7]CONRAD, Arlington, United States

Background: Cervical and vaginal (CV) biopsies are commonly performed in clinical studies of microbicides for HIV prevention and contraceptive research to assess biologic responses, investigate product safety and determine local drug tissue levels. Similar genital biopsies are commonly performed clinically, however, safety data from genital biopsies performed for research purposes have yet to be collectively analyzed and published. Summary data on biopsy safety in special populations, including postmenopausal, HIV+ and women with reproductive tract infections, are also lacking.
Methods: We searched PubMed and ClinicalTrials.gov and contacted principal investigators from trials of microbicides, multipurpose prevention technologies and contraceptives to collect data on biopsy protocols and procedures. Data on adverse events (AEs) that were deemed related to biopsy procedures were abstracted.
Results: We identified 34 studies (21 microbicide, 8 contraceptive and 5 others) in which CV biopsies were taken. A total of 1,409 women donated 8,330 CV biopsies (2,911 cervical, 5,419 vaginal). On average, 3 CV biopsies (range 1 - 5) were obtained at each visit. Three days was the shortest interval between consecutive biopsies (range 3 - 90 days). All clinicians reported using no pre-procedure antiseptic preparations. Investigators reported using either no pre-procedure pain control methods or combinations of topical anesthesia (xylocaine spray, benzocaine gel) and distraction (cough). Biopsy sites were treated for hemostasis with pressure, silver nitrate, Monsel's solution and, rarely, sutures. Biopsy-related AEs were reported in 45 (3.2%) of participants. Studies included special populations such as postmenopausal women (n = 17), women with symptomatic bacterial vaginosis (n = 33), HIV- Kenyan women (n = 38), HIV+ female sex workers (FSWs) (n = 20) and highly HIV exposed seronegative FSWs (n = 18). Among these special populations, no biopsy healing abnormalities were observed.

Biopsy-Related Adverse Event	Number of Participants with Adverse Event	Percent of Total AEs (n = 45)	Percent of Total Participants (n = 1409)
Cervico-vaginal bleeding requiring an unscheduled visit, additional procedures to resolve or estimated blood loss greater than expected	33	73.3	2.3
Cervico-vaginal pain after procedure	6	13.3	0.4
Vasovagal Episode	3	6.7	0.2
Asymptomatic erythema at biopsy site seen at follow up, more than expected with normal healing process	2	4.4	0.1
Contraceptive ring damaged by biopsy forceps	1	2.2	0.1
TOTALS	45	100	3.2
Adverse event graded mild or moderate with resolution	44	97.8	3.1
Serious Adverse Event with resolution	1	2.2	0.1

[Biopsy Related Adverse Events]

Conclusions: CV biopsies are associated with a low rate of AEs that are usually mild with complete resolution. Post-procedure bleeding is the most common AE. Although most studies with biopsies were performed in developed countries on healthy premenopausal women, there are emerging data that CV biopsies among special populations of women, including HIV+ women and women living in high HIV prevalence areas are also safe and well tolerated.

TUPEC523

Pharmacokinetics of tenofovir and emtricitabine delivered by vaginal tablets

C. Mauck[1], A. Thurman[2], M. Keller[3], D. Archer[2], T. Kimble[2], A. Kashuba[4], C. Sykes[4], D. Friend[1], G. Doncel[1]
[1]CONRAD, Arlington, United States, [2]CONRAD, Norfolk, United States, [3]Albert Einstein College of Medicine, Bronx, United States, [4]University of North Carolina, Chapel Hill, United States
Presenting author email: cmauck@conrad.org

Background: Vaginal tablets offer advantages over gels. Elimination of plastic applicators reduces cost and environmental impact and allows for discreet storage and insertion. Tablets are smaller and lighter than gels in applicators, lowering shipping/storage costs and increasing convenience.
Methods: This prospective parallel, double-blinded, randomized study examined the pharmacokinetics (PK) of: 1) 40 mg tenofovir (TFV); 2) 40 mg emtricitabine (FTC); 3) 40 mg TFV combined with 40 mg FTC; and 4) placebo. 48 healthy, non-pregnant, HIV-uninfected women (12 per group), aged 18-50 and protected from pregnancy by non-hormonal methods used vaginal tablets in a single use phase followed by a multiple use phase (14 days of daily dosing). Women were randomized to treatment, number of tablets inserted in the single use phase (1 tablet or 1 tablet followed by a second tablet 2 hours later to mimic BAT24 dosing), and 1 of 4 collection time-points (2, 4, 6, or 24 hours) for assessments after the last dose of the multiple use phase. Vaginal biopsies were assessed for concentrations of TFV, its active metabolite (TFV-DP), FTC, and its active metabolite (FTC-TP) 5 hours after the single use and 2, 4, 6, or 24 hours after the last dose of the multiple use phase.
Results: Subject participation is complete. Preliminary results show that median TFV tissue levels were at the target of 10^{1-2} ng/mg after administration of TFV and TFV+FTC tablets. Concentrations after 14 days were similar to those after a single dose. Importantly, median TFV-DP concentrations were above the target of 10^3 fmol/mg after TFV and TFV+FTC tablets, with concentrations 1 log higher after 14 days than after a single use. FTC levels in tissue were at least an order of magnitude higher than the FTC EC_{50}. In some cases, the tablet disintegration rate was slower than the target of 30 minutes.
Conclusions: This first human study of vaginal microbicide tablets demonstrates efficient drug release and intracellular metabolism. TFV and TFV-DP tissue concentrations were comparable to the clinical TFV 1% gel. Combination with FTC added consistently high FTC and FTC-TP tissue concentrations. Further work to improve disintegration speed is ongoing.

Barriers and facilitators to adherence to biomedical HIV prevention strategies

TUPEC524

Factors linked to transitions in adherence to antiretroviral therapy among HIV-infected illicit drug users in a Canadian setting

B. Joseph[1], T. Kerr[1,2], C. Puskas[1,3], J. Montaner[1,2], E. Wood[1,2], M.-J. Milloy[1,2]
[1]British Columbia Centre for Excellence in HIV/AIDS, Vancouver, Canada, [2]University of British Columbia, Faculty of Medicine, Vancouver, Canada, [3]Simon Fraser University, Faculty of Health Sciences, Burnaby, Canada
Presenting author email: bjoseph@ualberta.ca

Background: HIV-positive people who use illicit drugs typically achieve lower levels of adherence to antiretroviral therapy and experience higher rates of sub-optimal HIV/AIDS treatment outcomes. Given the dearth of longitudinal research into ART adherence dynamics, we sought to identify factors associated with transitioning into and out of optimal adherence to ART in a longitudinal study of HIV-infected people who use illicit drugs (PWUD) in a setting of universal no-cost HIV/AIDS treatment.
Methods: Using data from a prospective cohort of community-recruited HIV-positive illicit drug users confidentially linked to comprehensive HIV/AIDS treatment records, we estimated longitudinal factors associated with losing or gaining ≥ 95% adherence in the previous six months using two generalized linear mixed-effects models.
Results: Among 703 HIV-infected ART exposed PWUD, becoming non-adherent was associated with periods of homelessness (Adjusted Odds Ratio [AOR] = 2.52, 95% Confidence Interval [95% CI]: 1.56 - 4.07), active injection drug use (AOR = 1.25, 95% CI: 1.01 - 1.56) and incarceration (AOR = 1.54, 95% CI: 1.10 - 2.17). Periods of sex work (AOR = 0.51, 95% CI: 0.34 - 0.75) and injection drug use (AOR = 0.62, 95% CI: 0.50 - 0.77) were barriers to becoming optimally adherent. Methadone maintenance therapy (MMT) was associated with becoming optimally adherent (AOR = 1.87, 95% CI: 1.50 - 2.33) and was protective against becoming non-adherent (AOR = 0.52, 95% CI: 0.41 - 0.65).
Conclusions: In conclusion, we identified several behavioural, social and structural factors that shape adherence patterns among PWUD. Our findings highlight the need to consider these contextual factors in interventions that support the effective delivery of ART to this population.

TUPEC525

The impact of health literacy and physician-patient dynamics on health outcomes in adult HIV patients

A. Wawrzyniak[1], A. Falcon[2], A. Parra[3], A. Rodriguez[4]
[1]University of Miami Miller School of Medicine, Psychiatry and Behavioral Sciences, Miami, United States, [2]Eastern Virginia Medical School, Norfolk, United States, [3]University of Miami, School of Nursing and Health Studies, Coral Gables, United States, [4]University of Miami Miller School of Medicine, Division of Infectious Diseases, Miami, United States
Presenting author email: awawrzyniak@miami.edu

Background: Health literacy has been shown to impact health in HIV-infected patients. However, little research has examined the characteristics of the relationship between the patient and the provider in an adult HIV outpatient setting. Physician-patient dynamics, notably communication styles and modalities, are integral to maximizing health outcomes, particularly in HIV-infected patients.
Methods: HIV-related health literacy (HIV Health Literacy Scale) and patients' perceptions of their providers (Patient Satisfaction Questionnaire) were determined via questionnaire in 201 HIV-infected outpatients (mean age = 50.4 ± 10.1 years; 45.8% female; 80% Black; 19% Hispanic/Latino) from the University of Miami/Jackson Memorial Medical Center Adult Outpatient HIV Clinic. Health outcomes were defined by patients' most recent CD4 counts and if patients had achieved viral suppression (< 20 copies/mL).
Results: After controlling for age, gender, and education level, patients with higher HIV-related health knowledge had higher CD4 counts (β = .238, p = .011; model R^2 = .091, p = .025). Greater ratings of physicians' interpersonal ratings were significantly associated with greater CD4 counts
(r = .21, p = .003) and lower viral loads (r = -.18, p = .014); those who were virally suppressed had significantly higher interpersonal ratings of their physician than those who did not (t(193) = 2.12, p = .036); controlling for age, gender and HIV knowledge, each 1-point increase in physicians' interpersonal ratings were associated with a 1.46 times greater odds that the patient was undetectable (OR = 1.46, 95% CI 1.005-2.119). Furthermore, after adjusting for age, gender, and HIV knowledge, patients with higher interpersonal ratings of their physicians had higher CD4 counts (β = .221, p = .015; model R^2 = .11, p = .009).
Conclusions: Although peripheral to the standard course of treatment, health knowledge, communication styles, and interpersonal interaction are an integral part of HIV patient care that impacts health outcomes. The additional importance of education and physician-patient communication should be incorporated in provider training; system-level policy changes should include the value of both education and interpersonal style in treatment protocols and address the potential to improve communication.

Approaches to improving adherence to prevention interventions

TUPEC526

Prevalence and correlates of non-disclosure of maternal HIV status in Kenya

J. Kinuthia[1], C. McGrath[2], B. Odeny[3], B. Singa[4], A. Langat[5], A. Katana[5], L. Nganga[5], J. Pintye[3], G. John-Stewart[3]
[1]Kenyatta National Hospital, Research & Programs, Nairobi, Kenya, [2]University of Texas, Medical Branch, Galveston, United States, [3]University of Washington, Seattle, United States, [4]Kenya Medical Research Institute, Nairobi, Kenya, [5]United States Centers for Disease Control and Prevention (CDC), Nairobi, Kenya
Presenting author email: kinuthia@u.washington.edu

Background: Prevention of mother-to-child HIV transmission programs (PMTCT) usually test pregnant women alone for HIV. Non-disclosure of maternal HIV results to their male partner may deter utilization of PMTCT interventions to reduce HIV transmission.
Methods: We enrolled mother-infant pairs attending week 6 and month 9 immunizations at 140 maternal and child health clinics across Kenya, with a second survey of HIV-positive moth-

ers in 30 clinics in Western Kenya to increase statistical power to assess HIV-related outcomes. Consenting women completed a questionnaire that assessed disclosure of HIV status (positive or negative) and among HIV-positive women, utilization of PMTCT interventions. Multivariate logistic regression, adjusting for facility-level clustering, was used to determine correlates of HIV test results non-disclosure among women reporting current partnership and association with uptake of PMTCT interventions.

Results: Between June and December 2013, 2819 women were enrolled of whom 2491 (88.4%) reported having a current partner. Of these, 128 (5.2%) reported non-disclosure of HIV results to their partners. Being unmarried [aOR=3.41 (1.65-8.54)], unemployed [aOR=3.59 (1.21-10.6)], partner antenatal clinic non-attendance [aOR 3.11 (1.84-5.24)], maternal HIV-positive status [aOR=4.12 (2.76-6.27)] and frequent threats of harm [aOR 5.16 (1.76-15.16)] were independently associated with non-disclosure of HIV test results. Among 420 HIV-positive women who reported having a current partner, male partner status was HIV-positive in 54.3%, HIV-negative in 21% and unknown status in 24.8%. Fifty three (12.6%) HIV-positive women with a current partner reported non-disclosure. Of these, 8 (15.1%) had HIV-positive partners, 10 (18.9%) HIV-negative partners and 35 (66.0%) had partners of unknown HIV status. HIV-positive women who did not disclose results were less likely to use antiretrovirals during pregnancy [aOR 0.26 (0.14-0.49)], during labour [aOR 0.40 (0.21-0.74], during breastfeeding [aOR 0.43 (0.24-0.79)] or give their infants antiretrovirals [aOR=0.08 (0.02-0.25)].

Conclusions: We found low rates of non-disclosure of maternal HIV status among all women, but higher among those who were HIV-positive. Non-disclosure among HIV-positive women was associated with reduced use of antiretrovirals during all time periods. Promoting male partner antenatal clinic attendance may be a useful strategy to facilitate disclosure. There is need for innovative strategies to facilitate PMTCT interventions uptake by HIV-positive women reluctant to disclose their status.

TUPEC527

African women's perceptions of honesty and dishonesty about product use adherence in the context of HIV prevention research during the VOICE (MTN-003) trial

E. Montgomery[1], P. Musara[2], K. Woeber[3], J. Etima[4], B. Mensch[5], A. van der Straten[6,7]
[1]RTI International, Women's Global Health Imperative, San Francisco, United States, [2]UZ-UCSF Collaborative Reserch Programme, Harare, Zimbabwe, [3]HPRU, South African Medical Research Council, Durban, South Africa, [4]MU-JHU, Kampala, Uganda, [5]Population Council, New York, United States, [6]RTI International, Womens Global Health Imperative, San Francisco, United States, [7]UCSF, San Francisco, United States
Presenting author email: emontgomery@rti.org

Background: Following null effectiveness results and evidence of low product use from pharmacokinetic drug testing in VOICE, the VOICE-D (MTN 003D) ancillary study used a variety of strategies in an attempt to elicit candid accounts from participants about why actual product use was lower than reported.

Methods: 175 former VOICE participants were enrolled between December 2012 and March 2014 in South Africa (n =49), Uganda (n=61) and Zimbabwe (n=65). Participants were randomly selected from a list of those permitting further research contact and who met pre-specified eligibility characteristics. Data from 156 in-depth interviews and 12 Focus Groups collected in 2 study stages were coded and analyzed thematically in Nvivo10, following audio-recording, transcription and translation from local languages. Interviews were conducted by non-VOICE social scientists in offsite locations.

Results: Women at all sites apparently understood the importance of daily product use and honest reporting, but widely acknowledged that research participants lie. While some indicated there were "habitual liars", many emphasized that telling the truth about product nonuse was "very difficult" and described how participants felt ashamed of admitting nonuse because they had not followed study instructions and then "wasted" (discarded) products. Some participants spoke of selling unused products. Women were afraid of being reprimanded, "talked about" or scolded by trial staff, particularly nurses, but yet most acknowledged that staff were friendly and non-punitive. Many narratives were analogous to pupil/teacher relationship dynamics, whereby participants wanted their behavior to appear "good" and believed that the truth about product nonuse would lead to being "expelled" from the study. Early study termination was primarily undesirable because of reimbursement money, and not wanting to "fail". Many suggested real-time blood-monitoring during trials would improve use and honest reporting. Narratives of dishonesty suggested a wider social context of hiding products from partners and distrust about research, influenced by rumors circulating in clinic waiting-rooms and surrounding communities.

Conclusions: Participants valued participation in VOICE. Nevertheless, widespread dishonesty reporting product use was acknowledged, and was said to have occurred for multiple reasons including human nature and fear of repercussions. When feasible, real-time adherence monitoring with feedback to participants should be implemented in future trials.

TUPEC528

Difficulty accessing addiction treatment predicts injection initiation among street-involved youth in a Canadian setting

K. DeBeck[1,2], T. Kerr[2,3], H. Dong[2], J. Montaner[2,3], E. Wood[2,3]
[1]Simon Fraser University, School of Public Policy, Vancouver, Canada, [2]BC Centre for Excellence in HIV/AIDS, Urban Health Research Initiative, Vancouver, Canada, [3]University of British Columbia, Department of Medicine, Vancouver, Canada

Background: Preventing transitions to injection drug use is central for reducing HIV transmission risk among vulnerable street-involved youth. Although addiction treatment is a key intervention to reduce problematic high-risk drug use, engagement with addiction treatment and injection initiation among youth has not been well explored. To help identify potential areas for intervention, this study examines the relationship between having difficulty accessing addiction treatment and injection initiation among street-involved youth.

Methods: Data were derived from the At-Risk Youth Study (ARYS), a prospective cohort of street-involved youth aged 14-26 who use illicit drugs, from September 2005 to May 2013. Cox proportional hazards regression was used to identify factors independently associated with time to injection initiation.

Results: Among 462 participants who were injection naive at baseline, 97 (21%) initiated injection drug use over study follow-up and 129 (27.9%) reported having difficulty accessing addiction treatment at some point during the study period. The median and IQR for the number of study visits was 4 (2-6). In a multivariate Cox analysis, which was adjusted for gender, ethnicity, number of years since initiated non-injection 'hard' drug use (e.g., cocaine, heroin, crystal methamphetamine), recent non-injection cocaine use, recent crack cocaine smoking, recent crystal methamphetamine use, and recent non-injection heroin use, having difficulty accessing addiction treatment remained independently associated with injection initiation (Adjusted Odds Ratio= 1.94; 95% Confidence Interval: 1.11 - 3.38; p-value =0.02).

Conclusions: Study findings suggest that having difficult accessing addiction treatment is a common experience among street-involved youth and is associated with injection initiation. Numerous barriers to accessing addiction treatment among youth have been previously described and include age restrictions, wait times, and stigma among others. Addressing these barriers may support efforts to prevent injection initiation and subsequent risk of HIV transmission among at-risk youth and should be made a public health priority.

Prevention for the general population

TUPEC529

How do HIV-negative individuals in sub-Saharan Africa change their sexual risk behaviour upon learning their serostatus? A systematic review

S. Ramachandran, N. Condie, M. Pickles, S. Mishra
Imperial College London, Department of Infectious Disease Epidemiology, London, United Kingdom

Background: HIV/AIDS imposes a significant public health burden on sub-Saharan Africa (SSA). While mathematical modelling studies have highlighted the potential of universal testing and treatment (UTT) as an HIV elimination strategy, behavioural patterns of the majority HIV-negative population are often overlooked. We aimed to determine how sexual risk behaviour of HIV-negative individuals in SSA changes upon learning their serostatus.

Methods: We systematically reviewed the published literature according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Two electronic databases - EMBASE and Medline - were searched for studies published between 2004 and 2014. We included studies that measured quantitative behavioural changes (condom use or number of partners) in HIV-negative adults in SSA.

Results: From 2185 unique citations, 14 studies representing 29,668 participants met our inclusion criteria. Most studies were at high risk of sampling bias (n=13) and social desirability bias (n=12). Pooling of data was prohibited by marked heterogeneity in study outcome measures. However, many studies showed improvements in both condom use (n=8 of 13) and number of partners (n=5 of 11), while only one study demonstrated slight increases in risk behaviour with condom use. Members from the general population appear to undergo modest improvements in risk behaviour and to sustain these over follow-up periods of 12-24 months. In contrast, evidence from three studies suggests that HIV-negative partners in serodiscordant relationships engage in more extrarelational sex. The remaining three studies evaluating number of partners found negligible changes post-testing.

Conclusions: With the exception of serodiscordant couples, we have found little evidence suggesting that awareness of one's serostatus causes behavioural disinhibition among HIV-negative individuals. Promisingly, there is reasonable evidence that testing can result in improvements in risk behaviour. Our findings have implications for UTT in SSA as well as future modelling studies. Future work should include qualitative studies exploring the determinants of behavioural modification and the precise role of counselling in driving these changes.

TUPEC530

Development and initial validation of an instrument to measure beliefs among women in Puerto Rico about biomedical interventions and the biological factors that facilitate inbound and outbound HIV transmission

K. Fitzgerald, J. Martínez González
Universidad Carlos Albizu, Department of Clinical Psychology, San Juan, Puerto Rico
Presenting author email: 2015kfitz@gmail.com

Background: High rates of sexual mixing with MSM contribute significantly to the HIV burden among women in San Juan, Puerto Rico, where female HIV incidence is attributed primarily to heterosexual contact (67%). Some women do not possess accurate beliefs about the biomedical interventions inhibiting transmission or biological variables enhancing transmission. Knowledge in these areas could potentially increase HIV prevention behaviors.
This study developed and initially validated a Spanish-language instrument measuring beliefs about HIV transmission in the presence of the following: factors facilitating inbound transmission (STIs/oral infections, adolescent cervical ectopy, postmenopausal elevated CCR5 expression, and hormonal contraception), factors facilitative of outbound male to female transmission (viral load and STIs), and PrEP, PEP and HAART efficacy.
Methods: Women recruited via social media (*N* = 100) in October, 2014, responded to a 67-item Likert scale, illustrating scenarios of unprotected vaginal intercourse in the presence of varying biological risk factors or biomedical interventions. Responses were based on their opinion about HIV transmission likelihood. Principle Component Analysis (PCA) was used to perform dimension reduction, and to confirm internal validity.
Results: The majority of respondents were Hispanic (94%), ages 21-30 yrs (72%), with no children (67%), and a baccalaureate degree or beyond (72%). Reliability analysis indicated that the instrument is internally consistent (Cronbach's Alpha = .80). PCA revealed four respective sub-dimensions, accounting for 71% of total variance, related to beliefs about HIV transmission in the presence of the following: biomedical interventions (BMI), STIs and infections (STI/I), hormonal contraception (HC), and outbound infectivity (IX).
Most respondents did not possess accurate beliefs about the augmented inbound risk of HIV infection during adolescence (70%), or post-menopause (79%); nor did they perceive heightened risk in the presence of hormonal contraception (74%), or STIs/oral infections (60%). The majority had incorrect beliefs about PrEP (69%) and PEP (62.%); and most participants did not relate HAART non-adherence to transmitted drug resistance (62%).
Conclusions: Results suggest that this brief, Spanish-language, clinically-administered measure of women's beliefs about factors facilitating or inhibiting HIV transmission may contribute to knowledge-based interventions helping women adopt prevention behaviors. Further scale validation is recommended on a larger, less homogenous Hispanic population.

TUPEC531

Factors associated with uptake of HIV counseling and testing in Cross River State, Nigeria

C. Oyom[1], M. Mbukpa[1], O. Idogho[1], G. Eluwa[2], A. Oginni[2]
[1]Society for Family Health, Abuja, Nigeria, [2]Population Council, Abuja, Nigeria
Presenting author email: oidogho@sfhnigeria.org

Background: HIV counselling and testing (HCT) is a key intervention strategy for effective HIV control in most developing countries as it increases access and knowledge of HIV status, encourages safer sex and is an entry point for HIV care treatment and support services. We determined factors associated with uptake of HCT among the general population in Cross River state.
Methods: The survey sampled females aged 15-49 years and males aged 15-64 years in Cross River State using probability sampling. Interviewer administered questionnaire was used to obtain data on HCT uptake and assessed using a cross-sectional analysis. Logistic regression was used to identify factors associated with uptake of HCT while controlling for potential confounding factors.
Results: A total of 950 respondents were surveyed with equal representation of both male and female (50%). Majority of respondents had at least secondary level education (73%) and were older than 24 years (65%). Overall, uptake of HCT was 62%, with more females than males ever tested for HIV (66% vs. 59%;p=0.04). Compared to those with no formal education, those with primary (AOR:2.11; 95%CI:1.30-3.44), secondary (AOR:4.14; 95%CI:2.55-6.73) and tertiary education (AOR:5.73; 95%CI:3.02-10.88) were more likely to have ever tested for HIV. Females (AOR:1.40; 95%CI:1.06-1.86) compared to males and those with comprehensive HIV knowledge (AOR:2.66; 95%CI:1.99-3.57) were more likely to have ever tested for HIV. Compared to those who were currently married/cohabiting, singles were less likely (AOR:0.67; 95%CI:0.45-0.98) to have ever been tested for HIV. Compared to those aged < 25 years, those aged >=25 years were more likely to have ever tested for HIV
(AOR:2.06; 95%CI:1.40-3.04).
Conclusions: Females, those with comprehensive HIV knowledge and aged >25 years were more likely to have ever tested for HIV. Evidence based and targeted interventions are needed to reach more males and younger population in Cross River state. Increased educational status was associated with increased uptake of HCT and suggests that out of school adolescents and young people are significantly marginalized in HIV programming in Cross River state. Programs that deliver HCT must device new strategies to ensuring out of school adolescents and young people are reached with HIV prevention interventions including HCT.

Prevention for youth and adolescents

TUPEC532

HIV decline associated with changes in risk behaviors among vulnerable young people in Nepal: analysis of population-based HIV prevalence surveys between 2001-2012

K. Deuba[1], D. Kumar Karki[2], A.M. Ekström[1], G. Tomson[1], G. Marrone[1]
[1]Karolinska Institutet, Public Health, Stockholm, Sweden, [2]National Health Insurance Support Project (NHISP), KOICA-Nepal, Kathmandu, Nepal
Presenting author email: gaetano.marrone@ki.se

Background: Objective of the study was to assess changes in HIV risk behaviors and HIV prevalence among young key populations in Nepal, through repeated anonymized unlinked HIV prevalence surveys.
Methods: A total of 7505 young key populations aged 16-24 years [2767 injecting drug users (PWID); 852 men who have sex with men/transgender (MSM/TG); 2851 female sex workers (FSW) and 1035 male labour migrants (MLM)] were recruited randomly over a 12-year period, 2001- 2012 . Local epidemic zones in Nepal were analyzed separately.
Results: We found a very strong and consistent decline in HIV prevalence over the past decade in all local epidemic zones in Nepal among most young vulnerable groups: PWID (from 32% to 1%, p< 0.001), MSM (from 4% to 1%, p= 0.005) and FSWs (from 3% to 1%, p= 0.291), most likely due to a parallel increase in safe needles and syringes use among PWID (56% to 92%, p< 0.001) and an increased condom use among MSM (from 72% to 80%, p= 0.098) and FSW (76% to 86%, p= 0.011). The HIV prevalence among young MLM was low overtime (< 1%) and condom use during sexual intercourse with FSW in abroad was increased (from 73% to 84%, p= 0.059) but decreased overtime with Nepalese FSW (from 40% to 26%, p=0.001). Changes in mean age at starting first injection and frequency of injection among young PWID were dissimilar across the epidemic zones. Young MSM/TG with knowledge of HIV/AIDS was increased over time but no change was observed in mean age at starting anal sex. The age of starting labor work abroad was decreased overtime among young MLM and the knowledge of HIV/AIDS was low among them (< 12%). A variation in places to solicit clients was observed differently across local epidemic zones among young FSW.
Conclusions: In Nepal, the decline in HIV prevalence was consistent and most likely associated with an increase in use of condoms and safe needles/syringes. The large reduction in HIV related risk behaviors may have resulted from available interventions (peer education, HIV testing and counselling, harm reduction programme), and continuation and expansion of such interventions is recommended in Nepal.

TUPEC533

Using peer to peer approach to promote uptake of HIV/SRH services among young people (10-24 years): experience with young key populations (YKPs) in 3 central districts of Uganda

W. Musubika[1], D. Bukenya[2], H. Ntale[3], P. Mpinga[4], R. Egadu[1], S. Kadokech[5], S. Nabadda[3], R. Nabossa[1]
[1]Naguru Teenage Information and Health Center, Service Delivery Department, Kampala, Uganda, [2]Naguru Teenage Information and Health Center, Training Department, Kampala, Uganda, [3]Naguru Teenage Information and Health Center, BCC/Advocacy Department, Kampala, Uganda, [4]Naguru Teenage Information and Health Center, Kampala, Uganda, [5]Naguru Teenage Information and Health Center, M&E Department, Kampala, Uganda
Presenting author email: winibika@yahoo.com

Background: Naguru Teenage Information and Health Centre adopted a peer to peer approach to popularize and promote HIV/SRH uptake for young people in 3 districts in central region. Like many other development programs, the use of peer educators has become very popular especially in the broad field of HIV prevention, however not much is known about the impact of peer to peer approach on uptake of services among key populations. This project chose to assess the impact of peer education on the uptake of HIV/SRH services among YKPs in the 3 districts.
Methods: Young people from key populations including People living with HIV, men having sex with men, sex workers, fisher folks and bodaboda/truck drivers between 14- 24 years were selected and equipped with knowledge and skills, through basic training in SRH/HIV integra-

tion. After training, they were deployed to mobilise and engage their peers through home visits, community dialogues and health information dissemination. They were further provided with data collection tools to record the people they have seen and those referred for services to selected facilities. Service data from completed referral forms was collected from the facilities and analysed for numbers of YKPs accessing HIV/SRH services in the 4 months before and after intervention.

Results: A total of 31,522 YKPs including 16,486 males and 15,036 females were reached in the 8 months with 7,495 and 24,027 accessing services before and after the intervention respectively. YKPs between 10 and 14 years accessing services increased from 476 before to 1,620 after the intervention, those between 15 and 19 years increased from 2,123 before to 7,519 after the intervention and those between 20 and 24 years increased from 4,896 before to 14,888 after the intervention. Highest impact was registered among the fisher folks from 37 before to 5996 after the intervention.

Conclusions: Peer to peer approach seems to yield high return and could be effectively used to increase uptake of HIV/SRH services among YKPs if they are well facilitated to reach out to fellow peers. However there is need for further studies to ascertain its effectiveness among the different YKPs.

TUPEC534

Street culture, survival and HIV risk among street-connected girls in a resource-limited setting

J. Wachira[1], A. Kamanda[2], L. Embleton[3], V. Nanyu[4], D. Ayuku[4], P. Braitstein[3,5,6]
[1]AMPATH, Social and Behavioral Team, Eldoret, Kenya, [2]Moi Teaching and Referral Hospital, Eldoret, Kenya, [3]University of Toronto, Dalla Lana School of Public Health, Toronto, Canada, [4]Moi University, Behavioral Sciences, Eldoret, Kenya, [5]Moi University, School of Medicine, Eldoret, Kenya, [6]AMPATH, Monitoring and Evaluation, Eldoret, Kenya
Presenting author email: pbraitstein@gmail.com

Background: The objective was to describe how the culture and survival strategies of street connected girls and adolescent women (SCGAW) in Eldoret, Kenya, put them at high risk for HIV.

Methods: This qualitative study was conducted from August 2013 to February 2014. A total of 65 street connected boys and girls aged 11-24 years were purposively sampled from the three referral points:

1) A dedicated study clinic for vulnerable children and youth at Moi Teaching and Referral Hospital;
2) Primary locations in which street children reside "bases/barracks";
3) Street youth community-based organizations.

In-depth interviews and focus group discussions were used to collect data. All data were audio recorded, transcribed, translated to English, and a content analysis performed.

Results: The overall median age was 18 years (IQR 14-20.5 years); 30.8% were female. None had gone beyond primary level of education. The majority (81.5%) reported to be sexually active. HIV was highly stigmatized, yet unsafe sexual practices played a significant role in the street culture. Street rules favored boys and involved SCGAW engaging in high-risk sexual behaviors to survive. SCGAW were viewed as sexual objects; instilling low self-esteem and affecting their psychological well-being. During initiation rituals, girls were forced to acquire a sexual partner or risk being raped/gang raped. Rape/gang rape of SCGAW was normalized and identified as a form of punishment for 'unruly' SCGAW. There were no appropriate law-enforcing structures for dealing with perpetrators of rape among SCGAW. Once on the street, SCGAW were pressurized to get pregnant and bear children to satisfy the 'egos' of street boys and avoid stigmatization. Meanwhile, unsafe transactional sexual encounters with street boys and members of the larger society was a common source of income. Although contraceptives were easily accessible, misconceptions around injectable contraceptives and condoms were dominant. In addition, SCGAW did not have the autonomy to make decisions regarding safe sex practices and had to seek consent from their sexual partners.

Conclusions: The street culture promoted high-risk sexual behaviors among SCGAW that increased their risk of HIV transmission including mother to child transmission. Interventions that promote the sexual health and life skills of this vulnerable group are needed.

Themes	Sub-themes	Quotes
Initiation rituals	Girls viewed as sexual object	Female (20 years): The boys at the base must also welcome the girl by raping her although if she agrees with one of them, he can take her as the wife and then he will be the one to protect her.
Initiation rituals	Low self-esteem	Female FGD (14-17 years): Yes, because the same was done to me. It hardens her. I will accept it because I want her to feel what I felt...okay, aha. [Interviewer: So you will allow your man to do a ‚combination' (gang rape) on another girl because the same was done to you?]...I will accept.
Rape	Normalization of rape	Female (21 years): Yes rape is acceptable. If you are being forced to have sex or being…raped by a fellow street boy and another person passes there and sees the action, he…will just tell you to cooperate and finish but will not interfere. Even the leaders of the …base cannot help. He will just tell the boy to give him something small so that he doesn't ….call a group of boys to beat him.
Rape	Managing unruly girls	"...you can even threaten her with a knife or ‚kumpigangeo'…. (interviewer: what is ‚kumpigangeo'?)...catching her on the throat with your elbow…ooh (Interviewer) ‚kumpigangeta'?... (Respondent) ...you can be like two boys. He holds her while you rape her and after that you exchange positions...(interviewer: okay, who mostly rape girls? The big boys or the small boys?)... The big boys...big in age or size?...people around my age..."(Male, 20 years).
Rape	Lack of law-enforcing structures at society level	Male FGD (18-24 years): You know "Gavaa" is just a name for a police, if you are "mshefa"(street youth) and you go to the police, they just say that you know each other ...You know each other... You know streets is just considered as one thing...One thing, so if you go to the police they say you know each other, aha another one?...If you rape a girl even if she is not from the base, when she goes to report, the first thing they will ask is "where have you been raped"? And if it "mangula" (SCCY barracks) they ask you if you know the person who has raped you, they also tell you that, that place is dangerous, "Why did you choose to pass through there?" so it depends on where you have been raped. So if you have been raped at the base...There is no problem; there is nothing they can do. You can't be caught.
Promotion of Pregnancy	Satisfying male ego	Female barracks leader 20 years: For example if you are married and your husband sees other girls on the streets with children…. because most of the street girls give birth to boys, you will find your husband beating you up for no reason. He will later tell you that you don't give birth. He will say "You don't want to give me a child and other people's (SCCY males) wives are giving birth." So you just have to conceive and give birth so that you make him happy and he will not beat you.
Transactional sexual encounters	Multiple sexual partners Sex for money	Female 15 years: "Yes. For example if I have a boyfriend who doesn't give me money, I will prefer to go to the one with money. So I will have sex with the one with money so that he gives me money then in the evening I go back to my boyfriend. My boyfriend doesn't need to ask me where I got the money because if he doesn't give me money and only provides is food and clothing, then what does he expect me to do."
Misconceptions about contraceptives	Injectable contraceptives	Female 15 years: Some girls also say that they cannot use family planning methods because they say that the injection makes people lose their fertility. And some also say that if they use a condom, it makes sex not sweet…The girls prefer condoms but boys don't want. They (referring to the SCCY boys) have now ended up impregnating all of my friends. There are only two who are not pregnant.
Misconceptions about contraceptives	Condom use	Barracks Leader 24 years: Because they tell us (referring to health educators) that condoms should not be in contact with oil but it already has oil in it. As for me, I wouldn't advise others to do as I do, but what I know is that the hole (referring to vagina) that I enter because it's not like I just get a woman and I enter (sex). When you find a woman and she tells you to buy a condom, you buy then you go to the base (SCCY meeting place), and because we are known there, we take two polythene bags, we put them on before we put on the condom. They say you leave some space at the front of the condom, and then imagine you did leave some sweat at your front, so the oil gets into your ‚deki' (penis)… So you find that, with the condom only even if you wanted to go 5 rounds you will only go once because of the oil… You know when you pump, your blood also gets hot and thus the ‚deki' (penis) becomes hot too and that's when you get the oil…

[Emerging themes and quotes around street]

TUPEC535

Understanding opportunities for HIV prevention and care for street connected children and youth in western Kenya

L. Embleton[1,2], J. Wachira[3], A. Kamanda[4], V. Naanyu[3,5], S. Winston[6,7], D. Ayuku[5], P. Braitstein[1,8,9]
[1]University of Toronto, Dalla Lana School of Public Health, Toronto, Canada, [2]Moi University, College of Health Sciences, Department of Medicine, Eldoret, Kenya, [3]AMPATH, Eldoret, Kenya, [4]Moi Teaching and Referral Hospital, Eldoret, Kenya, [5]Moi University, College of Health Sciences, Department of Behavioural Sciences, Eldoret, Kenya, [6]Brown University, Warren Alpert Medical School, Providence, United States, [7]Rhode Island Hospital/Hasbro Children's Hospital, Providence, United States, [8]Indiana University, Fairbanks School of Public Health, Department of Epidemiology, Indianaopolis, United States, [9]Regenstrief Institute, Indianaopolis, United States
Presenting author email: pbraitstein@gmail.com

Background: To effectively inform HIV prevention and care programs based on the needs of street connected children and youth (SCCY), we sought to elucidate the contextual and cultural factors rooted in street life that impact SCCY's sexual behaviours and their perceptions of sexually transmitted infections (STIs) in western Kenya.
Methods: This qualitative study was conducted from August 2013 to February 2014 in Eldoret, Kenya. We recruited SCCY aged 11-24 years who had lived on the street for ≥ 3 months to participate in 25 in-depth interviews and 5 focus group discussions stratified by age and sex, that were audio recorded, transcribed, translated to English, and thematically analyzed.
Results: In total we interviewed 65 SCCY; 69% were male with a median age of 18 years (IQR: 14-20.5 years), and 81.5% participants reported being currently sexually active. Sex played a central role in the context and culture for youth on the street. Commencement of street-involvement, acceptance into street culture, and expectations about roles and responsibilities all largely revolved around sexual activity making early sexual debut, multiple partners, and the inability to remain celibate realities of street life. Rules based on cultural norms dictated acceptable and unacceptable sexual acts. Gender inequities were prominent in SCCY's sexual practices and were at the core of misconceptions related to STI transmission and prevention. Boys sought sex for pleasure, power, and dominance in the street social hierarchy. Whereas for girls, engaging in sex was perceived as the primary tool for survival and protection, with little choice in the matter, resulting in profound sexual and gender-based violence. Male SCCY discussed that females were responsible for spreading STIs due to women's hygiene, urination, and promiscuity, and that circumcision increased the risk of HIV transmission. Boys had a general distrust of condoms and perpetuated fallacies associated with their use.
Conclusions: Our findings revealed many misconceptions and practices that are a result of the sociocultural context on the streets, which are essential to consider when implementing an effective HIV prevention and care program for SCCY. There is an urgent need for distinct HIV prevention programs for boys and girls focusing on sexual education.

TUPEC536

Effects of the PREPARE multi-component, school-based HIV prevention programme on adolescent sexual risk behavior and access to condoms, contraception and HIV testing: cluster randomized controlled trial (RCT)

C. Mathews[1,2], S.M. Eggers[3], L.J. Townsend[4], L.E. Aarø[5], P.J. de Vries[6], A.J. Mason-Jones[6,7], P. De Koker[6], T. Mcclinton Appollis[6], J. Koech[6], Y. Mtshizana[4], A. Wubs[5], N.T.D. Naledi[8], H. De Vries[3]
[1]South African Medical Research Council, Health Systems Research Unit, Cape Town, South Africa, [2]University of Cape Town, Adolescent Health Research Unit, Department of Psychiatry and Mental Health, Cape Town, South Africa, [3]University of Maastricht, Maastricht, Netherlands, [4]South African Medical Research Council, Cape Town, South Africa, [5]University of Bergen, Bergen, Norway, [6]University of Cape Town, Cape Town, South Africa, [7]University of York, York, United Kingdom, [8]Department of Health, Western Cape Government, Cape Town, South Africa
Presenting author email: cathy.mathews@mrc.ac.za

Background: Unwanted pregnancies and sexually transmitted infections, including HIV, are among the social and health consequences of early adolescent sexual debut and unprotected sex. We evaluated the effects of a multi-component, school-based HIV prevention intervention to delay sexual debut and increase condom use (primary outcomes), decrease IPV, and increase access to condoms, contraception and HIV tests (secondary outcomes) among young adolescents in the Western Cape, South Africa.
Methods: During 2013-2014 we conducted a cluster RCT among Grade 8 students in 42 randomly selected public high schools. After agreeing to participate, schools were randomly allocated to intervention or comparison arms. In intervention schools we implemented a 21-session after-school sexual health educational programme, school health service and school sexual violence prevention programme. Comparison schools had usual care. Participants completed questionnaires at baseline, 6 and 12 months. Regression was undertaken to provide outcomes at 6 and 12 months with ORs for dichotomous variables and coefficients for continuous variables, adjusted for baseline demographics, the baseline measure in question and clustering.
Results: One school dropped out before data collection. Of 6244 sampled adolescents in 41 schools, 3451 (55.3%) had signed parental consent and assented to participate. Retention at 12 months was 87.6%. In the intervention arm 614 participants (33.6%) attended at least 50% of educational sessions and 16.0% used the health service. At 12 months, there were no differences between arms in one year incidence of sexual debut (10.4% versus 9.3%; OR= 1.09; 95% CI: 0.81-1.44), condom use at last sex (74.1% versus 80.3%; OR: 0.70, CI: 0.30-1.63), procurement of condoms or HIV tests. Participants in the intervention arm (versus comparison arm) had better knowledge (mean: 0.49, SD: 0.24 versus mean: 0.43, SD: 0.22; Beta: 0.06; CI: 0.03-0.09), were less likely to report IPV (34.6% versus 39.7%; OR: 0.77, CI: 0.61-0.99) and were more likely to have accessed contraception (24.8% versus 18.7%; OR: 1.47; CI: 1.12-1.92). Stronger effects were obtained among participants who attended more sessions.
Conclusions: The intervention may not have changed some sexual behaviours, but may have led to less violent sexual relationships and lower risk of unwanted pregnancy. We need effective ways to improve intervention uptake.

TUPEC537

Correlates of intimate partner violence perpetration among young urban Tanzanian men

M. Mulawa[1], H.L.M. Reyes[1], V. Foshee[1], S. Martin[2], L. Kajula[3], S. Maman[1]
[1]University of North Carolina at Chapel Hill, Health Behavior, Durham, United States, [2]University of North Carolina at Chapel Hill, Maternal and Child Health, Durham, United States, [3]Muhimbili University of Health and Allied Sciences, Psychiatry and Mental Health, Dar es Salaam, Tanzania, United Republic of
Presenting author email: mulawa@live.unc.edu

Background: Evidence suggests that interventions with youth that prevent intimate partner violence (IPV) perpetration may also reduce HIV risk. However, to date, few studies have examined determinants of young men's perpetration of IPV in sub-Saharan Africa. As a result, we have a limited understanding of the etiology of IPV perpetration that could inform prevention efforts. The objective of this study was to examine associations between exposure to childhood violence, alcohol use, and normative beliefs (gender role attitudes and acceptance of IPV) and physical IPV perpetration among young urban Tanzanian men.
Methods: To address this objective, we used baseline data from an ongoing cluster-randomized HIV prevention trial with 1,268 men, (mean age = 26), who were recruited through social clubs called "camps" in Dar es Salaam, Tanzania. Camps are stable social networks with elected leadership and mostly male members. Past-year physical IPV perpetration was assessed using an adapted version of the World Health Organization violence against women instrument. Multilevel modeling was used to examine associations between the hypothesized set of determinants of IPV and the frequency of physical IPV perpetration while adjusting for clustering within camps.
Results: Decreasing age (γ=0.005, p=.02) and increasing number of past-year sexual partners (γ=0.027, p< .0001) were associated with increasing IPV perpetration. Men who were married
(γ=0.089, p=.006), reported having experienced sexual violence before the age of 12
(γ=0.237, p< .0001), or had ever consumed alcohol (γ=0.109 , p< .0001) reported higher levels of IPV perpetration than men who were unmarried, had not experienced childhood sexual violence, and had never used alcohol, respectively. More equitable attitudes towards gender roles were negatively associated with IPV perpetration, but this association was attenuated to non-significance when attitudes towards IPV were added to the model. Less accepting attitudes towards IPV were protective of past-year IPV perpetration (γ=-0.046, p=.03).
Conclusions: Interventions seeking to reduce HIV among Tanzanian men should target youth and aim to eradicate childhood exposure to sexual violence, prevent alcohol use, and change attitudes towards partner violence. While more research is needed, changing attitudes specifically related to violence may be more effective than more broadly shifting gender norms.

TUPEC538

Optimising adolescent HIV care in a large Kenyan care and treatment centre

N. Gitahi-Kamau[1], S. Ilovi[1], L. Njagi[1], E. Njuguna[2], K. Mutai[2], I. Katei[1], I. Inwani[3], J. Mecha[1]
[1]University of Nairobi, Department of Internal Medicine and Therapeutics, Nairobi, Kenya, [2]Kenyatta National Hospital, Respiratory and Infectious Disease Unit, Nairobi, Kenya, [3]University of Nairobi, Department of Paediatrics and Child Health, Nairobi, Kenya
Presenting author email: gnyawira@gmail.com

Background: The global increase in adolescent HIV-related deaths between 2005 and 2012 has been attributed to lack of prioritization of adolescents in national HIV programmes. In 2013, the Kenya Ministry of Health (MOH) developed and piloted a standardized adolescent package of care (APOC) for adolescents living with HIV/AIDS (ALHIV). Although the MOH has not rolled out the APOC, Kenyatta National Hospital (KNH) fully rolled out APOC in February 2014. We evaluated quality of care of ALHIV following the implementation of the package of care at KNH.

Methods: We analysed data from a clinical care database of HIV positive adolescents on follow up at a national teaching and referral centre (KNH), before and after implementation of APOC (October 2012 to September 2014). The care components included provision of antiretroviral therapy, health education, Tanner staging, reproductive health services, facilitated disclosure, and adherence, mental health and family social assessment. Paired comparisons were analysed using Mc'Nemar test on SPSS.
Results: Data on 495 HIV positive adolescents (10-19 years) was analysed. Mean age was 13.6 years (Standard Deviation 2.2 years), and males were 51.8%. The proportion on ART in the current period was 93.5%, median treatment duration of 68.5 months (Inter Quartile Range 38-87 months). After implementation of the standardised APOC, adherence assessment increased from 32.6% to 54.0% (p<0.001). Self-reported adherence did not increase significantly (p = 0.100). There was improved documentation of key clinical care indicators including family and social status (84.6% to 95.1%, p<0.001), Tanner staging (0.2% to 16%, p<0.001), mental status (27.7% to 55.7%, p<0.001) and health information provision (0.4% to 52.2%, p<0.001). Condom provision improved from 5.7% to 9.1%, p=0.047 for all adolescents. Incremental disclosure assessment increased from 22.3% to 84.4%(p=<0.001). The proportion of adolescents with completed disclosure increased from 10.9% to 55.3% (p<0.001) after controlling for baseline age and stage of disclosure.
Conclusions: Implementation of a comprehensive package of care with optimization of adolescent focussed components can contribute to improved quality of care and outcomes. Long term impact on treatment outcomes and quality of life of HIV infected adolescents require further evaluation.

TUPEC539

Towards adolescent friendly voluntary medical male circumcision services: older adolescents report relatively less satisfaction with counseling

D. Boyee[1], E. Peacock[2], K. Andrinopoulos[2], M. Plotkin[1], A. Hellar[1], H. Mahler[1], E. Edouard[3], E. Mlanga[4], R. Kisendi[5]
[1]Jhpiego, Dar es Salaam, Tanzania, United Republic of, [2]Tulane School of Public Health and Tropical Medicine, New Orleans, United States, [3]Consultant, London, United Kingdom, [4]USAID, Dar es Salaam, Tanzania, United Republic of, [5]Ministry of Health and Social Welfare, Dar es Salaam, Tanzania, United Republic of
Presenting author email: dorica.boyee@jhpiego.org

Background: Voluntary Medical Male Circumcision (VMMC) is a WHO recommended HIV prevention strategy, with HIV counseling and testing (HTC) and VMMC counseling forming part of this comprehensive prevention package. Majority of the VMMC clients in Tanzania (75%), as in most countries, are adolescents aged 10-19 years; however there are younger and older boys at different sexual maturity stages, with potentially different needs for information. This presents counselors with a challenge and has the potential to result in variations in client satisfaction with counseling.
Methods: 320 VMMC clients aged 15 years and above and from 11 purposefully sampled health facilities (out of a total of 25 facilities) were observed during service and interviewed afterwards, as part of a cross sectional study conducted in Iringa and Njombe regions, Tanzania in 2013 to examine integration of HTC within VMMC services. STATA 12.1 was used for analysis to calculate percentages; construct client satisfaction scale; X^2 test was applied to look for significance.
Results: Mean age of participants was 22 years (15-64 years). Overall client satisfaction with counseling was high; a minimum of 87% of clients agreeing or strongly agreeing that the counselor had met individual assessed criteria. However, 18-19 year olds reported being relatively less satisfied in comparison to other age groups (see table below). Assessment of individual items in the satisfaction scale reveals a consistent lower rating by 18-19 year olds across all items, with items related to perceptions of privacy and confidentiality being statistically different. Older adolescents were less likely to have been exposed to some prevention messages, including reducing the number of sexual partners (64% were exposed versus 76% of those 20+ years, p<0.05) and wearing condoms correctly and consistently (71% versus 88%, respectively, p<0.05).

Client satisfaction (N)	Weighted percentages			
	15-17 yrs.	18-19 yrs.	20+ yrs.	Total
Relative satisfaction with overall counseling*				
Very satisfied (160)	47.7	31.9	57.5	47.1
	52.3	68.1	42.5	52.8
Relative satisfaction with counselor related factors				
Very satisfied (147)	42.9	32.6	51.6	43.7
Less satisfied (173)	57.1	67.4	48.4	56.2
Relative satisfaction with facility related factors*				
Very satisfied (195)	66.9	46.4	65.6	59.6
Less satisfied (125)	33.1	53.6	34.4	40.3

**p<0.05*
[Table. Counseling satisfaction by VMMC clients' age]

Conclusions: The relatively lower client satisfaction with counseling among the 18-19 year olds could be explained by desire for more information and need for privacy and confidentiality assurance. Older adolescents are at a critical transition to adulthood, presenting increased HIV risk, and getting appropriate HIV prevention messages is critical. VMMC programs are urged to revisit materials, messages, and approaches to counseling older adolescents.

TUPEC540

The impact of food insecurity on sexual HIV risk negotiation with clients among youth sex workers living with and affected by HIV

D. Barreto[1,2], K. Shannon[1], C. Taylor[1], S. Dobrer[1], J. Brown[2], S. Goldenberg[1], K. Deering[1]
[1]British Columbia Centre for Excellence in HIV/AIDS, Vancouver, Canada, [2]YouthCO HIV & Hep C Society, Vancouver, Canada
Presenting author email: dbarreto@cfenet.ubc.ca

Background: Previous research has determined that food insecurity is associated with heightened vulnerability to HIV and reduced access and retention in HIV care. Much of this research has been conducted in resource-poor countries, with limited data from resource-rich settings, despite evidence that food insecurity is concentrated among key affected populations, such as youth and sex workers (SWs). The objective of this research was to longitudinally examine the independent effect of food insecurity on sexual HIV risk negotiation with clients among youth SWs (aged 14-29 years) in Vancouver, Canada.
Methods: Longitudinal data (baseline and six bi-annual follow-up questionnaires) was drawn from An Evaluation of Sex Workers' Health Access ("AESHA"), a prospective community cohort of 723 street and off-street SWs between 01/2010-08/2013. Youth and adult SWs are recruited through street, indoor and online outreach to sex work venues. Bivariable and multivariable generalized estimating equations (GEE) logistic regression was used to examine the independent effect of measures of food insecurity (e.g. modified Radimer/Cornell Food Insecurity Scale; such as food-related financial concerns/cost of food; concerns of food running out; exchanging sex for food) and client condom refusal.
Results: Of the 708 SWs included in this study, 220 (31.1%) were youth, contributing 639 observations over the 3.5-year study. Of the 220 youth SWs, 34.6% (n=76) reported client condom refusal during the study period. In multivariable GEE analysis, after adjusting for other HIV risk pathways (e.g. injection and non-injection drug use; client sexual/physical violence), financial food insecurity retained an independent effect on client condom refusal (adjusted odds ratio: 2.19, 95% confidence interval: 1.28-3.74).
Conclusions: Despite food banks and charitable food sources in a high-income setting, one third of youth were considered food insecure. This study underscores the necessity of access to nutritious food for marginalized youth, HIV/STI education and services among youth involved in sex work, and food security for youth as a prerequisite to positive health outcomes for those both living with and affected by HIV. This research highlights the need for youth-centered programs to address the social determinants of health, including food security, that are directly linked to HIV risk negotiation and access to treatment.

Prevention for people who use drugs, including harm reduction

TUPEC541

Characteristics of drug use in coastal and mainland Tanzania: a mixed methods, rapid assessment in 12 regions

J. Tiberio[1], A. Ngonyani[2], Y.I. Laurent[2], A. Msami[2], M. Makumbuli[2], S. Mwankemwa[2], J. Ndayongeje[3], E. Matiko[4], S. Welty[1], M. Morris[1]
[1]University of California, Global Health Sciences, San Francisco, United States, [2]Drug Control Commission, Dar es Salaam, Tanzania, United Republic of, [3]Global Programs, Dar es Salaam, Tanzania, United Republic of, [4]CDC-Tanzania, Dar es Salaam, Tanzania, United Republic of
Presenting author email: j_ndayongeje@hotmail.com

Background: Tanzania has a generalized HIV epidemic, with an estimated 1.6 million persons living with infection. Because drug use and HIV are linked worldwide and require specific prevention interventions, understanding drug use is needed for a comprehensive, evidence-based response, including in generalized epidemics. Our study aimed to characterize the magnitude and trends in drug use within twelve regions in Tanzania.
Methods: We conducted a rapid assessment, triangulating data from (1) in-depth key informant interviews (PWUD/PWID, police officers, community members, service providers); (2) physical (GPS) and ethnographic mapping of drug use hotspots to describe drug use; and (3) PWUD/PWID population size estimates using Wisdom of the Crowds, enumeration, and modified Delphi. Epidemic trends were categorized as (1) nascent: drug use is beginning to

take root; (2) established: drug use has existed for some time; or (3) pervasive: drug use is spreading into new sub-groups/areas.

Results: We conducted 436 in-depth interviews from September 2013 to August 2014, corroborating illicit drug use increasing across all regions, with rapid increases in female PWUD in some regions. Most PWUD were 18-35 years and worked as bus touts, laborers, fishermen, miners or sex workers or stole to survive or support their habit; most were concentrated around bus stops along the coastal transit corridor, in abandoned buildings, and in low-income residential areas. A minority of "invisible" PWUD were reported among military officers, police, or working-class people. Cannabis was the most commonly used drug, smoked alone or combined with tobacco and heroin ("cocktail"). Heroin was available in all regions and reported to originate from Dar es Salaam. Cocaine was less common, likely due to high price and variable availability. Substances such as petrol, shoe polish, and glue were used as inhalants; diazepam misuse was common. Regional findings are reported in Table 1.

Region	Description of drug use epidemic	Region	Description of drug use epidemic
Tanga	Drug use is pervasive and increasing, and has spread to villages outside of the regional capital. Female PWUD are present but not visible.	Mbeya	Drug use is established, and has limited spread in towns along the road throughout the border region.
Mwanza	Drug use is pervasive and increasing, concentrated in the regional capital. Female PWUD are visible.	Kilimanjaro	Drug use appears to be established and increasing. Most users are young men in Moshi Municipality.
Arusha	Drug use is pervasive and increasing, and the epidemic is concentrated in the regional capital. Female PWUD are visible.	Shinyanga	Drug use is established, and can be found in towns outside of the regional capital where there is heightened economic opportunity from mining activities.
Pwani	Drug use is pervasive and increasing, and was found in more small towns than other regions visited.	Geita	Drug use is nascent and concentrated in the regional capital, with limited spread to areas with mining activities.
Dodoma	Drug use appears to be pervasive and increasing in both men and women, and also youth.	Kigoma	Drug use is nascent, concentrated only in the regional capital, with no established hotspots. No female PWUD were identified.
Morogoro	Drug use appears to be established and increasing in both men and women and also youth.	Mtwara	Drug use is nascent and increasing, currently concentrated in Mtwara Municipality. No female PWUD were identified.

[Region-level trends in illicit drug use]

Conclusions: Illicit drug use is widespread, with variable features across the Tanzanian hinterlands. Improving transportation infrastructure and economic opportunities combined with poverty and inequality appear key factors for increasing drug use. Our findings build upon work in the Tanzanian cosmopolitan cores of Zanzibar and Dar es Salaam to draw attention to increasing drug use nationally.

TUPEC542

Evidence-based recommendations for essential and novel HIV prevention and harm reduction services for people who use drugs in Canada and are at risk for HIV, HCV and other harms

C. Strike[1], T.M. Watson[1], S. Hopkins[2], H. Gohil[1], M. Miskovic[1], P. Leece[1], S. Robinson[1], C. Arkell[1], L. Challacombe[1], Working Group on Best Practices for Harm Reduction Programs in Canada

[1]University of Toronto, Dalla Lana School of Public Health, Toronto, Canada, [2]Toronto Public Health, Toronto, Canada

Presenting author email: carol.strike@utoronto.ca

Background: Drug use practices that can lead to transmission of HIV and other harms are issues affecting communities throughout Canada and the world. Our goal was to create and disseminate evidence-based recommendations to guide delivery of essential and novel interventions by Canadian HIV prevention and harm reduction programs that provide service to people who use drugs.

Methods: Our Canadian, community-based team includes people with lived experience, service providers, researchers, and policymakers. We used a consensus process to design the project and make all decisions. Narrative synthesis methods were used to search, retrieve, assess, and synthesize the most up-to-date scientific evidence from Canada, United States, Europe, and other countries with public health systems similar to Canada. Systematic review methods were used to produce overdose prevention recommendations. Multi-layered dissemination methods were used to promote uptake of the recommendations. An upcoming online survey of program managers will evaluate uptake.

Results: Starting in July 2013, evidence-based recommendations were disseminated about the following practice areas: needle and syringe distribution(e.g., recommendations to place no limits on distribution); other injecting equipment distribution (e.g., recommendations to distribute cookers without limits); safer crack cocaine smoking equipment distribution (e.g., recommendations regarding when to replace used equipment); safer disposal and handling of used drug use equipment; safer drug use education (e.g., brief and long-format interventions); naloxone and overdose prevention. In May 2015, another set of recommendations will be released focussed on service model design (e.g., recommendations for fixed, mobile, pharmacy, vending machine, and peer-based outreach models); equipment distribution for steroid/hormone injection, piercing and tattooing, smoking heroin, and smoking crystal methamphetamine; testing and vaccination; skin and vein care; referrals to HIV and HCV treatment, substance use treatment, mental health services, and housing services; education and other services for the prison context; and relationships with law enforcement. As of January 2015, there have been 12,337 downloads of the full English document and 1,225 downloads of the French version hosted online.

Conclusions: Our recommendations are used across Canada to reduce inequities in access to safer injection and smoking supplies, safer drug use education, and other essential services to improve the quality of HIV prevention and harm reduction interventions.

TUPEC543

Urgent need for harm-reduction interventions in Mozambique: results from the Integrated Biological and Behavioral Surveillance Survey among people who inject drugs

E. Teodoro[1], M. Boothe[2], C. Sema Baltazar[3], P. Young[4], H. Frank[2], I. Sathane[5], M.L. Gouveia[1], R. Horth[2]

[1]Ministry of Health, Department of Mental Health, Maputo, Mozambique, [2]University of California, San Francisco, United States, [3]Institute of Health, Ministry of Health, Maputo, Mozambique, [4]Centers for Disease Control and Prevention, Maputo, Mozambique, [5]ITECH Mozambique, Maputo, Mozambique

Presenting author email: isabels@itech-mozambique.org

Background: While studies highlight the importance of a comprehensive package of harm-reduction interventions to reduce HIV transmission among people who inject drugs (PWID), little is known about behaviors among PWID in Mozambique that increase their risk of HIV infection. Mozambique conducted its first Integrated Biological and Behavioral Surveillance (IBBS) Survey in 2014 using respondent-driven sampling to estimate HIV prevalence and associated risk behaviors among PWID.

Methods: Survey implementation occurred in two major urban areas: Maputo (n=353) and Nampula/Nacala (n=139). Specimens were collected for STI testing and a behavioral questionnaire was administered to PWID, defined as anyone ever having injected drugs. We present RDSAT-adjusted point estimates.

Results: Participants were mostly male (94.1% and 97.1% from Maputo and Nampula/Nacala, respectively) with mean age of 22 (range 19-56) and 28 (range 18-60). HIV prevalence was 50.3% and 36.8%, while 7.5% and 7.6% screened positive for hepatitis B, and 44.6% and 7.0% screened positive for hepatitis C. STI symptoms or diagnosis in the last 12 months was reported by 9.6% and 38.4%, of which 61.7% and 77.3% sought treatment. Contact with an HIV peer educator was reported by 9.5% and 40.8%, while 26.8% and 60.0% received condoms in the past 12 months. Access to new injection equipment was reported by 89.6% and 78.9%, however, 53.9% and 65.9% reported needle sharing; of those who injected in the past 30 days, 14.3% and 8.0% injected with a used needle at last injection. Among those who had sex in the last 12 months, non-condom use at last sex was reported by 47.6% (n=121) and 68.9% (n=93), while 11.4% (n=47) and 10.3% (n=20) received drugs in exchange for sex.

Conclusions: PWID are at high risk of HIV infection in Mozambique. A comprehensive package of harm-reduction interventions, with consideration of regional differences, is urgently needed to reduce the risk of infection among this population. Mozambique can gradually introduce harm-reduction policies beginning with enhanced peer education programming targeting PWID, distribution of safe injection kits and integrated HIV and STI health services within addiction treatment services. Additional studies are required to assess the feasibility of needle and syringe programs or opioid substitution therapies in Mozambique.

TUPEC544

Seek, test, treat and retain (STTR) for people who inject drugs (PWID) in Kenya: findings from the third intervention period of a stepped wedge study

J. Lizcano[1], A. Kurth[1], C. Cleland[1], P. Cherutich[2]

[1]New York University, College of Nursing Global, New York, United States, [2]Ministry of Health, Nairobi, Kenya

Presenting author email: jl3731@nyu.edu

Background: HIV infections in sub-Saharan Africa increasingly occur among people who inject drugs (PWID). Needle and syringe programs (NSPs) and PWID-specific ART support have been nearly non-existent, though Kenya is among the first to implement NSP at a country-wide level starting in 2013. The World Health Organization (WHO) recommends earlier antiretroviral therapy (ART) to enhance viral suppression among persons at high risk of transmission including people who inject drugs (PWID). We present data from an implementation science study to improve testing, linkage and retention in HIV care of PWID in Kenya.

Methods: Evaluation is being done using a stepped wedge cluster-randomized design. We are using respondent-driven sampling (RDS) to reach PWIDs for HIV-1 prevalence and

viral load determination [SEEK]. We continue collecting study data in additional time periods as PWID service sites roll out, including behavioral data collected using tablets, rapid HIV testing [TEST], POC CD4 determination for HIV-positives, and assignment of peer case managers (PCMs) to those with CD4 < 500/μL to link to ART with adherence [TREAT]. Both PCMs and PWID will receive small conditional cash transfers for PWID adherence to HIV care visits [RETAIN]. Recently, we added phylogenetics and HepatitisC Virus testing to our methods.
Results: 1346 individuals were screened during the third intervention period with 1293 found to be eligible and enrolled (96.1%). Most enrolled participants were male (88.2%). Median age was 32 years; age ranged from 18 to 82 years. Median age at first injection was 27 years. 213 of 1293 (16.5%) were HIV-positive. About 14.1% (n = 30) of those with HIV infection (n = 213) were newly diagnosed by our study. 54 participants were eligible to be assigned to a PCM and initiate ART. Of those, 50 initiated ART, 49 successfully continued on ART, 0 stopped taking ART, and 1 died. Thus 98% were retained in care (49/50 retained).
Conclusions: Current Kenyan guidelines restrict access to ART among PWID. The combination of RDS and rapid testing is an effective strategy for finding PWID with HIV infection, including those not previously diagnosed. Linkage to care by PCMs has been very effective for ART initiation and retention.

TUPEC545

More vulnerability, more risk: findings from a cross-sectional qualitative study on the multiple vulnerabilities experienced by people who inject drugs (PWID) in Bihar and Manipur, India

V. Arumugam, K. Biswas, C. Sharma, F. Joseph, S.W. Beddoe, S. Mehta, J. Robertson
India HIV/AIDS Alliance, New Delhi, India
Presenting author email: aviswanathan@allianceindia.org

Background: While sexual transmission remains the primary mode of HIV transmission in India, drug users are also disproportionately affected. People who Inject Drugs (PWID) are at high risk of acquiring HIV and other blood-borne viruses, such as Hepatitis B and C. Studies report that unsafe injection practices along with low condom use put PWID at dual risk for HIV. As part of the Hridaya programme, the Indian component of the five-country, Dutch government-funded Community Action on Harm Reduction initiative (CAHR), operational research was conducted to gain in-depth knowledge on multiple vulnerabilities for HIV acquisition among PWID in the states of Bihar and Manipur.
Methods: A cross sectional qualitative study was conducted with PWID in two Hridaya programme states, Bihar and Manipur. A total of 40 in-depth interviews were undertaken with PWID diagnosed with HIV recently (2010-2013). Four focus group discussions with PWID and with female injecting drug users (FIDUs), spouses and partners of PWID were conducted. Lastly, ten key informant interviews were conducted. Atlas.ti software (version 7) was used to code and categorise data into themes. In thematic analysis, the various topics that emerged from the interviews were analysed.
Results: Findings showed that there is overlap between injecting networks and sexual networks. Within injecting networks, each and every aspect — from the type of substances used, the sourcing of substances, and the accessing of harm reduction services to the interaction of social, structural, politico-legal barriers — has the potential to contribute to vulnerability of PWID. Similarly, sexual networks of PWID constitute a complex web in which HIV awareness is in conflict with actual behaviour to access prevention services and disclose HIV status. Partners or spouses of PWID are also at higher risk which further increases the vulnerability of both PWID and their spouses/partners.
Conclusions: The interventions required to achieve harm reduction with PWID are complex. Injection drug use needs to be understood holistically, considering (a) the reasons for drug use in a particular community; (b) the options and opportunities for intervention; and (c) the necessity for support provided in a non-judgemental and sensitive way through peers, service providers, families and the community.

TUPEC546

Reach them early: identifying risk behaviours after onset of injecting to reduce sharing of injecting equipment: findings from the Hridaya drug use pattern assessment in India

V. Arumugam[1], J. Robertson[1], K. Biswas[1], C. Sharma[1], F. Joseph[1], S.W. Beddoe[1], S. Mehta[1], A. Ambekar[2], U. Sharma[3], R.K. Raju[3], S. Singh[3], A. Biswas[1]
[1]India HIV/AIDS Alliance, New Delhi, India, [2]All India Institute of Medical Sciences, National Drug Dependence Treatment Centre, New Delhi, India, [3]Consultant, New Delhi, India
Presenting author email: abiswas@allianceindia.org

Background: Injecting drug use has emerged as an important route for HIV transmission in India. There are an estimated 200,000 People Who Inject Drugs (PWID) in India with an HIV prevalence of 7.14% (NACO, 2011). Injecting drug users are vulnerable to HIV infection due to risky injecting practices. The pattern of drug use through injecting and its association with vulnerability to blood-borne infections have not been well studied in Indian settings. As part of the Hridaya programme, the Indian component of the five-country, Dutch Government-funded Community Action on Harm Reduction initiative, India HIV/AIDS Alliance conducted a Drug Use Pattern Assessment to understand the profile of PWID, their patterns of drug use and risk behaviours, and the accessibility and availability of harm reduction services among PWID.
Methods: A multi-site, cross-sectional study was conducted with a mixed-methodology (quantitative and qualitative) approach. A total of 1,091 semi-structured interviews and 65 FGDs with PWID, and 34 key informant interviews were conducted in four states (Bihar, Haryana, Jammu and Uttarakhand). Respondents for semi-structured interviews were selected through simple random sampling using client information available from partner NGOs. Appropriate analytical techniques were employed using SPSS 20.0.
Results: 20% of PWID respondents initiated illegal injection at the age of 18 years or less. PWID respondents started injecting illicit drugs at the mean age of 23, after a progression from initial illicit substance use at the mean age of 16 and non-injecting illicit drug usage at the mean age of 19. Of the 35% of respondents who shared injecting equipment, 86% had shared injecting equipment within one month of onset of injecting practice. Ever shared injecting equipment is significantly higher among those initiated illegal injection at earlier age (18 years or less) when compare with those who started illegal injection above 18 years old ($p< 0.05$).
Conclusions: Though it takes a mean of seven years from the first licit drug use to onset of injecting illicit drugs, sharing injecting equipment happens within one month of onset of injecting. In addition to early identification of PWID, appropriate strategies need to respond to client's specific stage of substance use to reduce vulnerability towards HIV.

TUPEC547

Effective services for HIV prevention among people who inject drugs (PWIDs) in Ukraine

I. Sazonova[1], T. Mykhalchuk[1], T. Salyuk[1], O. Varetska[2]
[1]ICF 'International HIV/AIDS Alliance in Ukraine', M&E, Kyiv, Ukraine, [2]ICF 'International HIV/AIDS Alliance in Ukraine', Kyiv, Ukraine

Background: HIV epidemic in Ukraine was estimated to be one of most rapidly growing in Europe and was driven primarily by PWID. Since 2003 Ukraine has been implementing nationwide prevention programs for PWID: in 2013 196,460 PWIDs received HIV prevention services (63% of estimated population size). The study explores the level of HIV seroconversion and the most effective HIV services for its prevention.
Methods: Data on HIV test results were collected during 2013 using program monitoring database (SYREX) of ICF "International HIV/AIDS Alliance in Ukraine" which accumulates national data on prevention service provision. PWIDs who were tested for HIV 2 or more times with the first negative result were included into analysis (n=33,000): 19,677 PWIDs have been tested twice during 2013; 7,792 PWIDs had 3 tests and 5,531 PWIDs had 4 and more HIV tests during the year. Regression analysis was performed to define the association between number and typology of services received and HIV seroconversion.
Results: Among all HIV negative IDUs in the cohort seroconversion occurred in 3% cases. The majority of new HIV positive cases occurred between first and second test (60%). 23% of additional infections occurred between second and third test, 9.5% between third and fourth, and 7.5% between fourth more rounds of testing. Consultation of outreach worker turned out to be one of the most effective methods to prevent HIV, even one consultation in a year decreased the odds to be HIV-infected by almost 2 times (OR=2.3 [1.3; 4.0]). The syringe and condoms distribution programs also have shown their effectiveness: increasing the number of distributed syringes (OR=3.65 [1.35; 9.8]) and condoms (OR=3.4 [1. 5; 7.7]) decreased the odds to have HIV seroconversion. Needles separate distribution as well as distribution of informative materials did not have significant influence on seroconversion ($p>0.05$).
Conclusions: The analysis presents the complex array of the level of service effectiveness for PWID. The motivation to safer behaviour formed through outreach worker's consultations together with syringe and condom distribution are significantly associated with negative HIV test results.

TUPEC548

Exploring HIV risks and treatment outcomes among people who use drugs enrolled in unregulated recovery house programs in British Columbia, Canada's Lower Mainland region: a qualitative study

R. McNeil[1], T. Kerr[1], S. Anderson[1], L. Maher[2], W. Small[1]
[1]BC Centre for Excellence in HIV/AIDS, Urban Health Research Initiative, Vancouver, Canada, [2]UNSW Australia, Kirby Institute for Infection & Immunity in Society, Sydney, Australia
Presenting author email: rmcneil@cfenet.ubc.ca

Background: The treatment of drug dependence has been increasingly identified as critical to reducing drug-related HIV risks and promoting optimal HIV treatment outcomes. Across North America, largely unregulated group housing programs operating under abstinence-based (e.g., 12-step) models, known as Recovery Houses, are among the most commonly available drug treatment programs. In British Columbia (BC), Canada, Recovery Houses are not

regulated and operate with little oversight from health authorities. Despite the proliferation of Recovery Houses, little research has been undertaken examining their impacts on drug-related outcomes, including HIV-related outcomes. We undertook this study to explore how the regulatory contexts and treatment approaches of Recovery Houses in BC's Lower Mainland region influence HIV-related outcomes.

Methods: We conducted qualitative interviews with 27 people who use drugs (PWUD) who reported enrollment in Recovery House programs within the previous five years. These individuals were recruited from among participants in two ongoing prospective cohort studies comprised of HIV-negative and HIV-positive PWUD. We analyzed interview transcripts thematically and by drawing on the 'Risk Environment' framework.

Results: Participant accounts underscored how the social-structural contexts of Recovery Houses (e.g., lack of regulation, abstinence-based philosophies) fostered conditions that increased the potential for HIV risks and other adverse outcomes. Participants emphasized how many unregulated Recovery Houses promoted continued engagement in drug scene activities (e.g., injection drug use) due to their proximity to street-based drug scenes. Meanwhile, abstinence-based treatment philosophies adopted by Recovery Houses failed to accommodate participants' drug use trajectories (e.g., lower frequency or episodic drug use) and undermined access to supports (e.g., harm reduction supplies) necessary for enacting risk reduction. In turn, our findings underscore how this interplay of social and structural factors fostered high-risk drug use practices within Recovery Houses (e.g., syringe-sharing), while evictions stemming from breaches of abstinence-based treatment contracts resulted in cascading harms (e.g., homelessness, public injecting) that increased vulnerability to HIV risks and treatment interruptions.

Conclusions: Our findings underscore the potential of unregulated drug treatment programs to perpetuate adverse HIV-related outcomes, highlighting the importance of ensuring that these programs operate under evidence-based treatment models and with sufficient oversight from health authorities.

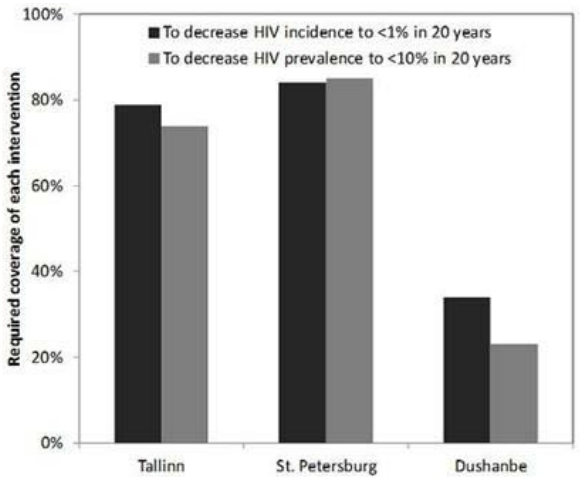
TUPEC549

Controlling HIV among people who inject drugs in Eastern Europe and Central Asia: insights from modelling

P. Vickerman[1], L. Platt[2], E. Jolley[2], T. Rhodes[2], M. Kazatchkine[3], A. Latypov[4]
[1]University of Bristol, SSCM, Bristol, United Kingdom, [2]LSHTM, London, United Kingdom, [3]United Nations, Geneva, Switzerland, [4]Management Sciences for Health, Kiev, Ukraine
Presenting author email: peter.vickerman@bristol.ac.uk

Background: Although there is evidence that needle and syringe programmes (NSP), opioid substitution therapy (OST) and antiretroviral therapy (ART) reduce HIV transmission, most Central and Eastern European sub-regions still have low coverage of these interventions.

Methods: We conducted a modelling analysis to estimate the impact on HIV transmission of OST, NSP and ART in St. Petersburg (Russia), Tallinn (Estonia) and Dushanbe (Tajikistan). For each site, we estimated the coverage needed of each intervention separately or in combination to:
(1) achieve a 30%/50% relative reduction in HIV incidence or prevalence over 10 years; and
(2) reduce HIV incidence to < 1% or prevalence < 10% after 20 years.
A sensitivity analysis for St. Petersburg considered the implications of including varying degrees of risk heterogeneity or sexual HIV transmission, as well as assuming the initial acute phase of HIV does not have such heightened HIV transmission risk.



[Figure. Projected coverage required for each intervention to decrease HIV incidence to <1% or HIV prevalence to <10% in 20 years]

Results: For St. Petersburg, when OST, NSP and ART are combined, only 14% coverage of each intervention is required to achieve a 30% reduction in HIV incidence over 10 years. Similar findings are obtained for Tallinn and Dushanbe. To achieve the same reduction in HIV prevalence, over double the coverage level of each intervention is required. To either reduce HIV incidence to < 1% or HIV prevalence to < 10% over 20 years (see Figure), with all interventions combined, projections suggest that very high coverage levels (74-85%) are required for the higher prevalence settings (Tallinn/St.Petersburg), whereas lower coverage levels (23-34%) are needed in the lower prevalence setting of Dushanbe. The sensitivity analysis suggested the predicted intervention coverage requirements are robust to changes in the model assumptions.

Conclusions: The lack of political support and resources for the implementation of combination interventions has caused the HIV epidemic to spread unchecked among PWID in these high prevalence settings, to such an extent that large reductions in prevalence and incidence will be hard to achieve. The immediate implementation and scale up of combined interventions are urgently needed to start reducing HIV transmission.

TUPEC550

HIV risk factors associated with risky and illegal income generation among street-involved youth in a Canadian setting

T. Cheng[1,2], T. Kerr[1,3], P. Nguyen[1], E. Wood[1,3], K. DeBeck[1,4]
[1]British Columbia Centre for Excellence in HIV/AIDS, Urban Health Research Initiative, Vancouver, Canada, [2]Simon Fraser University, Faculty of Health Sciences, Burnaby, Canada, [3]University of British Columbia, Vancouver, Canada, [4]Simon Fraser University, School of Public Policy, Burnaby, Canada

Background: Although youth who are street-involved face increased risk of HIV infection through a range of social and structural factors, little is known about the HIV risks associated with deriving income from illegal and risky quasi-legal sources. This study investigates risky income generation activities among a sample of street-involved youth.

Methods: Data were collected between 2005 and 2012 from the At-Risk Youth Study (ARYS), which is a prospective cohort study of street-involved youth aged 14-26 in Vancouver, Canada. Generalized estimating equations were used to identify factors associated with risky income generation defined as reporting income from dealing drugs, sex work, recycling, squeegeeing, pan-handling, theft, robbing, stealing, or other criminal activities. We also examined which sources of income respondents would eliminate if they did not require money to purchase drugs.

Results: Among 1,008 participants, 826 (82%) reported engaging in risky income generation activities at some point during the study period. Drug dealing was the most prevalent form of income generation (52%). Factors positively and independently associated with risky income generation included: homelessness, high-intensity stimulant drug use, binge drug use, non-fatal overdose, interactions with police, and experiencing violence; regular employment was negatively associated with the outcome (all $p < 0.05$). Among those who reported risky income generation, 440 (53%) were willing to give up these income sources if they did not need money to purchase drugs, and those who reported drug dealing were most likely to give up this income source (n=283, 64%). These youth were significantly more likely to be older, homeless, engage in high-intensity drug use, have interactions with police, and have recently accessed addiction treatment (all $p < 0.05$).

Characteristic	Unadjusted		Adjusted	
	Odds Ratio (95% CI)	*p* - value	Odds Ratio (95% CI)	*p* - value
Older Age (yes vs. no)	1.06 (1.02 – 1.10)	0.001		
Gender (female) (yes vs. no)	0.88 (0.72 – 1.07)	0.205		
Aboriginal ancestry (yes vs. no)	1.05 (0.85 – 1.30)	0.662		
Education (≥high school) (yes vs. no)	0.86 (0.71 – 1.05)	0.131		
Homeless* (yes vs. no)	2.87 (2.49 – 3.31)	<0.001	2.33 (2.00 – 2.73)	<0.001
Heavy alcohol use* (yes vs. no)	1.07 (0.91 – 1.25)	0.441		
Binge drug use*† (yes vs. no)	2.54 (2.19 – 2.94)	<0.001	1.73 (1.45 – 2.06)	<0.001
Daily crystal meth use*‡ (yes vs. no)	2.62 (1.94 – 3.56)	<0.001	2.52 (1.80 – 3.53)	<0.001
Daily crack use*‡ (yes vs. no)	3.72 (2.87 – 4.82)	<0.001	2.99 (2.20 – 4.05)	<0.001
Daily cocaine use*‡ (yes vs. no)	2.90 (1.54 – 5.46)	0.001	2.02 (0.95 – 4.28)	0.067
Daily heroin use*‡ (yes vs. no)	1.88 (1.25 – 2.82)	0.002	1.37 (0.83 – 2.25)	0.220
Any injection drug use* (yes vs. no)	2.44 (1.98 – 3.00)	<0.001	2.03 (1.64 – 2.53)	<0.001
Any non-fatal overdose* (yes vs. no)	2.47 (1.88 – 3.25)	<0.001	1.78 (1.28 – 2.48)	0.001
Encounters with police* (yes vs. no)	2.89 (2.45 – 3.41)	<0.001	2.30 (1.91 – 2.77)	<0.001
Experienced violence* (yes vs. no)	1.87 (1.62 – 2.16)	<0.001	1.47 (1.26 – 1.73)	<0.001
Incarceration* (yes vs. no)	1.78 (1.47 – 2.17)	<0.001	1.18 (0.94 – 1.48)	0.143
Addiction treatment* (yes vs. no)	1.09 (0.92 – 1.28)	0.316		
Regular employment* (yes vs. no)	0.80 (0.69 – 0.92)	0.002	0.80 (0.68 – 0.94)	0.006

° Includes dealing drugs, sex work, recycling, squeegeeing, pan-handling, theft, robbing, stealing, other criminal activities
* All behavioural variables refer to activities occurring in the last six months
† Includes injection and non-injection drug use
‡ Non-injection drug use

[Table 1. Bivariate and multivariate GEE analyses of factors associated with risky income generation activities° (n = 1,008)]

Conclusions: Risky income generation was prevalent in our sample, and associated with known social and structural risk factors for HIV, such as higher intensity drug use, housing marginalization, and interactions with the criminal justice system. The majority of participants were willing to give up their risky income sources if they did not need money for drugs, indicating that increasing youths' access to addiction treatment and low-threshold employment opportunities may reduce risky income generation and related HIV vulnerabilities.

TUPEC551

Defining public disorder: conceptual implications for HIV prevention efforts

D. Werb[1], D. Fast[2]
[1]*University of California, San Diego, Division of Global Public Health, Toronto, Canada,* [2]*University of British Columbia, Vancouver, Canada*
Presenting author email: dwerb@ucsd.edu

Background: Public disorder is commonly used to describe a variety of activities such as public injecting, public drug dealing, and homelessness or street involvement among people who inject drugs (PWID). HIV prevention interventions among PWID have often focused on reducing public disorder in an effort to reduce HIV risk. However, observers have noted that open drug scenes, while appearing 'disorderly', are often highly ordered spaces within which behavior is circumscribed by structural factors within strict, and often complex, shared codes of social conduct. This complexity has implications for the development and implementation of HIV prevention efforts.
Methods: We employed Rhodes' Risk Environment Framework, as well as notions of structural violence to elucidate how definitions of public disorder impact the effectiveness of structural HIV prevention efforts. We reviewed current HIV prevention approaches, identified their underlying approach to public disorder, and assessed how this impacted their effectiveness.
Results: Structural approaches to HIV prevention generally seek to re-order spaces to produce a lower incidence or intensity of HIV risk behaviors. For example, medically supervised injection facilities seek to reduce syringe sharing by altering injecting spaces, as do abstinence-based or supported housing interventions. However, the failure of certain housing interventions suggests that the provision of 'ordered space' to replace 'public disorder' can, paradoxically, increase HIV risk. For example, abstinence-based housing may reduce the frequency of public drug use, but increase risky or rushed injection drug use in an effort to evade detection.
Conclusions: The effectiveness of structural HIV prevention approaches may be impacted by their potential for unintended consequences that paradoxically increase HIV risk among exceptionally vulnerable PWID subpopulations. Such unintended consequences may result from overly restrictive definitions of public disorder that fail to identify the underlying structural and social factors that order seemingly stochastic open drug scenes. We propose a re-thinking of public disorder, which takes into account the shared codes of conduct and socioeconomic hierarchies that are embedded within drug scenes, in order to improve HIV prevention outcomes.

Prevention for male, female and transgender sex workers

TUPEC552

Interventions for commercial sexual workers: lessons and challenges from Rakai, Uganda

J.L. Ssembatya[1], G. Nakigozi[2], J.B. Ssemanda[3], R. Kairania[3], E. Kato[3], F. Nalugoda[4], J. Kagaayi[5], D. Serwadda[6], N. Sewankambo[7], M.J. Wawer[8], R.H. Gray[9]
[1]*Ministry of Health, Uganda Virus Research Institute, Community Services, Kalisizo, Uganda,* [2]*Rakai Health Sciences Program, Clinical Services, Kalisizo, Uganda,* [3]*Rakai Health Sciences Program, Community Services, Kalisizo, Uganda,* [4]*Rakai Health Sciences Program, Head, Kalisizo, Uganda,* [5]*Rakai Health Sciences Program, M& E, Kalisizo, Uganda,* [6]*Makerere, Public Health, Kampala, Uganda,* [7]*Makerere University, College of Health Sciences, Kampala, Uganda,* [8]*John Hopkins University Bloomberg, School of Public Health, Baltimore, United States,* [9]*John Hopkins University, Public Health, Baltimore, United States*
Presenting author email: jssembatya@rhsp.org

Background: Commercial Sex Workers (CSWs) face a high burden and risk for HIV and other sexually transmitted infections (STIs). Despite this, coverage with prevention, treatment and support programs remains low among CSWs. We present data on the uptake of HIV prevention, treatment and support services among CSWs in Rakai District, Uganda following an intensive program targeting them.
Methods: Groups of up to 25 CSWs were identified in trading centres using local leaders and snowball sampling who were engaged in group discussions. Topics included self- assessment, of risk associated with HIV testing and counseling (HTC), and linkage into HIV /STI care and treatment. CSWs were offered free HTC services and HIV-positives were linked to HIV Care using existing referral systems. HIV counselors visited health facilities after one month and to ascertain linkage to HIV care.
Follow-up meetings were held with CSWs after six months to share experiences and challenges and their data on utilization of services was abstracted from clinic registers
Results: Between January and October 2014 a total of 734 CSWs participated in the meetings and 515 (70.2%) accepted HTC. Of those who accepted HTC, 313 (60.7%) tested HIV positive. 184 (59 %) of those who tested HIV positive were already enrolled in HIV care programs. Among the HIV-positive persons not in care 109 (84%) were successfully linked into HIV care. Over 70% of CSWs were seen at the six month follow up meetings.
During the initial and follow-up discussions, CSWs reported lower condom use with steady partners than with casual partners. Some CSWs reported reluctance to seek services because of mistrust of the health care system and fear of losing income if they were seen seeking HIV care.
Conclusions: Our approach identified and engaged the majority of CSWs in HTC and HIV care. However, future programs for CSWs need to identify care naïve CSWs to reduce redundancy and HIV care strategies sensitive to needs of CSWs need to be introduced into health units.

TUPEC553

Understanding high HIV risk behavior, gender identity, stigma and violence among transgender women in urban Uganda

R. King[1], J. Nanteza[2], Z. Sebyala[2], T. Poteat[3], R. Apondi[4], W. Hladik[5]
[1]*University of California, San Francisco, United States,* [2]*Makerere University, School of Public Health, Kampala, Uganda,* [3]*Johns Hopkins Bloomberg School of Public Health, Department of Epidemiology, Center for Public Health and Human Rights, Center for AIDS Research, Baltimore, United States,* [4]*Centers for Disease Control and Prevention, Entebbe, Uganda,* [5]*Centers for Disease Control and Prevention, Atlanta, United States*
Presenting author email: rach@vtx.ch

Background: A recent review estimated transgender women (TGW) have a pooled HIV risk across 15 countries (none in Africa) as 49 times higher than the general population. In Kampala, TGW, face stigma, high HIV risk and poor access to health services. We explored the HIV and gender-related context of their lives.
Methods: TGW were defined as being 18+ years, living in Kampala, born male, but identifying female. Snowball sampling was used to enroll 45 participants between July and September 2013. Data collection included ACASI, qualitative face-to-face interviews, and blood tests for HIV, CD4. Topics explored in interviews were: sexual behavior, HIV risk and prevention, gender identity and expression, self and enacted stigma and violence related to gender expression, and access to health services.
Results: Median age was 23 years; HIV prevalence was 20%. Emergent themes revealed a highly varied gender identity and expression. HIV-related themes included limited access to non-stigmatizing health services, inconsistent condom use, inaccurate perceptions of self and partners' risk, alcohol use, anal sex with men, high rates of multiple partners, high rates of self and enacted stigma and violence. These themes reveal the broader structural context as well as personal and relational behavioral factors related to HIV risk behavior. Social, cultural and policy issues surrounding TGW revealed HIV prevention attitudes, risk and health-promoting behaviors that could inform interventions. Stigma and violence were reported by almost all respondents. One participant mentioned, *"They called me " Devil" and wanted to kill me, they told mum that we don't want to associate with your child . . . I was sent away from home and my mother felt very bad and didn't know what to do . . . my mother's house was burnt down; they tortured and beat me."*
Conclusions: There are no estimates of TGW population size in Uganda or the region, estimates might suggest TGW are <1% of general population. Our qualitative findings highlight the urgency to target this hidden key population with innovative, comprehensive and effective HIV prevention interventions that address high-risk behaviors such as inconsistent condom use, multiple partners, and structural issues of stigma, violence and alcohol use.

TUPEC554

Transactional sex and the challenges to safer sexual behaviors: a study among male sex workers in Chennai, India

B. Thomas[1], K. Biello[2,3], E. Closson[2], P. Navakodi[1], A. Dhanalakshmi[1], S. Menon[4], K. Mayer[2,5,6], S. Safren[2,7], M. Mimiaga[2,3,7]
[1]*National Institute for Research in Tuberculosis, Department of Social and Behavioral Research, Chennai, India,* [2]*Fenway Health, The Fenway Institute, Boston, United States,* [3]*Harvard T. H. Chan School of Public Health, Department of Epidemiology, Boston, United States,* [4]*Sahodaran, Chennai, India,* [5]*Harvard Medical School/Beth Israel Deaconess Medical Center, Div. of Infectious Diseases, Boston, United States,* [6]*Harvard T. H. Chan School of Public Health, Department of Global Health and Population, Boston, United States,* [7]*Harvard Medical School/Massachusetts General Hospital, Department of Psychiatry, Boston, United States*

Background: Male sex workers (MSWs) are a significant but invisible population in India with elevated levels of HIV/STI risk. Baseline sex work-related risk behavior data from a pilot randomized controlled trial that aimed to decrease HIV risk behaviors among MSWs in Chennai, India are examined.

Methods: Between December 2013 and May 2014, 100 MSWs completed a baseline assessment. Participants were ≥18 years, and reported current sex work. We report medians (with interquartile ranges [IQR]) for continuous variables and proportions for categorical variables. Wilcoxon-Mann-Whitney tests are used to examine differences between underlying distributions of sexual behavior measures by income source.
Results: Most (76.8%) participants identified as Kothi, and 50% completed secondary education or less. Participants were engaged in sex work for 5.0 years (IQR=21.0-31.5), and earned 3,000 (IQR=2000-8000) Rupees (< 50 USD) per month from sex work. Sixty-four percent reported ever testing for HIV and 20.2% for any STI. The most common reasons for starting and continuing sex work were money (83.0% and 93.0%, respectively) and pleasure (56.0% and 50%, respectively). Participants reported 8.0 (IQR=3.0-15.0) male clients and 2.0 (IQR=0.0-6.0) non-paying male partners in the past month. Participants reported 7.0 (IQR=4.0-15.0) condomless anal sex acts with male clients and 3.0 (IQR=1.0-6.0) with non-paying male partners in the past month. Compared to participants who indicated an additional source of income, participants whose only source of income was sex work reported significantly more male clients in the past week (7.5 vs. 4.0, p=0.001) and in the past month (10.0 vs. 6.0, respectively, p=0.017), as well as more condomless anal sex acts with male clients (8.5 vs. 5.0, respectively, p=0.007) and non-paying male partners (5.0 vs. 2.0, respectively, p=0.024) in the past month. Nearly 70% were offered more money to not use a condom during a sex work encounter, and two-thirds reported having difficulty using condoms with clients.
Conclusions: MSWs in India engage in high levels of sexual risk for HIV/STIs. Money appears to be a driving factor for engaging in sex work and higher risk sex with clients. HIV prevention interventions should focus on increasing safe sexual practices in the face of monetary disincentives to do so.

TUPEC555

Prevalent syphilis predicts HIV acquisition among men who have sex with men who received money, or gifts in exchange for sex, Bangkok, Thailand

S. Pattanasin[1], W. Wimonsate[1], P. Luechai[1], K. Pancharoen[1], W. Sukwicha[1], S. Lertpruek[1], J. Tongtoyai[1], P. Sirivongrangson[2], E.F. Dunne[1,3], T.H. Holtz[1,3]
[1]Thailand MOPH - U.S. CDC Collaboration, Department of Disease Control, Nonthaburi, Thailand, [2]Ministry of Public Health, Department of Disease Control, Nonthaburi, Thailand, [3]Division of HIV/AIDS Prevention, U.S. Centers for Disease Control and Prevention, Atlanta, United States

Background: Male sex workers (i.e. men who receive money or gifts in exchange for sex (MSW)) are at increased risk for HIV infection and syphilis. We assessed the incidence of HIV infection and syphilis, and risk factors for incident infection among men who have sex with men (MSM) who reported as MSW in the Bangkok MSM Cohort Study (BMCS).
Methods: We enrolled Thai MSM age ≥ 18 years old from the greater Bangkok metropolitan area in the BMCS during 2006-2010 and followed every 4 months for 3-5 years. HIV testing was performed at every visit on oral fluid; with serological confirmation of all reactive specimens. *Treponema pallidum* (TP) screening was performed at enrollment and annually using the rapid plasma reagin (RPR) and, if reactive, with a TP-specific antibody test; we considered incident syphilis as a reactive TP-specific antibody test or RPR titer ≥ 1:8. At every visit, participants answered HIV risk behavior questions. We calculated factors for incident HIV and syphilis using Cox regression ; models were adjusted for baseline demographic and behaviors, and prevalent syphilis or prevalent HIV infection.
Results: Of 1,744 participants enrolled, the 334 (19.1%) who reported being MSW had a median age of 24 years (Interquartile Range: 21-27 years). Among 334 men, the prevalence was 27.8% (n=93) for HIV and 7.5% (n=25) for syphilis. Among HIV uninfected men (n=241), the HIV incidence per 100 person-years (PY) was 6.9 (95% CI 5.1-9.2). Among men without syphilis (n=309), the syphilis incidence was 3.3/100 PY (95% CI 2.3-4.7). Factors independently associated with incident HIV were prevalent syphilis (Adjusted HR [AHR] 4.1, 95% CI 1.6-10.8), reporting meeting a casual sex partner via Internet (AHR 2.6, 95% CI 1.4-4.6), and reporting sex with a foreign partner (AHR 2.0, 95% CI 1.1-3.5). Factors independently associated with incident syphilis were living with a partner (AHR 8.4; 95% CI 3.0-23.6), and reporting paying for sex (AHR 0.2; 95% CI 0.05-0.9).
Conclusions: MSW-MSM in Bangkok is at high risk for HIV and syphilis and should be targeted for prevention. Prevention efforts might effectively be targeted to MSM working in sex exchange venues, and through Internet-based sites.

TUPEC556

Concealment and stigma in the context of adherence to ARV therapy amongst female sex workers in Bamenda, Cameroon, a qualitative report

R.T. Nyenti[1], F.P. Ijang[2], N. Atiabet[3], G. Njoyah[4], FSW-REACH OUT Study Group
[1]Cameroon National Association For Family Welfare (CAMNAFAW), HIV/AIDS, Bamenda, Cameroon, [2]Cameroon Medical Women Association, HIV/AIDS and Reproductive Health, Bamenda, Cameroon, [3]Day Care Treatment Center, Counselling, Bamenda, Cameroon, [4]Cameroon Medical Women Association, Receptionist/ FSW Coded Coupon Distribution Point, Bamenda, Cameroon
Presenting author email: tabokorogan898@gmail.com

Background: Good ART adherence is needed to retain drug efficacy, minimize resistance and HIV transmission. Considering the adherence procedures given by the nurse adherence is not good in HIV positive female sex workers (FSW) in Bamenda. Then the aim of our study is to describe the potential barriers to ART adherence.
Methods: Study participants included were only HIV positive FSW receiving ART at Bamenda Day Care Treatment Centre. We conducted 5 Focus Group Discussions (FGDs), 7 in-depth interviews (IDI) with FSW experiencing virological failure and 3 FGDs with health care workers. Participants were divided into three adherence groups (poor, average and good), which were mixed together during FGDs.
Results: The participants included 53 female sex workers with a mean age of 28.5. Many patients viewed their CD4 counts as the ultimate 'test' of adherence; it was notable how many patients were able to remember their first CD4 counts. Participants talked about concealment of their HIV status as a strategy to protect their clients, avoid being talked about and avoid being perceived as a burden. Behaviour designed to conceal one's HIV status from others fell in three broad categories: not disclosing status to others, avoiding being seen taking pills, and not being seen at a HIV clinics. "I just don't think I can handle somebody finding out, even the idea of someone finding out scares me". Many but not all participants had experienced stigma were recounted: de-valuing, fear of contagion, gossiping, discriminating against, insulting and revealing prejudiced views. Due to this stigma, patients often chose not to disclose to those around them, which in turn created barriers to taking pills and attending clinic visits. Patients were afraid of showing visible signs of disease, as this might result in a "forced" disclosure, which provided strong motivation for adhering.
Conclusions: Perception of stigma can have both a positive and negative effect. On the one hand, FSW adhere to avoid showing visible signs of disease. On the other hand, stigma deters patients from disclosing to others which can lead to problems taking medicine and visiting clinics. Therefore the need for behaviour change communication targeting FSW.

TUPEC557

Determinants of non-condom use among female sex workers in Iran: findings of the first national bio-behavioural study

M. Karamouzian[1], A. Mirzazadeh[1,2], H. Sharifi[1], A. Sedaghat[3], M. Shokoohi[1], A. Haghdoost[1]
[1]Regional Knowledge Hub and WHO Collaborating Center for HIV Surveillance, Institute for Future Studies in Health, Kerman University of Medical Sciences, Kerman, Iran, Islamic Republic of, [2]University of California, Global Health Sciences, San Francisco, United States, [3]National AIDS Office, Center for Disease Control, Ministry of Health and Medical Education, Tehran, Iran, Islamic Republic of
Presenting author email: karamouzian.m@gmail.com

Background: The prevalence of HIV among female sex workers (FSW) is approximately 4.5% and condom-related behaviours among them reported to be low in Iran. We assess the determinants of non-condom use with paying and non-paying partners among FSW through Iran's first and only national bio-behavioural surveillance survey conducted to date.
Methods: This survey was conducted in 2010, by recruiting 872 FSW through facility-based sampling from 21 sites in 14 cities in Iran. Data were collected through face-to-face interviews using a pilot-tested standardized risk assessment questionnaire. All analyses were weighted based on the response rate and adjusted for the clustering effect of the sampling sites. A multivariable logistic regression model was constructed to investigate the determinants of non-condom use among FSW in Iran.
Results: Mean age of participants was 32, 50% had primary school educations, 36% were married, and the majority reported sex work as their primary source of income. The frequency of non-condom in the last sexual contact with their paying and non-paying partners was 36.8% (95% CI: 33.6-40.1) and 63.0% (95% CI: 58.6-67.4), respectively. Regarding paying partners, older age (AOR=1.02, 95 % CI: 1.00-1.04), being tested for HIV (AOR=0.47, 95% CI: 0.35-0.64), alcohol consumption before sex (AOR=0.65, 95% CI: 0.46-0.90), and number of paying partners in the last day of sex work (AOR= 0.91, 95% CI: 0.79-1.04) were significant predictors of non-condom use. For non-paying partners, older age (AOR= 1.06, 95% CI: 1.03-1.06), higher level of education (AOR=0.74, 95% CI: 0.54-1.00), number of sexual contact with monetary partner in previous month (AOR= 1.10, 95% CI: 1.03-1.14), being tested for HIV (AOR=0.64, 95% CI: 0.40-0.98), alcohol consumption before sex (AOR=0.54, 95% CI: 0.31-0.92), condom rupture (AOR=0.33, 95% CI: 0.16-0.67), and having an alternative source

of income (AOR=0.52, 95% CI: 0.32-0.84) were significantly associated with non-condom use.
Conclusions: The prevalence of non-condom use among FSWs in Iran is alarmingly high. Several personal and client-related barriers still need to be addressed to observe safer sex, particularly with their non-paying partners, as a common practice among female sex workers in Iran.

TUPEC558

Testing for HIV among female sex workers in Iran; findings of the first national bio-behavioural survey in 2010

H. Sharifi[1], A. Mirzazadeh[1,2], M. Karamouzian[1], M. Shokoohi[1], A. Sedaghat[3], A. Haghdoost[1]
[1]Regional Knowledge Hub and WHO Collaborating Centre for HIV Surveillance, Institute for Futures Studies in Health, Kerman University of Medical Sciences, Kerman, Iran, Islamic Republic of, [2]University of California, San Francisco, San Francisco, United States, [3]National AIDS Office, Center for Disease Control, Ministry of Health and Medical Education, Tehran, Iran, Islamic Republic of
Presenting author email: karamouzian.m@gmail.com

Background: HIV testing is crucial to detect infected people and link them to services. HIV testing rate among female sex workers as one of the key populations at risk for HIV, serves as one of the major indicators for access to prevention and care services. While the prevalence of HIV among FSW in Iran is 4.5%, frequency of testing for HIV is poorly understood among them. Here we are presenting the rate of HIV testing and determinants of testing for HIV among FSW in Iran.
Methods: This survey was conducted in 2010, by recruiting 872 FSW through facility-based sampling from 21 sites in 14 cities in Iran. Data was collected through face-to-face interviews using a pilot-tested standardized risk assessment questionnaire. Using dried blood spot (DBS) technique, the blood samples were drawn and were tested for HIV antibodies by ELISA. All analyses were weighted based on the response rate and adjusted for the clustering effect of the sampling sites. A multivariable logistic regression model was constructed to investigate the determinants of testing for HIV.
Results: Overall, 817 consented to provide blood samples and be tested for HIV. Mean age of participants was 32, around 50% had primary school educations, and 35% were married. Overall 47.8% (95% CI: 4.5-51.1) of study participants had ever tested for HIV; 84.4% of which knew their results. Around 55.3% (95% CI: 52.1-59.0) perceived themselves at risk of HIV infection. In the multivariable model for testing for HIV, condom use in the previous sexual contact with a non-paying partner (AOR: 2.3 95% CI: 1.72-3.06), history of abortion (AOR: 0.66 95% CI: 0.49-0.88) and group sex (AOR: 0.41 95% CI: 0.26-0.64) were significant predictors of having tested for HIV.
Conclusions: The low prevalence of testing for HIV, among younger FSW in particular, calls for appropriate HIV testing and counseling programs to educate FSW on the importance of HIV testing and promote testing. As testing for HIV is a stigmatized behaviour in the context of Iran, identifying barriers to testing for HIV in Iran is also critical.

TUPEC559

Induced abortion among female sex workers in Iran: findings of the first national bio-behavioural study in 2010

H. Sharifi[1], M. Karamouzian[1], A. Mirzazadeh[1,2], A. Sedaghat[3], M. Shokoohi[1], A. Haghdoost[1]
[1]Regional Knowledge Hub and WHO Collaborating Centre for HIV Surveillance, Institute for Futures Studies in Health, Kerman University of Medical Sciences, Kerman, Iran, Islamic Republic of, [2]University of San Francisco, Global Health Sciences, San Francisco, United States, [3]National AIDS Office, Center for Disease Control, Ministry of Health and Medical Education, Tehran, Iran, Islamic Republic of
Presenting author email: ali.mirzazadeh@ucsf.edu

Background: It is estimated that around 80,000 female sex workers (FSW) live in Iran, who are an extremely hidden and hard-to-reach population due to the sensitive nature of sex work in the religious and conservative context of Iran. FSWs are at an increased risk of reproductive health hazard and vulnerability for unintended pregnancies. Here, we focused on the prevalence of induced abortion and its associated determinants.
Methods: This survey was conducted in 2010, by recruiting 872 FSW through facility-based sampling from 21 sites in 14 cities in Iran. Data were collected through face-to-face interviews using a pilot-tested standardized risk assessment questionnaire. The self-report induced abortion was measured after rapport building between the interviewer and the interviewee in a private consulting room. All analyses were weighted based on the response rate and adjusted for the clustering effect of the sampling sites. We applied the logistic regression model to investigate the determinants of induced abortion among FSW.
Results: Mean age of participants was 32, 50% had primary school educations, 36% were married, and most of them reported sex work as their primary source of income. Of the 863 participants with valid responses to the abortion variable, 35.3% (95% CI: 32.1-38.6) had ever had induced abortion. In our multivariable model for induced abortion, older age (AOR=1.01; 95% CI: 1.00-1.04), being longer in sex market, (AOR= 1.03; 95% CI=1.00-1.06), start sex at an earlier age (AOR= 0.94; 95% CI=0.90-0.98), being tested for HIV(AOR= 1.41; 95% CI= 1.06-1.90), ever group sex (AOR= 1.92; 95% CI=1.25-2.94), ever drug injection (AOR=1.50; 95% CI= 1.00-2.25), and ever condom rupture
(AOR= 1.74=1.10-2.72) were significant predictors of induced abortion.
Conclusions: One in third of FSW reported induced abortion which is concerning, a figure likely to be an underestimate. The real number is expected to be even higher, with a rough national estimate of 29.4 per 1,000 FSW per year. Scaling-up effective condom distribution programs and empowering FSW to have safer sex practices may help them to prevent from unintended pregnancies and further risk of HIV transmission.

TUPEC560

Recent incarceration correlated with reduced access to HIV prevention in a longitudinal study of sex workers who inject drugs in a Canadian urban centre

M.E. Socías[1,2], K. Shannon[1,3], M. Horton[1], P. Nguyen[1], T. Lyons[1,3], R. Martin[4], M. Mannoe[1], K. Deering[1,3]
[1]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada, [2]University of British Columbia, Interdisciplinary Studies Graduate Program, Vancouver, Canada, [3]University of British Columbia, Department of Medicine, Vancouver, Canada, [4]University of British Columbia, School of Population and Public Health, Vancouver, Canada
Presenting author email: esocias@cfenet.ubc.ca

Background: Evidence suggests that criminalized approaches to both sex work and drug use intersect with heightened exposure to violence, other criminalized activities, and exposure to correctional facilities among female sex workers who inject drugs (FSW-IDU). Given the high vulnerability to HIV among FSW-IDU, we sought to investigate the impact of recent incarceration on access to HIV prevention supplies among FSW-IDU in Vancouver, Canada.
Methods: Longitudinal data (baseline and six bi-annual follow-up questionnaires) were drawn from an ongoing prospective cohort of 723 SWs recruited through street, indoor and online outreach across Metropolitan Vancouver ("An Evaluation of Sex Workers' Health Access") between 01/2010-08/2013.To account for repeated measures, bivariate and multivariable generalized estimating equations (GEE) logistic regression were performed to model the independent effect of exposure to recent incarceration (e.g. jail/detention/prison in the last 6 months) on difficulty accessing sterile syringes and male condoms in the same period among FSW-IDU.
Results: Of 720 female sex workers included in this analysis, 338 (46.9%) currently injected drugs (FSW-IDU), contributing 1047 observations. Over the study period, one-third (32.3%) of FSW-IDU were incarcerated, with 29.3% and 20.1% reporting difficulty accessing sterile syringes and condoms, respectively. In multivariable analysis, after adjusting for key confounders, episodes of incarceration remained independently correlated with difficulty accessing sterile syringes (AOR=1.65, 95% CI 1.02-2.66). In bivariable analysis, there was little evidence that exposure to incarceration had an effect on access to condoms (OR=1.48, 95% CI 0.88-2.47).
Conclusions: This study found that FSW-IDU in Vancouver were incarcerated at alarming rates, and that recent incarceration had an independent effect on reduced access to sterile syringes. Despite efforts to reduce barriers, these findings suggest limited access to harm reduction supplies for women while in prison, as well as barriers to healthcare, HIV prevention and harm reduction resources that occur during entry or release from jail, detention or prison. Results suggest a critical need to scale up access to harm reduction supplies for highly marginalized women during these transition periods and supports national and international calls for the decriminalization of sex work and drug use.

Prevention for MSM

TUPEC561

The emergence of undetectable viral load as a HIV risk reduction strategy by Australian gay and bisexual men who have condomless sex with casual partners

M. Holt[1], T. Lea[1], L. Mao[1], I. Zablotska[2], G. Prestage[2], J. de Wit[1,3]
[1]UNSW Australia, Centre for Social Research in Health, Sydney, Australia, [2]UNSW Australia, The Kirby Institute, Sydney, Australia, [3]Utrecht University, Social and Organizational Psychology, Utrecht, Netherlands
Presenting author email: m.holt@unsw.edu.au

Background: Gay and bisexual men (GBM) use various risk reduction strategies (RRS) to reduce the risk of HIV transmission during anal intercourse. The international focus on HIV treatment as prevention suggests that some GBM may be more willing to rely on having an undetectable viral load to prevent HIV transmission during sex without condoms, although there has been little evidence of the use of this strategy between casual male partners.

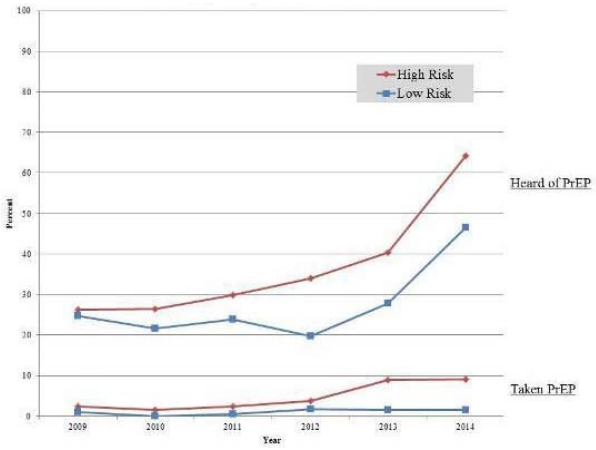
Methods: Using data from routine behavioural surveillance surveys conducted at gay venues and events in four Australian cities in 2013, we analysed the frequency of use of different RRS by GBM with casual partners, comparing different HIV status groups with chi-square tests.
Results: Data from 6,161 participants were analysed (575 HIV-positive, 4,655 HIV-negative and 931 untested/unknown status), of whom 1,346 (22%) reported any condomless anal intercourse with casual partners (CAIC). CAIC was most commonly reported by HIV-positive (46%) then HIV-negative (20%) and untested (16%) men (p≤0.001). Among men who had CAIC, 75% frequently practised at least one RRS (25% did not). Frequently practising at least one RRS was reported by 83% of HIV-positive, 78% of HIV-negative and 45% of untested men who had CAIC (p≤0.001). The most common strategy among men who had CAIC was serosorting (44%), followed by condoms (35%), withdrawal before ejaculation (21%), strategic positioning (20%), undetectable viral load (20%) and taking anti-HIV medication before/after sex (5%). Use of RRS varied by HIV status. Among men who had CAIC, undetectable viral load was frequently used by 58% of HIV-positive, 12% of HIV-negative and 8% of untested men (p≤0.001). Frequent serosorting was reported by 55% of HIV-positive and 47% of HIV-negative men who had CAIC (p=0.01). Frequent condom use was reported by 17% of HIV-positive, 41% of HIV-negative and 30% of untested men who had CAIC (p≤0.001).
Conclusions: In Australia, serosorting remains the most common RRS reported by GBM who have sex without condoms with casual partners. However, having an undetectable viral load is now the most commonly reported RRS by HIV-positive men who have CAIC, and notable minorities of HIV-negative and untested men also report checking on viral load with HIV-positive partners.

TUPEC562

Awareness & utilization of HIV prevention innovations among men who have sex with men in Seattle

J. Hood[1], S. Buskin[1], E. Barash[1], D. Katz[1,2], J. Dombrowski[1,2], M. Golden[1,2]
[1]Public Health - Seattle & King County, Prevention Division, Seattle, United States, [2]University of Washington, Department of Medicine, Seattle, United States
Presenting author email: julia.hood@kingcounty.gov

Background: Recent innovations in HIV prevention include pre-exposure prophylaxis (PrEP), HIV treatment as prevention (TasP), and home HIV testing. The extent to which members of key populations are aware of these innovations and use them is uncertain. We assessed awareness and utilization of new HIV prevention interventions among men who have sex with men (MSM) in Seattle.
Methods: We analyzed six years of cross-sectional survey data collected annually (2009-2014) at the Seattle Pride Parade. Parade spectators who identified as MSM were eligible to complete a self- or interviewer-administered survey. The survey included items that assessed participants' awareness and utilization of PrEP; knowledge of TasP; and use of home HIV tests. Respondents were considered 'high risk' if they reported an STD diagnosis, methamphetamine or popper use, 10+ sex partners, or non-concordant condomless anal sex in last year. We used descriptive statistics and multivariable logistic regression to assess awareness and utilization and their correlates.



[Figure. Percent of HIV-negative Pride Survey respondents who have heard of and taken PrEP, by survey year and HIV risk level]

Results: Across all study years (n=2095), 91% of MSM had ever tested for HIV and 63% of sexually active, HIV-negative MSM tested ≥2 times in the past 2 years. Between 2013 and 2014, use of home HIV tests among sexually active, HIV-negative men increased from 8% to 17%. Between 2009 and 2014, awareness of PrEP and TasP increased significantly: the proportion of HIV-uninfected respondents who had heard of PrEP increased from 25% to 51% (p< 0.0001); the proportion believing that HIV medications reduce the likelihood of HIV transmission increased from 17% to 40% among HIV-negative MSM and from 25 to 72% among HIV positive MSM (p< .0001 for both). Higher levels of awareness of PrEP and TasP were associated with elevated HIV risk, higher income and educational attainment, and more recent year of survey. PrEP was utilized by 44 respondents. Among high-risk MSM without a prior HIV diagnosis, utilization of PrEP increased from 2% in 2009 to 9% in 2014 (p=.003). Higher income and elevated HIV risk were significantly associated with PrEP use.
Conclusions: In this sample of MSM, awareness of PrEP and TasP has increased substantially. Use of PrEP and home testing also increased, though PrEP use remains relatively low.

TUPEC563

When and how male couples form a sexual agreement in their relationship: qualitative findings toward development of a tailored online HIV prevention 'toolkit' for at-risk HIV-negative male couples

J. Mitchell[1], J.-Y. Lee[1], J. Bauermeister[2], C. Woodyatt[3], S. Patrick[2], S. Lim[2], P. Sullivan[3], R. Stephenson[4]
[1]University of Miami Miller School of Medicine, Department of Public Health Sciences, Miami, United States, [2]University of Michigan, School of Public Health, Ann Arbor, United States, [3]Emory University, School of Public Health, Atlanta, United States, [4]University of Michigan, School of Nursing, Ann Arbor, United States
Presenting author email: jwm35@med.miami.edu

Background: Although between one- and two-thirds of MSM in the US acquire HIV from their primary relationship partners, few evidence-based HIV prevention interventions exist for male couples. Researchers have assessed how dynamics of male couples' relationships affect their risk for HIV, including sexual agreements. A sexual agreement is an explicit mutual understanding between two main partners about which sexual and other relational behaviors are allowed to occur within their relationship, and if applicable, outside the relationship. Many aspects of couples' agreements have been well studied. However, how and when male couples form a sexual agreement in their relationship remains poorly understood, yet relevant for development of a tailored online HIV prevention 'toolkit' which aims to assist at-risk HIV-negative male couples, who lack an agreement, to form and adhere to one.
Methods: The present study is part of a larger intervention project aimed to help male couples form and adhere to a sexual agreement via an online interactive prevention toolkit. Active and passive recruitment strategies were used to enroll 29 consented HIV-negative male couples from Detroit, MI and Atlanta, GA to participate in semi-structured individual- and couple-level interviews. Interviews focused on couples' sexual agreements and attitudes toward other preventive methods; all couples had an agreement. Interviews were digitally recorded, transcribed verbatim, and anonymized. Grounded theory was used to identify themes from the codes developed.
Results: Themes pertinent to when the agreement formed included early on (e.g., first date) to within the first year; themes related to how the agreement was formed ranged from 'purposeful' to 'circumstantial' instances. Differences of when and how the agreement was formed existed by couples' agreement type: couples with closed agreements were purposeful about having their conversations early compared to those with an open agreement, which tended to occur later in time and were oriented around circumstances or events.
Conclusions: Our findings highlight how and when male couples typically form a sexual agreement in their relationship, which can be used toward developing content and activities in an online HIV prevention 'toolkit' aimed at helping at-risk HIV-negative male couples form and adhere to a sexual agreement.

TUPEC564

Awareness and willingness to take pre-exposure prophylaxis (PrEP) among men who have sex with men and transgender women: preliminary findings from the PrEP Brasil study

B. Hoagland[1], V.G. Veloso[1], R.B. De Boni[1], J.V. Madruga[2], E.G. Kallas[3], N.M. Fernandes[1], R.I. Moreira[1], A.Y. Liu[4], B. Grinsztejn[1]
[1]Fiocruz, Rio de Janeiro, Brazil, [2]Centro de Referência DST/AIDS, São Paulo, Brazil, [3]University of São Paulo, São Paulo, Brazil, [4]Bridge HIV, San Francisco Department of Public Health, San Francisco, United States
Presenting author email: brenda.hoagland@ipec.fiocruz.br

Background: Brazil is experiencing a severe HIV epidemic among men who have sex with men (MSM) and transgender women (TGW), particularly the youngest. The WHO issued recommendations for PrEP use in such populations; however, it is not yet implemented in most resource limited settings. Understanding awareness and willingness to use PrEP is essential to inform public policy formulation. In this study, PrEP awareness and willingness among MSM and TGW were assessed.
Methods: Using gay-friendly HIV testing venues in Rio de Janeiro (RJ) and São Paulo (SP), including 1 mobile unit and a LGBT NGO in RJ, a convenience sample of 780 MSM/TGW was evaluated from April/2014 to January/2015. Of these, 734 individuals ≥ 18 years, male at birth, who reported having sex with men within 12 months completed a self-administered ques-

tionnaire. Two logistic models were fitted to predict factors associated with PrEP awareness (positive answer to "Have you heard about PrEP for HIV prevention before?") and willingness ("Totally agree" on a five-point *likert* scale measuring "I would be willing to use PrEP to prevent HIV infection").

Results: Median age was 29 years (IQR 24-36), 56.9% non-white, 89.1% had ≥12 years of education; 80.9%, 11% and 5.6% identified themselves as homosexual, bisexual or TGW. HIV prevalence was 9.2%. Overall, 60% were aware of PrEP. Older age, having a steady partner and prior history of HIV testing increased the odds of PrEP awareness while recruitment in RJ and having an HIV positive result decreased it (Table). Nearly 95% (n=695) demonstrated willingness to use PrEP to prevent HIV. Factors associated with PrEP willingness were: recruitment in RJ *vs.* SP (aOR 0.25; 95% CI 0.07-0.85), reporting condomless anal intercourse with≥ 2 men vs. < 2 (aOR 2.12, 95% CI 1.03-4.39) and prior PrEP awareness (aOR 2.07, 95% CI 1.03-4.16).

		Have you heard about PrEP for HIV prevention before?		Unadjusted Model				Adjusted Final Model		
		No N=294 (%)	Yes N=440(%)	OR	95% C.I. Lower	Upper	p-value	OR	95% C.I. Lower	Upper
Age - Mean (S.D.)*		28 (24-34)	30 (25-37)	1.04	1.02	1.06	<0.001	1.04	1.02	1.06
Color/Race	White	105 (33.2)	211 (66.8)	Ref				-		
	Non-white	189 (45.2)	229 (54.8)	0.60	0.45	0.82	0.001	-		
Schooling**	<12 years	47 (58.8)	33 (41.3)	Ref				-		
	12 /more years	247 (37.8)	407 (62.2)	2.35	1.46	3.76	<0.001	-		
Sexual identity	Homosexual	224 (37.7)	370 (62.3)	Ref				Ref		
	Bisexual	39 (48.1)	42 (51.9)	0.65	0.41	1.04	0.07	0.79	0.48	1.30
	Trans	19 (46.3)	22 (53.7)	0.70	0.37	1.32	0.27	0.79	0.40	1.57
	Other	12 (66.7)	6 (33.3)	0.30	0.11	0.82	0.02	0.25	0.09	0.70
Steady Partner	No	167 (44.5)	208 (55.5)	Ref				Ref		
	Yes	127 (35.4)	232 (64.6)	1.47	1.09	1.97	0.01	1.40	1.01	1.93
City	Rio de Janeiro	231 (47.3)	257 (52.7)	0.38	0.27	0.54	<0.001	0.51	0.35	0.74
	São Paulo	63 (25.6)	183 (74.4)	Ref				Ref		
Perceived likelihood of getting HIV on the next year	0-25%	181 (42.1)	249 (57.9)	Ref				-		
	50-100%	113 (37.2)	191 (62.8)	1.23	0.91	1.66	0.18	-		
Previous HIV test (last 12 months)	No	133 (58.8)	93 (41.2)	Ref				Ref		
	Yes	161 (31.7)	347 (68.3)	3.08	2.23	4.26	<0.001	2.30	1.62	3.27
HIV testing result	Negative	236 (38.6)	375 (61.4)	Ref				Ref		
	Positive	40 (59.7)	27 (40.3)	0.42	0.25	0.71	0.001	0.53	0.31	0.91
	Indeterminate/ Undone	18 (32.7)	37 (67.3)	1.29	0.72	2.32	0.39	0.89	0.48	1.68
# Male condomless anal sex partners (last 12 months)	<2	157 (40.4)	232 (59.6)	Ref				-		
	2 or more	137 (39.7)	208 (60.3)	1.03	0.76	1.38	0.86	-		
Anal sex with HIV-positive partners(12 months)	Yes	87 (34.1)	168 (65.9)	1.40	0.99	1.97	0.05	-		
	No	73 (45.6)	87 (54.4)	0.86	0.59	1.27	0.45	-		
	I dont know	134 (42.0)	185 (58.0)	Ref				-		
STD diagnosis (last 12 months)	No	261 (41.5)	368 (58.5)	Ref				-		
	Yes	33 (31.4)	72 (68.6)	1.55	1.00	2.41	0.05	-		

Variables with p<0.1 in the univariate analysis were included in the initial logistic model. Variables with p<0.05 remained in the final logistic model. *S.D.= standard deviation. OR refers to per year increase in age. **12 years=High School. STD=Sexual Transmitted Disease

[Table. Sample characteristics and factors associated to PrEP awareness after logistic regression]

Conclusions: The high willingness to use PrEP among MSM and TGW and its association with riskier behavior is reassuring. Its association with previous PrEP knowledge indicates that dissemination of PrEP information among these key populations must be implemented. Young MSM and TGW must be prioritized as they bear the lowest PrEP awareness and the highest HIV incidence.

TUPEC565

Community mobilization intervention with men who have sex with men (MSM) increases uptake of regular HIV-testing in South Africa: 12-month impact evaluation results from project Boithato

T. Lane[1], T. Osmand[1], A. Marr[1], S. Shade[1], N. Mlotshwa[2], A. Bilankulu[2], R. Gaobepe[2], T. Sandfort[3], H. Struthers[2], S. Kegeles[1], J. McIntyre[2]
[1]University of California, Center for AIDS Prevention Studies, San Francisco, United States, [2]Anova Health Institute, Johannesburg, South Africa, [3]Columbia University, HIV Center for Clinical and Behavioral Studies, New York, United States
Presenting author email: tim.lane@ucsf.edu

Background: Few South African MSM test regularly for HIV. Project Boithato was adapted from Mpowerment, a community mobilization intervention for MSM in the USA proven to increase HIV prevention behaviors through peer support. This evaluation of Boithato assessed effects on regular HIV testing uptake among MSM in two communities: Gert Sibande, the Boithato intervention community, and Ehlanzeni, the comparison community. Baseline HIV prevalence estimates were 28.3% and 13.7% respectively, with 22.1% and 39.6% of infections in each sample occurring within the prior year. Trained MSM-competent HIV services in non-stigmatizing clinical settings are available in both communities.

Methods: We conducted serial cross-sectional surveys using RDS recruitment in both MSM communities at baseline, and repeated 12 months following Boithato implementation. Participants took 90-minute sexual and health behavior surveys, and were offered HIV testing and counseling. Regular testing was defined as having more than one lifetime HIV test, and testing independently between study visits; testing only at study visit was not categorized as regular testing. Linked to care was defined as seeking HIV care within 30 days of diagnosis. We present results of generalized estimating equations showing sample proportions and odds ratios (OR) with 95% Confidence Intervals (CI).

Results: We recruited N=307 in Gert Sibande and N=298 in Ehlanzeni at baseline, and N=277 and N=393 respectively at follow-up; 14.3% and 24.8% respectively participated in both assessments.

Over 12 months, there was a nearly four-fold increase in regular testing in Gert Sibande (20.2% to 49.8%; OR 3.7, 95%CI 2.6-5.5, p< .001), and a decrease in Ehlanzeni (26.5% to 22.1%;

OR 0.6, 95%CI 0.4-0.9, p< .05). Increase over baseline in the intervention community was six times greater than the comparison (OR 6.0, 95% CI 3.5-10.3, p< .001). In addition, more HIV-positives in Gert Sibande were linked to care at 12-month follow up than in Ehlanzeni (28.3% versus 12.9%).

Conclusions: Implementation of Boithato was associated with increased regular testing among MSM in non-stigmatizing, trained MSM-competent clinical settings in a high-incidence community. Mobilizing MSM peer support for HIV testing will increase timely diagnosis and linkage to care. Additional research on optimally mobilizing HIV-positive MSM for treatment is urgently needed.

TUPEC566

An event-level analysis of substance use, relational, and psychosocial factors affecting condom use during anal intercourse among self-identified HIV-negative and unknown status gay and other MSM in Vancouver, British Columbia

N. Lachowsky[1,2], J. Jollimore[3], A. Rich[1], Z. Cui[1], P. Sereda[1], A. Lal[1], R. Hogg[1,4], D. Moore[1,2,5], E. Roth[6,7]
[1]British Columbia Centre for Excellence in HIV/AIDS Research, Vancouver, Canada, [2]Faculty of Medicine, University of British Columbia, Vancovuer, Canada, [3]Health Initiative for Men, Vancouver, Canada, [4]Faculty of Health Sciences, Simon Fraser University, Burnaby, Canada, [5]British Columbia Centre for Disease Control, Vancouver, Canada, [6]Faculty of Social Sciences, University of Victoria, Department of Anthropology, Victoria, Canada, [7]Centre for Addictions Research BC, Victoria, Canada
Presenting author email: nlachowsky@cfenet.ubc.ca

Background: We sought to identify psychosocial and event-level factors associated with condom-use during anal intercourse among self-identified HIV-negative and HIV status unknown MSM in the Greater Vancouver Area.

Methods: We analyzed data from Momentum Health Study participants collected at enrollment on their most recent sexual encounter with each of up to five sexual partners in the past six months. Explanatory factors included event-level factors (substance use, partner's serostatus, sexual history with partner, and sexual position), psychosocial scales (i.e., Van Den Ven et al., 2000 *HAART Optimism*; Nimmons & Folkman, 1999 *Sexual Altruism*; Kalichman & Rompa, 1995 *Sexual Sensation Seeking*; and McKirnan et al., 2001 *Cognitive Escape*), and demographics. Of all sexual encounters where anal intercourse was reported, factors associated with condom-use versus not were determined using manual backward stepwise multivariable generalised linear mixed models.

Results: The majority of participants reported at least one anal intercourse event in the past six months (85.0%, n=436/513). Two-thirds of all sexual encounters involved anal intercourse (64.1%, n=1196/1866) during which condoms were used for 56% of events. Condom-use was positively associated with higher sexual altruism community sub-scale scores (AOR=1.98, 95%CI:1.46-2.68) and negatively associated with greater HAART optimism (AOR=0.95, 95%CI:0.91-0.99), sexual sensation seeking (AOR=0.94, 95%CI:0.89-0.98), and cognitive escape (AOR=0.97, 95%CI:0.94-0.99). At the event-level with that partner, longer time since first sex and higher frequency of recent anal sex were both negatively associated with condom-use (AOR=0.99, 95%CI:0.99-0.99 and AOR=0.96, 95%CI:0.95-0.98, respectively). Compared with men who didn't know their partner's serostatus, participants who were certain their partner was HIV-negative or HIV-positive were less likely to report condom-use (AOR=0.24, 95%CI:0.08-0.72 and AOR=0.11, 95%CI:0.03-0.39, respectively). Event-level participant alcohol use was positively associated with condom-use (AOR=1.43, 95%CI:1.02-2.00) while partner crystal methamphetamine use was negatively associated (AOR=0.19, 95%CI:0.07-0.55). Event-level receptive-only versus both insertive and receptive sexual position was positively associated with condom use (AOR=1.81, 95%CI:1.20-2.74). Lower odds of condom-use were associated with annual income >$30,000 (AOR=0.66, 95%CI:0.45-0.95) and being in relationship >1 year versus single (AOR=0.57, 95%CI:0.34-0.96).

Conclusions: Health promotion for gay and other MSM must consider how substance use, HAART optimism, partner familiarity, discussions of HIV serostatus, and psychosocial traits collectively affect condom-use decision-making.

Prevention for transgender persons

TUPEC567

Prevalence and correlates of injection of industrial silicone among transgender women in Argentina

M.E. Socías[1,2,3], T. Kerr[2,4], B.D.L. Marshall[5], I. Arístegui[1,6], C. Frola[1], P. Cahn[1], O. Sued[1]
[1]Fundación Huésped, Buenos Aires, Argentina, [2]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada, [3]University of British Columbia, Interdisciplinary Studies Graduate Program, Vancouver, Canada, [4]University of British Columbia, Department of Medicine, Vancouver, Canada, [5]Brown University School of Public Health, Department of Epidemiology, Providence, United States, [6]University of Palermo, Center for Psychology Research, School of Social Sciences, Buenos Aires, Argentina
Presenting author email: eugenia.socias@huesped.org.ar

Background: Transgender women continue to contend with high rates of HIV infection in many settings. To enhance their feminine appearance many transgender women undergo medically unsupervised body modification procedures, such as self or peer-administered injection of industrial silicone. The use of non-sterile equipment and assisted injecting has been associated with increased risk for HIV acquisition and skin and soft tissue infections, among other complications.
Methods: Data was drawn from a cross-sectional nation-wide study involving transgender women in Argentina conducted in 2013. We assessed the prevalence and correlates of industrial silicone injection among this population using multivariable logistic regression.
Results: In total, 450 transgender women were included. The median age was 30 (IQR 25-37) and 376 (83.6%) had a history of sex work. HIV or HCV infection was self-reported by 104 (23.1%) and 18 (4%) participants, respectively. Overall, 277 (61.6%) reported having ever injected industrial silicone (91.7% of them were injected by a transgender peer). In multivariable analysis, factors positively associated with injection of industrial silicone were: engagement in sex work (AOR =3.20, 95%CI 1.67-6.12), older age (AOR=1.05, 95%CI 1.02-1.08), having ever been arrested (AOR=2.00, 95%CI 1.06-3.80), having avoided healthcare due to transgender identity (AOR=1.61, 95%CI 1.01-2.56), and foreign-born status (AOR=3.22, 95%CI 1.38-7.52). No association was found with self-reported HIV or HCV infection.
Conclusions: Our findings revealed that injection of industrial silicone is a common practice among transgender women in Argentina, especially among those engaged in high risk activities and those experiencing barriers to healthcare. Although no association was found with HIV or HCV infection, this analysis was limited by self-report. Given the high prevalence of medically unsupervised and peer-assisted injecting in this sample, longitudinal studies are needed to investigate whether injection of industrial silicone is an important risk factor for HIV or HCV transmission among this population. Regardless, given the well-known morbidity associated with this practice, interventions to ensure appropriate access to transgender care are urgently needed.

TUPEC568

Transgenders in Ukraine: understudied and underserved

R. Kulchynska[1], T. Saliuk[2], O. Trofimenko[3], A. Meteliuk[1], M. Gates[1]
[1]State University of New York at Albany, Albany, United States, [2]International HIV/AIDS Alliance in Ukraine, Kyiv, Ukraine, [3]Center of Social Expertizes of the Institute of Sociology in Ukraine, Kyiv, Ukraine
Presenting author email: kulchynska@gmail.com

Background: The purpose of the research was to do the first-ever description of socio-demographic and behavioral characteristics of male-to-female transgenders (MFT) in Ukraine in the context of the ongoing HIV epidemic.
Methods: We conducted secondary analysis of cross-sectional data collected by HIV/AIDS Alliance in Ukraine in 28 Ukrainian cities during the 2013 behavioral surveillance survey among men who have sex with men (MSM). Data were collected using respondent-driven sampling; all participants were offered HIV rapid testing during the survey. Unweighted descriptive statistics were used to describe the sub-population of interest.
Results: Among 8,100 MSM, 247 individuals (0.03%) identified themselves as transgenders. Mean age of the respondents was 27.8 years (range 16 - 51). The majority of MFT (61%) lived in small cities with populations less than 200,000, and one third lived in the Western part of Ukraine. Forty-five percent had university level education or higher. Approximately 65% defined themselves as homosexuals, and 29% as bisexual. Over 98% had anal intercourse with a male partner within the last 6 months. Mean age at the first homosexual experience was 17 years, and 23% reported having their first homosexual intercourse before 14 years of age.
Only 35% of MFT reported receiving HIV prevention services. Of those with a permanent sexual partner (n=130), 35% reported not using condoms in the relationship. Among MFT who had sex with casual partner in the last 30 days (n=140), 15% reported no condom use during sexual intercourse. Almost one quarter reported having group sex in the last 6 months. Seventy-eight percent had recent sex under alcohol intoxication, while only 6% reported consistent condom use. During the last year, 63% were tested for HIV; 1.6% said they were HIV-positive, while 3.2% turned to be HIV-positive as the result of the testing conducted during the survey. Approximately 37% of transgenders had insufficient knowledge about HIV.
Conclusions: Only a small percentage of male-to-female transgenders currently receive HIV prevention services, whereas a high proportion demonstrates risky sexual behavior and lack of knowledge about HIV. Effective HIV prevention interventions should be provided for this marginalized population in Ukraine.

Prevention for immigrants, mobile and displaced populations

TUPEC569

Assessment of HIV associated risk behaviour among internally displaced persons (IDPs) in Northern Nigeria

C. Ifekandu[1,2], U. Bukar[1,2], E. Jegede[1]
[1]Ahmadu Bello University, Development Communications, Zaria, Nigeria, [2]Population Council, Nigeria Office, HIV Department, Lagos, Nigeria
Presenting author email: edukandu@yahoo.com

Background: Nigeria has the second highest burden of people living with HIV globally. Since 2010, the Boko Haram insurgency has forced over 10 million persons mostly women and children to flee from their places of habitual residence in order to avoid the effects of armed conflicts. This has rendered millions of women and children disproportionately vulnerable to HIV. Internally displaced Persons (IDPs) are not included in Nigeria's national HIV strategic plan. Moreover there is neither size estimate nor HIV data for IDPs in Nigeria.
Objective: Our study provides further insight into HIV vulnerability of internally displaced persons IDPs) in Northern Nigeria.
Methods: Through the cluster approach, quantitative research was conducted in December 2014 in the evacuation camps of the IDPs in Abuja and Nassarawa states of Nigeria. The study involved structured questionnaire administered to 200 IDPs. The respondents were recruited through the IDPs-Key Opinion Leaders identified by the Community Based Organizations providing succor in the two study location, while skilled interviewers administered the structured questionnaire. Respondents were assured of their confidentiality by using Unique Identifier codes and pseudonyms. Ethical IRB approval was also obtained for the study.
Results: The mean age of the 200 respondents was 22years +/- SD. 72% were women within the ages of 18-24years. 35% were married, while 50% have lost a key figure of their livelihood or separated from their families and cannot tell if they are still alive. 15% reported encountering sexual violence by armed groups and had no access to prophylaxis pre-exposure (PreP) or Health care Providers. Most of them lack employment opportunities, while 13% have resorted to survival sex work in exchange for jobs, money, shelter and other basic amenities and in most cases, condom was not used (a significant size of 19% are unsure of their HIV serostatus).
Conclusions: From this study, transactional sex, inconsistent condom use, sexual violence and lack of access to health facilities are factors that may increase the vulnerability of IDPs, Furthermore, a broader framework on comprehensive HIV comprehensive HIV and other sexual and reproductive health programming needs to be developed for the IDPs.

Prevention for HIV serodiscordant couples

TUPEC570

Implementation of HIV discordant couple care and treatment program in a Kenyan referral hospital

N. Gitahi-Kamau[1], J. Kiarie[2], S. Eshiwani[1], K. Mutai[3], L. Njagi[1], S. Ilovi[1], J. Mecha[1]
[1]University of Nairobi, Department of Internal Medicine and Therapeutics, Nairobi, Kenya, [2]University of Nairobi, Reproductive Health, Nairobi, Kenya, [3]Kenyatta National Hospital, Respiratory and Infectious Disease Unit, Nairobi, Kenya
Presenting author email: gnyawira@gmail.com

Background: Little has been reported about the care of discordant couples in programmatic settings. We report on the care of discordant couples in a HIV care and treatment in a discordant couple's care and treatment centre in Nairobi, Kenya.
Methods: We analysed data from a routine clinical care database of HIV discordant couples enrolled between April 2012 and September 2014 at Kenyatta National Hospital, Nairobi, Kenya. The clinic provides CD4 testing, initiation of antiretroviral therapy (ART) irrespective of CD4 cell count, contraception and other reproductive health services, fertility desire assess-

ment, pre-conception care and conception planning and assisted conception when indicated. Chi square test was used to test for associations and paired comparisons carried out using Mc'Nemar's and Wilcoxon matched pair signed rank tests.

Results: We enrolled 322 discordant couples. Majority (58%) of positive partners were female. Overall, 4.7% of clients expressed desire to conceive in the next 6 months and desire was higher in HIV negative compared to HIV positive male clients (9.7% vs 0.6% p< 0.001) and women (6.0% vs 2.4% p< 0.001). After 8,024 person-months of follow up 80% of enrolled clients were still in care with positive partners reporting higher retention compared to HIV negative partners (91% vs 70%, (p< 0.001). Baseline median CD4 of HIV positive partners was 430 cells/ml (IQR 260, 630) and was higher for women than men (491 vs 384 p=0.002). ART was started for 91.6% positive partners with 41.1% initiating ART at CD4 counts >500cells/ml. Median CD4 count increased significantly (p< 0.001) to 494 cells/ml. Incidence of sero-conversion in ART experienced individuals was 1.7 per 1,000 person-years

Conclusions: Focussed discordant couple care has shown successful aversion of transmission. Sero-negative partners in discordant unions are reported to have higher fertility desires and poorer retention. Challenges in follow up of negative partners should be addressed to prevent reversal of gains made in discordant couple HIV prevention.

TUPEC571

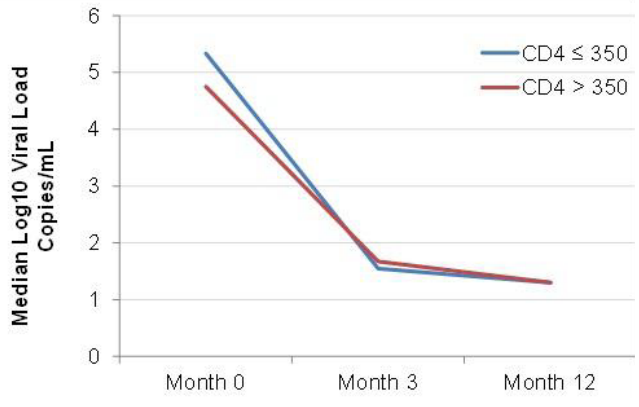
Couples testing and immediate antiretroviral therapy among serodiscordant couples in Vietnam: implementation study in resource-limited settings affected by drug use

D.D. Bui[1], T.N. Do[1], T.L.A. Tong[1], K.T. Duong[2], T.L. Pham[2], K.A. Lai[3], X.C. Hoang[4], H.A. Nguyen[5], T.V. Vu[6], T.X.L. Truong[7], T.T.V. Nguyen[8], V. Dao[9], M.H. Do[2], A. Suthar[8], P. Nadol[9], S. Lyss[9], T.L. Nguyen[10], M. Kato[8]
[1]Viet Nam Authority for HIV/AIDS Control, Hanoi, Vietnam, [2]Hanoi School of Public Health, Hanoi, Vietnam, [3]Can Tho Province AIDS Centre, Can Tho, Vietnam, [4]Dien Bien Province AIDS Centre, Dien Bien, Vietnam, [5]National DINADR Centre, Hanoi, Vietnam, [6]Bach Mai Hospital, Hanoi, Vietnam, [7]Hochiminh Pasteur Institue, Ho Chi Minh, Vietnam, [8]World Health Organization, Hanoi, Vietnam, [9]Centers for Disease Control and Prevention - CDC Vietnam, Hanoi, Vietnam, [10]Ministry of Health, Hanoi, Vietnam
Presenting author email: bdduong06@gmail.com

Background: Injection drug use and heterosexual transmission from people who inject drugs (PWID) are the dominant modes of HIV transmission in Vietnam. HPTN 052 indicates that antiretroviral therapy (ART) reduces HIV transmission from HIV-positive to uninfected partners in serodiscordant couples (SDC); however, it excluded PWID. We assessed feasibility of providing couples HIV testing and counselling (CHTC) and immediate ART among SDC in drug use-affected provinces in Vietnam.

Methods: From March to December 2013, CHTC and immediate ART for SDC were offered in Dien Bien and Can Tho provinces; following consent, HIV-positive partners initiated ART immediately (irrespective of CD4 count). In addition to routine monitoring, viral load (VL) was assessed in HIV-positive partners at baseline and months 3 and 12. Couples received behavioural counselling and completed surveys, and uninfected partners received HTC, at baseline and months 3, 6 and 12.

Results: There were 532 newly diagnosed people with HIV (PLHIV); 259 couples completed CHTC. Among 149 (57.5%) serodiscordant couples, 136 (91.2%) HIV-positive partners initiated ART immediately. Of these, 56.6% reported current or past illicit drug use, 85% were male, median age was 32 years, 51.9% had baseline CD4 count >350 cells/mm^3, and median baseline VL was 5.0 log10 copies/ml. 91.2% of HIV-positive partners were retained at month 12. Viral suppression (VL< 1000 copies/ml) was achieved by 85 (71.4%) of 119 infected partners with 3-month VL results and 95 (94.1%) of 101 with 12-month results to date. Twelve-month viral suppression among those with CD4 counts below and above 350 cells/mm3 was 88.8% and 95.1%, respectively. Consistent condom use in sexually active couples was 72.7% (80/110) at baseline and 99% (96/97) at month 12. Two uninfected partners seroconverted between enrolment and month 3



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Conclusions: The results suggest low uptake of CHTC and high uptake and adherence to ART in SDC, irrespective of CD4 count, in drug-use affected settings. No behavioural disinhibition was seen. Novel approaches to improve partner testing among newly diagnosed PLHIV are needed. Immediate ART among SDC likely presents a feasible and effective intervention to reduce HIV burden in Vietnam. Informed by this study, Vietnam is moving toward adopting immediate ART in SDC as national policy.

TUPEC572

Healthcare providers' understanding of HIV sero-discordance in South Africa and Uganda: implications for HIV prevention counselling

R.M. Greener[1], C. Milford[1], F.N. Mosery[1], F. Bajunirwe[2], L. Pillay[1], L. Moore[1], C. Ng[3], J. Kastner[4], R. Rifkin[3], J.A. Smit[1], D.R. Bangsberg[2,3], A. Kaida[4], L.T. Matthews[3]
[1]MatCH Research (Maternal, Adolescent and Child Health Research), Department of Obstetrics and Gynaecology, Faculty of Health Sciences, University of the Witwatersrand, Durban, South Africa, [2]Mbarara University of Science and Technology, Faculty of Development Studies, Mbarara, Uganda, [3]Center for Global Health and Division of Infectious Disease, Massachusetts General Hospital, Boston, United States, [4]Simon Fraser University, Faculty of Health Sciences, Burnaby, Canada
Presenting author email: rgreener@matchresearch.co.za

Background: HIV transmission within stable heterosexual couples accounts for nearly half of new HIV infections in sub-Saharan Africa, consequently the uninfected partner within HIV-serodiscordant partnerships is a priority population for prevention counselling. It is important then, to assess whether and how healthcare providers understand HIV serodiscordance and how this understanding may impact HIV prevention counselling.

Methods: In-depth interviews and focus group discussions were conducted with 42 healthcare providers from 6 public sector clinics in eThekwini District, South Africa (2012) and with 38 healthcare providers from 5 public sector clinics in Mbarara District, Uganda (2013). Interview guides were designed to assess whether and how providers counsel people living with HIV about reproductive goals and safer conception strategies. Provider understanding of HIV-serodiscordance was an emergent theme. Thematic analysis was used to explore provider understanding of serodiscordance and how this impacts safer conception counselling practices.

Results: In eThekwini, 93% of participants were women with a median age of 41 (range, 28-60) years. In Mbarara, 78% were female with a median age of 34 (range 24-57). Most providers in eThekwini assumed that HIV infected clients were in a seroconcordant relationship; in contrast, providers in Mbarara reported familiarity with caring for HIV serodiscordant couples. Providers displayed a range of understanding of how serodiscordance may occur, citing innate immunity, viral load suppression in the infected partner, chance and a very-extended window period. Incorrectly, occurrences of serodiscordance were also attributed to God or "good blood". Many providers stated that they did not know how one partner may be HIV-infected and the other is not. Providers who understood the mechanisms of serodiscordance provided more accurate peri-conception counselling to HIV-infected patients, while providers who articulated a misunderstanding of serodiscordance did not provide accurate counselling.

Conclusions: The ability to provide effective and relevant counselling to HIV serodiscordant couples is vital for HIV prevention efforts. Many providers express doubt and confusion regarding the epidemiology and mechanisms of serosdiscordance within stable sexual partnerships. Healthcare providers require ongoing training and support on serodiscordance in order to provide accurate and effective peri-conception counseling to infected men and women with uninfected partners.

TUPEC573

Community cultural beliefs and disclosure to primary sexual partners among women living with HIV in Brazil, Thailand and Zambia: results from HPTN063

B. Ojikutu[1,2], S. Pathak[3], S. Li[3], K. Mayer[2,4], S. Safren[2,5], HIV Prevention Trials Network 063
[1]Brigham and Women's Hospital, Division of Global Health Equity, Boston, United States, [2]Harvard Medical School, Boston, United States, [3]University of Washington, Statistical Center for HIV/AIDS Research and Prevention, Seattle, United States, [4]The Fenway Institute, Boston, United States, [5]Massachusetts General Hospital, Boston, United States
Presenting author email: bojikutu3@gmail.com

Background: Serostatus disclosure may be effective in decreasing HIV transmission between serodiscordant partners by raising risk awareness and heightening the need for prevention. For women living with HIV (WLWH), disclosure may be influenced by community cultural beliefs which shape relationship dynamics. Understanding the impact of cultural beliefs on disclosure among WLWH in different countries may inform intervention development.

Methods: HPTN063 was a longitudinal, observational cohort study of sexually active HIV-infected individuals, including heterosexual women, in care in Zambia, Thailand and Brazil. At baseline, a questionnaire measuring demographic, partner characteristics, intimate partner violence (IPV), fear of negative consequences following disclosure (loss of finances and IPV),

and perceived community cultural beliefs was administered. Disclosure was assessed by the statement, "I usually tell my sex partners about my HIV positive status". Multivariate logistic regression was conducted to determine predictors of disclosure.

Results: Among 299 women, 88% were on antiretroviral therapy and 88% reported adherence. Most (92%) were sexually active, 54% were married, and 72% were cohabiting with primary partners. Most partners (92%) were described as HIV negative or status unknown. History of IPV was reported by 42%, 66% screened positive for depression and 12% reported alcohol abuse. Almost half (45%) WLWH perceived that their communities believe HIV infection among women is associated with sexual immorality (prostitution and numerous partners), and 66% Zambian, 38% Thai and 24% Brazilian WLWH (p< 0.0001) perceived that their communities believe that women must be submissive to husbands, procreate and not use condoms. Fear of negative consequences post disclosure was expressed by 62% Brazilian, 38% Thai and 23% Zambian WLWH (p< 0.0001). Disclosure to partners was reported by 67% of WLWH. In univariate analysis, single women [OR 0.26, 95%CI (0.12-0.56)] and those who endorsed fear [OR 0.26, 95%CI (0.15-0.43)] were less likely to disclose. Women who were cohabiting[OR 3.97, 95%CI(2.27-6.93)] were more likely to disclose. Fear [OR 0.32 95%CI (0.18-0.57)] and cohabitation
[OR 2.86 95%CI (1.34-6.09] remained significant in MVA.

Conclusions: Perceived cultural beliefs promoting discrimination regarding sexual behavior, HIV stigma, and gender inequality persist in several countries. These beliefs may promote fear of negative consequences of disclosure which may affect prevention efforts.

Prevention for other vulnerable populations

TUPEC574

Perceptions of HIV burden and risk among Lake Victoria fishing communities: a qualitative study

V.C. Lee[1], T. Saliku[2], Z. Gura[3], E. Zielinski-Gutierrez[4]
[1]US Centers for Disease Control and Prevention, Kenya / CTS Global, Division of Global HIV and AIDS, Nairobi, Kenya, [2]University of California, San Francisco/Kenya Medical Research Institute, Nairobi, Kenya, [3]Field Epidemiology Laboratory Training Programme, Ministry of Health, Nairobi, Kenya, [4]US Centers for Disease Control and Prevention, Division of Global HIV and AIDS, Kisumu, Kenya
Presenting author email: vsr0@cdc.gov

Background: In Kenya, fishermen and others engaged in the fishing sector in Lake Victoria are a key population for HIV interventions given their high HIV risk. Previous studies conducted in 2005 to 2010 among the "fisherfolk" population in Kenya have estimated a HIV prevalence of 26% to 30%, which is much greater than the 6% prevalence of the general population (2012). We conducted a qualitative study among the Lake Victoria fishing communities to understand their perceptions about the HIV burden, their risk behaviors, and their utilization of health services.

Methods: This study was implemented in nine beaches located on the Kenyan border of Lake Victoria; study sites and participants were purposively selected through input from subject matter experts and community leaders. We conducted 25 focus group discussions and 29 key informant interviews among men and women engaged in the fishing sector. Interviews were conducted in Dholuo, the vernacular, or English and audio-recorded. After transcription and translation, interviews were coded using Nvivo and analyzed for emerging themes, using Protection Motivation Theory.

Results: Participants were aware of the high HIV burden in their communities and its impact on their livelihoods. There was a high level of knowledge about HIV prevention, specifically the importance of using condoms and getting tested for HIV. Nevertheless, high-risk sexual behaviors, like concurrent multiple partners, low or no condom use, transactional sex, and alcohol and drug use with sex, were commonly practiced at multiple beaches along the lake. There was widespread knowledge about the benefits of antiretroviral therapy (ART) for treating HIV; however, difficulty in routinely visiting health facilities due to their migratory lifestyles and the stigma of taking medication were barriers to accessing health services and ART adherence.

Conclusions: Despite high levels of awareness about prevention measures, lifestyle characteristics and HIV-related stigma were challenges to practicing protective behaviors and accessing HIV health services among the "fisherfolk." Further understanding is required to better tailor HIV prevention interventions to address their high-risk behaviors, while prevention and treatment interventions must account for their migratory lifestyles. Developing community-level initiatives to reduce stigma is also critical for improving uptake of HIV prevention and treatment services.

Prevention during acute and recent infection

TUPEC575

Influence of suspected source of infection on disclosure among people with acute HIV in Malawi

S. Hino[1], C. Grodensky[1], G. Hamela[2], C. Massa[2], C. Golin[1], S. Rutstein[1], K. Smith[1], L. Christmas[1], W. Miller[1], G. Kamanga[2], S. Phiri[3], A. Pettifor[1]
[1]University of North Carolina at Chapel Hill, Chapel Hill, United States, [2]UNC - Project Malawi, Lilongwe, Malawi, [3]Lighthouse Trust, Lilongwe, Malawi
Presenting author email: apettif@email.unc.edu

Background: Disclosure of HIV serostatus to sexual partners is a valuable opportunity to reduce HIV transmission, particularly among individuals diagnosed with acute HIV (AHI), who may be better able to identify and notify the partner who may have infected them. Little research has been conducted, however, on how identifying one's source of AHI can affect disclosure in Sub-Saharan Africa.

Methods: We conducted 40 in-depth interviews with 24 men and 16 women one month after their diagnosis of AHI in Lilongwe, Malawi. Participants were asked about their sexual behavior, disclosure to sexual partners, and reaction to AHI diagnosis. All interviews were conducted in the local language, simultaneously translated and transcribed, coded by a four-member team, and analyzed using a thematic analysis approach.

Results: Over half (23/40) of participants claimed to know who infected them, nine suspected but were not certain, and eight reported not knowing. Participants suspected individuals to be sources of their infection for a variety of reasons, including a sexual partner's physical appearance and timing between sexual encounter and emergence of symptoms. Participants frequently assumed that the suspected source of their infection was aware of his or her own HIV-positive status, and thus knowingly exposed the participant to risk. This led to some participants being unwilling to disclose to the suspected source due to feelings of betrayal. Overall, 16 of the 23 participants who reported knowing the source of their infection disclosed to at least one partner, but only nine disclosed to all partners (both main and casual). Of those who had multiple partners, most disclosed to main partners but not casual ones. Reasons for not disclosing to casual partners included fear of casual partners spreading the news of their status and feeling casual partners were not worthy of being told. Disclosing frequently resulted in improved condom use and abstaining, but participants also reported relationships being terminated and strained.

Conclusions: Identifying a suspected source of infection can lead to feelings of betrayal and assumptions that partners already know they are infected, which can complicate disclosure. Further counseling on the importance of and strategies for disclosing to casual partners is needed.

Prevention among HIV-infected individuals

TUPEC576

Prevention strategies during anal intercourse and prevention-related attitudes of HIV-positive gay, bisexual and other MSM in Vancouver, British Columbia

N. Lachowsky[1,2], T. Howard[3], Z. Cui[1], P. Sereda[1], A. Rich[1], A. Lal[1], E. Roth[4,5], R. Hogg[1,6], D. Moore[1,2,7]
[1]British Columbia Centre for Excellence in HIV/AIDS Research, Vancouver, Canada, [2]Faculty of Medicine, University of British Columbia, Vancovuer, Canada, [3]Positive Living B.C, Vancouver, Canada, [4]Department of Anthropology, Faculty of Social Sciences, University of Victoria, Victoria, Canada, [5]Centre for Addictions Research BC, Victoria, Canada, [6]Faculty of Health Sciences, Simon Fraser University, Burnaby, Canada, [7]British Columbia Centre for Disease Control, Vancouver, Canada
Presenting author email: nlachowsky@cfenet.ubc.ca

Background: Our objectives were to identify factors associated with condom-use during anal intercourse among HIV-positive gay, bisexual, or other men who have sex with men (MSM) in Vancouver and to determine what preventive attitudes and alternative strategies were employed by MSM who did not report using condoms.

Methods: We analyzed Momentum Health Study participants' data collected at enrollment on their most recent sexual encounter with each of up to five sexual partners in the past six months. Explanatory factors included psychosocial scales (Van Den Ven et al., 2000's *HAART Optimism*; Nimmons & Folkman, 1999's *Sexual Altruism*; Kalichman & Rompa, 1995's *Sexual Sensation Seeking (SSS)*; McKirnan et al., 2001's *Cognitive Escape*. Of all sexual encounters where anal intercourse was reported, factors associated with condom-use versus not were determined using manual backward stepwise multivariable generalised linear mixed models.

Results: A total of 648 sexual encounters were reported by 184 HIV-positive MSM (average=3.52/participant). Most encounters included anal intercourse (72.4%), during which condoms were used 22.6% of the time (11.6% with certain HIV-positive partners, 37.3% with certain HIV-negative partners, 35.3% with unknown status partners). Lower odds of condom-use were associated with being certain their partner was HIV-positive versus unknown: AOR=0.28,95%CI:0.11-0.73), reporting more prior anal sex events with this partner (AOR=0.86,95%CI:0.77-0.97), event-level GHB substance use (AOR=0.12,95%CI:0.02-0.77), and higher SSS and Cognitive Escape scores (AOR=0.86,95%CI:0.78-0.94 and AOR=0.93,95%CI:0.88-0.99, respectively). Higher Sexual Altruism community sub-scale scores were positively associated with condom-use (AOR=3.32,95%CI:2.00-5.50). HAART Optimism was not significantly associated with condom-use. HIV-positive MSM who reported condomless anal intercourse were more likely to ask partners their HIV status (AOR=3.43,95%CI:1.71-6.91), only have sex with other HIV-positive men (AOR=3.64,95%CI:1.78-7.43), only have sex with men on treatment or with low viral loads (AOR=2.32,95%CI:1.12-4.80) and hold differing prevention (e.g., more likely to agree that "knowing a sex partner's viral load is just as important as knowing their HIV status" (AOR=2.39,95%CI:1.09-5.21).
Conclusions: Psychosocial traits, attitudes, and substance use are important predictors of condom-use and HIV-positive men who report condomless anal intercourse employ various prevention strategies that consider HIV status and viral load. These strategies do not appear to consider other STIs, like syphilis.

TUPEC577

Relationship between social norms on condom use and inconsistent condom use among people living with HIV/AIDS in Guangzhou, China

Q. Zhou[1], W. Cai[2], Y. Hong[3], C. Yang[4], Y. Zhu[5], Z. Guo[5], Y. Guo[5]
[1]The First Affiliated Hospital of Sun Yat-sen University, Epidemiology Research Unit, Guangzhou, China, [2]Guangzhou NO.8 People's Hospital, Guangzhou, China, [3]Texas A&M University, Department of Health Promotion and Community, Health Sciences School of Public Health Health, Science Center, College Station, United States, [4]Johns Hopkins Bloomberg School of Public Health, Department of Health, Behavior and Society, Baltimore, United States, [5]Sun Yat-sen University, Department of Biostatistics and Epidemiology, School of Public Health, Guangzhou, China
Presenting author email: runninguoyan@163.com

Background: Previous studies have shown associations between social norms and risk behaviors among high risk populations for HIV infection. However, little is known about social norms and condom use among people living with HIV/AIDS (PLWHA). Since Chinese culture emphasizes collectivism and obedience of individual behaviors to social norms, the effects of social norms may be more pronounced. This study sought to examine the relationship between social norms on condom use and inconsistent condom use among PLWHA in Guangzhou, China.
Methods: We conducted a cross-sectional survey through convenience sampling among 412 PLWHA between March and June, 2013 in Guangzhou, China. Descriptive norm of condom use was measured as perception of number of friends thinking it necessary to use condoms when having sex. Inconsistent condom use was defined as not using condoms consistently in the last three sexual intercourses. Both bivariate and multivariate logistic regression analyses were performed to identify the independent association between inconsistent condom use and descriptive norm of condom use controlling for socio-demographic factors.
Results: About three fourths (*n*=301, 73.1%) of 412 PLWHA were sexually active since HIV diagnosis. Among the sexually active patients, the average age was 36.5 years; about two thirds were male; the majority was Han ethnicity (92.7%); 55.5% discussed condom use with their friends and the rate of inconsistent condom use was 29.2%. In multivariate logistic regression, PLWHA were 74% less likely to report inconsistent condom use if they perceived most of their friends considering necessary to use condoms when having sex (*aOR*=0.26, 95%*CI*:(0.11,0.61), *p*=0.002) compared to those who perceived less friends considering necessary to use condoms when having sex. HIV disclosure to family members was significantly related to reduced inconsistent condom use (*aOR*=0.16, 95%*CI*: (0.06, 0.41), p< 0.001), whereas living with family members compared to living with friends was associated with increased inconsistent condom use (*aOR*=8.06, 95%*CI*: (1.39, 46.63), *p*=0.020).
Conclusions: The results provide important evidence for developing social norm-based HIV interventions among PLWHA, especially in countries like China. Future interventions focused on changing social norms on risk behaviors in the social network of PLWHA have the potential to reduce risk behaviors and improve condom use among PLWHA.

TUPEC578

Ongoing HIV-transmission risks and factors associated with HIV transmission risks among young people living with HIV (YPLHIV) in Uganda

J.B. Zieman[1], C. Banura[2], R. Ampwera[3], D. Amanyire[4], M. Elang[3], G. Caswell[5], J. Okal[1], E. Yam[1], L. Vu[1]
[1]Population Council, Washington, United States, [2]Child Health and Development Centre, Kampala, Uganda, [3]Community Health Alliance Uganda, Kampala, Uganda, [4]Marie Stopes Uganda, Kampala, Uganda, [5]International HIV/AIDS Alliance, Brighton, United Kingdom
Presenting author email: bzieman@popcouncil.org

Background: Of new HIV infections worldwide, an estimated 40% occur among young people, either perinatally or sexually. In Uganda young people living with HIV (YPLHIV) face significant challenges regarding their health, development, and economicopportunities. Additionally, they find difficulties communicating with their partners about their HIV status, safer sex practices, and childbearing desires. This abstract aims to investigate HIV transmission risks and HIV disclosure practices among Ugandan YPLHIV.
Methods: These data were part of a baseline survey conducted under the Link Up project, which provides sexual and reproductive health (SRH) services to young people in Uganda. Between September-October, 2014, 473 YPLHIV aged 15-24 years were recruited through peer-support groups in Luweero and Nakasongola districts. The survey elicited information on HIV-related behaviors, use of SRH and HIV services, HIV status disclosure, and stigma and discrimination. We assessed key descriptive indicators and examined their associations with condom use and HIV disclosure using multiple logistic regression.
Results: Participants had a median age of 20 years, 70% were female, 67% were single, and had lived with HIV for an average of 3.6 years. Thirty percent reported acquiring HIV perinatally, 68% were on ART, and 40% experienced physical, sexual or emotional abuse (past 12 months).
Fifty-seven percent reported having sex in the past 12 months (n=274), of which 43% used condom at last sex and 42% knew partner's HIV status at last sex. Of YPLHIV with a recent sexual partner (n=229), 31% had disclosed their HIV status to their last sex partner.
Multivariate analysis showed that condom use was significantly higher among YPLHIV who were older (age 18-24; AOR=2.7; 95%CI:1.6-4.6), male (AOR=1.8; 95%CI:1.1-2.9), single (AOR=2.4; 95%CI:1.3-4.4), and who knew their partner's HIV status (AOR=4.0; 95%CI:2.4-6.6). HIV disclosure was higher among YPLHIV who were married/living together (AOR=8.1; 95%CI:3.7-17.6) and those knowing their partner's HIV status (AOR=5.4; 95%CI:2.5-11.6).
Conclusions: Over half Ugandan YPLHIV are sexually active and may engage in unprotected sex with HIV-negative partners. Program planners should tailor much-needed HIV counseling and behavioral interventions according to age, gender, and marital status. Further analyses and qualitative studies are needed to better understand YPLHIV relationships, and reasons for non-disclosure and condom non-use.

TUPEC579

Attitudes and preferences about cervical cancer screening among women living with HIV in Peru

I. Alva[1,2], A. Mühlbach[1], C. Diaz[3], E. Juárez[4], J.L. Castro[1], M. Blas[1,2], G. Mburu[5], P. García[2], R. Cabello[1]
[1]Via Libre, Lima, Peru, [2]Universidad Peruana Cayetano Heredia, Lima, Peru, [3]University of California, Los Angeles, United States, [4]Ministry of Health, Lima, Peru, [5]International HIV/AIDS Alliance, Hove, United Kingdom
Presenting author email: drisaacalva@gmail.com

Background: Cervical cancer was the first gender specific disease to be included in the AIDS case definition worldwide, due to the increased susceptibility of cervical cancer among women living with HIV. Although cervical cancer can be prevented with routine Pap-testing and timely treatment, its incidence in the context of antiretroviral treatment in Peru remains unclear. The objective of this study was to understand the attitudes and preferences of Peruvian women with HIV regarding Pap-testing.
Methods: From November to December 2014 we conducted a qualitative study of women living with HIV who attend the Via Libre HIV clinic in Lima Peru. We performed in-depth interviews to 14 women and 2 focus groups including additional 11 women.
Results: Participants age ranged from 19 to 54 years old. Our study found that:
1) Some women didn't want to undergo Pap-testing because they felt that they could not handle another severe health problem, especially in the absence of partner support;
2) Most women preferred not to disclose their HIV status when they underwent a Pap-test (even when the health provider was a female gynecologist).
3) Most women preferred to be tested at the end of the year when they are on vacation.
4) The physicians in charge of their HIV care only talked about Pap-testing at the first visit.
5) Although encrypted email or SMS reminders are acceptable, Facebook is considered as an innovative alternative to promote Pap-testing among HIV positive participants;
6) Women with HIV who had a relative with cervical cancer, or women who had their first Pap as part of previous antenatal care, got Pap-tests more frequently.

Conclusions: Women with HIV in this study had some clear attitudes and preferences regarding cervical cancer screening that should be taken into account in future interventions. HIV care providers should highlight the importance of having a Pap-test and should encourage women to disclose their HIV status when seeking health care, to ensure more timely diagnosis of cervical cancer. Our findings also highlight the potential importance of using email, SMS, and social media to motivate Pap-testing among women living with HIV.

TUPEC580

HIV-related stigma and depression among newly diagnosed HIV-infected men who have sex with men, in China

J. Tao[1], A.M. Kipp[1,2], Y. Liu[1], C. Zhang[1], Y. Ruan[3], L. Yin[1], K.R. Amico[4], Y. Shao[3], H.-Z. Qian[1,5,6], S.H. Vermund[1,5,6]
[1]Vanderbilt University, Vanderbilt Institution for Global Health, Nashville, United States, [2]Vanderbilt University, Epidemiology Center, Nashville, United States, [3]Chinese Center for Disease Control and Prevention, State Key Laboratory for Infectious Disease Prevention and Control and National Center for AIDS/STD Control and Prevention, Beijing, China, [4]University of Michigan, Department of Health Behavior and Health Education, Ann Arbor, United States, [5]Vanderbilt University, Department of Pediatrics, Nashville, United States, [6]Vanderbilt University, Department of Medicine, Nashville, United States
Presenting author email: barbaratao@gmail.com

Background: HIV-related stigma has a negative impact on the mental health of HIV long-term infected individuals. However, such an association among newly diagnosed HIV infected people has not been explored. Men who have sex with men (MSM) are vulnerable to depression due to social stresses, lack of family acceptance, and risks of HIV infection. We explored HIV-related stigma and depression among newly diagnosed HIV infected MSM in China.
Methods: A randomized clinical trial of HIV "prevention with positive" among newly diagnosed HIV infected MSM was conducted in China, with 367 eligible participants recruited at baseline. One participant was omitted in the analysis due to missing data. HIV-related stigma was measured with a validated scale (Steward, et al, 2008) with four components -enacted, felt, vicarious, and internalized stigma (component score range: 0-30). Factor analysis confirmed the four-component structure in the Chinese MSM population; Chronbach's alpha values were all >0.90. Depression was assessed from the Hospital Anxiety and Depression scale. Multivariable ordered logistic regression was conducted to analyze the associations between continuous stigma scores for each component and categorized depression groups (normal: 0-7, borderline: 8-10, and suspicious: 11-21), adjusting for age and education. The proportional odds assumption was satisfied.
Results: The mean age of our study participants was 30 years-old. The majority were of Han ethnicity (93%), well educated (77%, over 12-year education), and single (84%). Twenty percent (73/366) had suspicious depression, and 16% (59/366) had borderline depression. Mean scores for felt, vicarious and internalized stigma were 14.8, 4.9, and 8.1, respectively. Enacted stigma was excluded from the analysis, as one-third of participants did not respond to its items. A one-point increase in each of the stigma component scores was associated with a 5-11% increase in the odds of having depression (Table), with internalized stigma having the strongest association (OR=1.11, 95% confidence interval [CI]: 1.08, 1.14).

HIV Stigma Score	Mean Score (SD*)	Depression (adjusted odds ratio, 95% CI)+
Felt Stigma	14.8±11.2	1.05 (1.03, 1.07)
Vicarious Stigma	4.9±6.5	1.09 (1.05, 1.13)
Internalized Stigma	8.1±9.0	1.11 (1.08, 1.14)

* Standard Deviation; + Adjusted for age and education; other components of stigma were not mutually adjusted due to collinearity; NOTE: Enacted stigma was excluded, as one third of study participants did not respond to its items.

[HIV-related stigma and depression]

Conclusions: HIV-related stigma was positively associated with higher depression among newly diagnosed HIV infected MSM in China. Interventions to address coping with HIV stigma immediately following diagnoses, particularly for internalized stigma (shame, guilty and contact avoidance) may reduce depression and improve long-term mental health.

Prevention in other institutional settings (including workplace / school / prison / army)

TUPEC581

HIV/AIDS in prison: a global systematic review of HIV incidence and AIDS related mortality

K. Dolan[1], B. Moazen[2], A. Noori[2], S. Rahimzadeh[2], F. Farzadfar[2], F. Hariga[3]
[1]National Drug and Alcohol Research Centre, Program of International Research and Training, Wollongong, Australia, [2]Tehran University of Medical Sciences, Non-Communicable Diseases Research Center, Tehran, Iran, Islamic Republic of, [3]United Nations Office on Drugs and Crime, Vienna, Austria
Presenting author email: k.dolan@unsw.edu.au

Background: Prison populations have elevated levels of HIV infection and poor access to medical care including HIV prevention and treatment programs. Previous reviews have reported on HIV transmission and AIDS related mortality in the community setting but not in the prison setting.
Therefore we reviewed the global situation of HIV incidence, cases of HIV transmission and AIDS related mortality among prison populations.
Methods: We systematically searched the peer reviewed and grey literature for relevant data published from January 2008 to April 2013. Additional data sources were identified through direct communication with researchers, key experts and from a survey of UN staff and prison authorities.
Results: In 2011, over 10.1 million people were held in prisons, with an estimated 30 million persons passing through a prison annually. Rates of imprisonment varied greatly across Regions from 67.5 per 100,000 in West and Central Africa to 332 per 100,000 in the Caribbean. HIV incidence data for prisoners were found for six countries and ranged from 0.0% to 11.2% per year. Case reports of HIV transmission in prison were found for six countries and ranged from zero to 543 cases per year. AIDS-related mortality rates for prisoners were located for one country and ranged from 10.5% to 22.9%. Case reports of AIDS-related deaths of prisoners were found for four countries and ranged from zero to 388 per year.
Conclusions: The world's prisons hold vast numbers of individuals, many of whom are infected with HIV, yet information on HIV transmission and AIDS-related mortality was very scarce. HIV transmission in prison has substantial public health implications as tens of millions are imprisoned and released annually. HIV prevention and treatment strategies known to be effective in the prison setting, such as methadone maintenance treatment, needle and syringe programs, condoms and antiretroviral therapy should be provided to prisoners as a matter of urgency. Compassionate release should be available for inmates in the final stages of AIDS.

TUPEC582

Prevalence and correlates of occupational needle-stick injuries among active duty police officers in Tijuana, Mexico

M.L. Rolón[1,2], E. Patiño[1,2,3], L. Beletsky[1,4], J. Arredondo[1], T. Rocha[1], D. Abramovitz[1], V.M. Alaníz Morales[5], A. Bañuelos Pérez[5], M.G. Rangel Gómez[6], S.A. Strathdee[1]
[1]University of California San Diego, Division of Global Public Health, La Jolla, United States, [2]Universidad Xochicalco, School of Medicine, Tijuana, Mexico, [3]Dirección Municipal de Salud, Tijuana, Mexico, [4]Northeastern University, School of Law & Bouvé College of Health Sciences, Boston, United States, [5]Secretaría de Seguridad Pública Municipal, Dirección de Planeación y Proyectos Estratégicos, Tijuana, Mexico, [6]Secretaría de Salud, Tijuana, Mexico
Presenting author email: mlrolon@ucsd.edu

Background: For police officers, needle-stick injuries (NSI) are a serious occupational and healthcare risk for HIV and viral hepatitis. Despite legal syringe possession in Tijuana, 48-57% of people who inject drugs (PWID) report syringe-related arrests and confiscation by police, which has been associated with needle-sharing and HIV infection. Alarmingly, there is currently no NSI response protocol and/or affordable access to post-exposure prophylaxis for Mexican police.
We assessed prevalence and correlates NSIs among police officers to improve their occupational safety to inform a policing education program to reduce HIV risks among police and PWID.
Methods: Tijuana's Department of Municipal Public Safety is among Mexico's largest municipal police force. With full departmental collaboration, our binational, multi-sectoral team administered an anonymous work environment and occupational health survey (including handling and disposal of syringes, NSIs, access to healthcare) to active-duty police officers. Logistic regression was used to identify individual factors associated with NSIs.
Results: 503 officers surveyed in July 2014 were predominantly male (86.5%), 36-45 years old (46.3.%) and had worked as a Tijuana police officer a mean of 10.8 years. Most (94.0%) reported encountering syringes when performing daily duties; 15.3% reported ever having at least one NSI, of whom 14.3% was within the last year. Among those ever reporting encountering needles/syringes while on duty (n=407), factors independently associated with an elevated odds of NSIs included frequently finding syringes that contain drugs (Adj OR: 2.98; 95% CI: 1.56-5.67) and reporting breaking used needles (Adj OR: 2.25; 95% CI: 1.29-3.91), whereas

factors associated with a reduced odds of NSI were agreeing that they would contact emergency services in case of NSIs (Adj OR: 0.39; 95% CI: 0.22-0.69), and wearing needle-stick resistant gloves (Adj OR: 0.43; 95% CI: 0.19-0.91).
Conclusions: We found NSIs to be common and closely associated with inappropriate syringe handling by Tijuana police officers. After sharing these results, police academy officials endorsed an NSI surveillance and response program for post-exposure prophylaxis, and a police education program that aims to reduce their risk of NSIs while modifying policing behaviors (e.g. syringe confiscation) that can lead PWID to share syringes and experience elevated HIV risk.

TUPEC583

Endowment training intervention: changing attitudes toward opioid substitution therapy in 30 minutes

M. Polonsky[1], F. Altice[2]
[1]Yale University School of Medicine, Internal Medicine, New Haven, United States, [2]Yale School of Medicine, New Haven, United States
Presenting author email: frederick.altice@yale.edu

Background: Opioid substitution therapy (OST) is internationally recognized as the most effective form of treatment for opioid dependence and is also among the most effective HIV prevention strategies available. In the countries of Former Soviet Union (FSU), however, treatment for opioid dependence has been more influenced by myths and prejudices than by the scientific evidence. To challenge pervasively negative attitudes we developed a brief intervention called Endowment Training Intervention (EnTrI). Building upon work in decision sciences and behavioral economics, EnTrI targets attitude change via perceived ownership of a solution to a problem. The endowment effect documents that owning a particular good increases its value, even when ownership is experimentally induced and not necessarily sustained. Respectively,the ownership of ideas occurs by investing effort, and those ideas that are perceived to be of an internal origin are valued more. We expected that mental effort invested by prison medical administrators during a short task, is likely to bring about the desired effect: perceived ownership of an idea that OST is beneficial, and a preference for OST over other treatment methods.
Methods: ENTRI employs a pre/post-test experimental design, where the experimental treatment is a brief (10 minutes) exercise that provides study participants with a list of 12 indicators of efficiency and asks to rate the indicators' respective importance. A total of 94 prison medical administrators (57 male; 37 female) were randomized into either the experimental (n=50) or control (n=44) group. The control group was given 10 minutes to fill out a pre-test, which was then followed by the presentation, and the post-test attitude survey. The experimental group received a pre-test as well as the intervention, the presentation, and the post-test survey.
Results: The results of the study confirmed our key hypothesis, with the participants in the experimental group reporting more positive attitudes toward OST relative to those in the control group.
Conclusions: The inability of Ukrainian administrators to accept the scientific consensus regarding OST and a lingering bias toward thereof was successfully tackled by a brief intervention aimed at creating a perceived ownership of a solution to a problem.

Collectivization, mobilization, stigma reduction programmes

TUPEC584

Stigmatized health care: a challenging issue for Iranian HIV+ patients

N. Zarei, H. Joulaei, M. Amini Lari
Shiraz HIV/AIDS Research Center, Shiraz University of Medical Sciences, Shiraz, Iran, Islamic Republic of
Presenting author email: maminil@yahoo.com

Background: This study aimed to assess the stigmatized attitude among health providers toward people living with HIV/AIDS (PLWHA) and their willingness to provide service to these patients.
Methods: This is a descriptive-analytic study. The study population consisted of all medical personnel of public and private hospitals, in Shiraz, somehow dealing with PLWHA.The study was carried out on 575 health care providers of hospitals in Shiraz,as one of the metropolitan city of Iran. The data were collected from June to August 2014 and were analyze dusing $SPSS_{21}$.
Results: Almost half of the respondents are opposed to provide services to PLWHA. Most of the respondents stated that the reason for unwillingness to provide services was exposure to the disease (70.5%) and involvement of these patients in unethical behavior (65.6%).The respondents who had an experience dealing with PLWHA were asked to express their behavior; only 45.5% stated that their attitude was normal with patients, while other respondents had a discriminatory feeling; 42.42% of the subjects had a state of fear, 16.45% refused reception, 15.42% disgusted, and 8.74% experience danger. The most dominant attitude of the health care providers toward HIV/AIDS patients was dealing with fear. A significant reverse relationship existed between stigmatized attitude of the personnel and their willingness to provide services to the prostitute, drug injector, and homosexual patients ($p< 0.05$). Uni-variate regression also indicated the relationship of health care providers' stigmatized attitude with their religious beliefs, stigmatized attitude of the society, and knowledge of the transmission routes.
Conclusions: Stigmatized attitude of the health professionals as one of the key people in dealing with PLWHA may result in undesirable consequences, such as dealing with fear, disgust, anger, and in some cases refuse to accept the patients. Therefore, decreasing irrational fear of personnel is important to reduce their stigmatized attitude. Obviously, this will improve the quality of services to PLWHA.
Hence, it seems that creating an effective knowledge about transmission and correcting the socio-cultural beliefs of health providers are two key strategies to deal with this problem.

TUPEC585

Opinions and experiences of HIV-status disclosure to sex partners: a qualitative study with gay men in Lima, Peru

C. Sandoval[1,2], L. Najarro[3], K. Konda[4]
[1]Universidad Peruana Cayetano Heredia, Unidad de Salud, Sexualidad y Desarrollo Humano, Facultad de Salud Pública y Administración, Lima, Peru, [2]Instituto de Estudios en Salud, Sexualidad y Desarrollo Humano, Lima, Peru, [3]Instituto de Estudios en Salud Sexualidad y Desarrollo Humano, Lima, Peru, [4]UCLA, Department of Medicine, Division of Infectious Diseases, Los Angeles, United States
Presenting author email: kkonda@mednet.ucla.edu

Background: Improved treatment creates the possibility of living in health with HIV for many years, creating new challenges including decisions regarding sero-disclosure to sex partners. This study explored HIV-status disclosure among gay men in Lima, Peru.
Methods: A study on the relationships and lives of gay couples included 60 in-depth interviews with gay men, including people living with HIV (PLHIV) and HIV-negative men.
Results: PLHIV expressed fear of possible outcomes of divulging their HIV-positive status to a sex partner. Fears included abandonment and consequences of further disclosures to others, and/or the inability to obtain new sex partners due to their HIV-positive status. PLHIV also expressed fear that a sex partner would acquire HIV from them. Especially when the sex partner did not know their HIV-positive status, PLHIV said that they always used condoms, often due to guilt. However, many PLHIV eventually disclosed their HIV-positive status to their sex partners, after establishing a stable relationship, reporting that their fears of HIV-status disclosure were unfounded and that their relationships continued. All participants expressed that any HIV-status disclosure (positive or negative) would only occur with a trusted sex partner with whom they could see a future. HIV-negative participants thought they would not disclose a potential HIV-positive status due to fear of stigma and discrimination. The reaction of HIV-negative participants to a potential HIV-positive disclosure depended on their level of commitment to their partner. Some HIV-negative members of very committed relationship said the relationship would continue unchanged. Many HIV negatives said that the romantic relationship would end following an HIV-positive disclosure, but that they would continue as friends and provide emotional support to the HIV-positive partner.
Conclusions: Fear of HIV continues and affects HIV-status disclosure, despite knowledge and experience of improved HIV treatment. HIV negatives are scared of HIV and this perpetuates the fear of stigma and discrimination among PLHIV. Even though PLHIV now have access to treatment, their fears of other's reactions prevent or delay HIV-status disclosure. Interventions with PLHIV and HIV negative gay men are urgently needed to promote timely HIV-status disclosure in supportive situations and to alleviate fear of HIV as a disease.

TUPEC586

Development and reliability of scales to measure stigma among men who have sex with men and female sex workers in West Africa: tools for stigma reduction programmes

A. Grosso[1], S. Ketende[1], G. Ouedraogo[2], S. Anato[3], O. Ky-Zerbo[4], V. Pitche[5], E. Papworth[1], S. Baral[1]
[1]Johns Hopkins University, Center for Public Health and Human Rights, Baltimore, United States, [2]Institute de Recherche en Sciences de la Sante, Ouagadougou, Burkina Faso, [3]Arc en Ciel, Lomé, Togo, [4]Programme d'Appui au Monde Associatif et Communautaire, Ouagadougou, Burkina Faso, [5]Conseil National de Lutte contre le SIDA du Togo, Lomé, Togo
Presenting author email: grossoas@gmail.com

Background: Stigma is a multifaceted concept that affects key populations at higher risk for HIV, including men who have sex with men (MSM) and female sex workers (FSW). Appropriate tools to evaluate stigma reduction programmes for key populations are needed, but relatively few of these measures have been assessed in Sub-Saharan Africa. This study developed scales to measure stigma among MSM and FSW in two countries in West Africa.

Methods: Questionnaires were administered to 1,351 MSM and 1,380 FSW in two cities in Togo and two cities in Burkina Faso. Exploratory factor analysis was used. Factors were retained based on eigenvalues, the Kaiser's criterion, scree plots, and interpretability. For ease of interpretation, promax oblique rotation was used because some correlation between factors was expected. Consistency assessment was conducted using Cronbach's alpha and the Kuder-Richardson test.
Results: In total, 17 items were retained in the final MSM stigma scale. There were four factors, with 2-8 items loading on each factor. The factors were:
1) enacted stigma;
2) stigma from family and friends;
3) perceived healthcare stigma; and
4) enacted healthcare stigma.
The Cronbach's alpha varied by city and ranged from 0.7322 to 0.7906.
A total of 20 items were retained in the FSW stigma scale. The factors were similar to the MSM scale, with one additional factor: stigma from police. The Cronbach's alpha of the scale varied by city and ranged from 0.7079 to 0.8292.
Enacted stigma included physical and sexual violence, torture, arrest, blackmail, verbal harassment, and police refusing protection. Stigma from family and friends included rejection and gossip. Perceived healthcare stigma included avoiding or fear of seeking care. Enacted healthcare stigma included being denied services, not treated well, difficulties accessing care, and health workers gossiping.Stigma from police included witnessing, hearing about, or experiencing police confiscating condoms, or not carrying condoms to avoid trouble with police.
Conclusions: This preliminary study of metrics of stigma among MSM and FSW indicate that the scales have promising reliability. These scales will be used to examine stigma among MSM and FSW in Senegal and to assess the effectiveness of a stigma reduction programme in the health sector.

TUPEC587

Determinants of stigmatization of people living with HIV/AIDS in Burkina Faso

M. Kaboré[1,2], H. Badolo[3], N. Sawadogo[4], Y.J. Drabo[5], N. Méda[3]
[1]CHU Yalgado Ouedraogo, Médecine, Ouagadougou, Burkina Faso, [2]Association Burkinabé pour le Bien Etre Familial (ABBEF), Clinique, Ouagadougou, Burkina Faso, [3]Centre MURAZ, Bobo Dioulasso, Burkina Faso, [4]Université de Ouagadougou, Institut Supérieur des Sciences de la Population, Ouagadougou, Burkina Faso, [5]Université de Ouagadougou, UFR Sciences de la Santé, Ouagadougou, Burkina Faso
Presenting author email: mikailakab@gmail.com

Background: Stigmatization of people living with HIV/AIDS (PLWHA) negatively influences the response against the disease. Our goal was to identify the individual and contextual determinants of population's stigma towards PLHIV in Burkina Faso.
Methods: Secondary data set from the fourth Demographic and Health Surveys conducted in Burkina Faso in 2010 was analysed. The study included those who answered "yes" to the question «if they had ever heard about HIV/AIDS». Thus, the final sample included 16,571 women and 7,102 men. We performed a multilevel logistic regression with MLwiN 2.29 software. The contextual level was represented by the thirteen regions of the country.
Results: A total of 23,673 individuals (15 to 59 years) was surveyed, of which more than one third (36.8%) was under 25 years old. The prevalence of stigma was 89% [95% CI: 88.59 - 89.45%] (women : 92.70% versus men : 87.10%, p< 0.001). At the individual level, sociocultural factors (lack of knowledge about HIV/AIDS OR=2.41***, inaccessibility to media OR=1.60***, not doing the HIV test OR=1.34***) and sociodemographic factors (young age OR=1.39***, female gender OR=2.08***, coming from rural area OR=1.29***) were seemed to be more associated with stigmatizing behaviors than economic factors (no education OR=2.50***, informal occupation OR=1.13***).
At the contextual level, access to media (OR=1.70***) and knowledge about HIV contextual (0.70***) influenced stigmatizing behavior of individuals towards PLWHA. The entry of contextual factors in the final model lowered the contextual variance to 3.08% compared to the empty model (0.748***), but not significantly. In addition, there was no significant change of individual characteristics on stigmatization after taking into account contextual factors. The influence of contextual seroprevalence on stigmatization was not significant.
Conclusions: People with young age, female, less educated, with low knowledge about HIV/AIDS, living in the countryside with a low socioeconomic level in an environment with low awareness of the disease were more likely to stigmatize PLWHA. Therefore, there is a need to strengthen awareness programs through mass media for the benefit of this population, with the aim to move towards UNAIDS "zero discrimination" goal.

Policy-level HIV interventions including legal-policy reform

TUPEC588

Assessing changes in HIV-related legal and policy environments in sub-Saharan Africa

L. Ferguson[1], S. Gruskin[1], I. Henry[1], A. Nicholson[1], A. Saha[2], T. Sellers[2]
[1]University of Southern California, Program on Global Health and Human Rights, Institute for Global Health, Los Angeles, United States, [2]United Nations Development Programme, Addis Ababa, Ethiopia
Presenting author email: laura.ferguson@med.usc.edu

Background: Following the work of the Global Commission on HIV and the Law, there has been increased political interest in the impacts of law on vulnerability to HIV as well as access to HIV-related services. Implemented by the United Nations Development Programme, one such 3-year project seeks to use the Global Commission's recommendations to improve HIV-related legal and policy environments for key populations including LGBT populations and women and girls, in 11 countries in sub-Saharan Africa.
Methods: We carried out a mid-term review through a desk-based document review, as well as key informant interviews with project implementers and beneficiaries.
Results: Despite the specificity of country contexts, capacity to understand and address weaknesses in national legal and policy environments can be fostered in a number of ways. In many countries, multi-stakeholder assessments of the HIV-related legal environment were carried out, providing a comprehensive review of relevant laws and policies and allowing national prioritization of follow-up actions.
In others, emphasis was placed on national dialogues between government and civil society resulting in unprecedented opportunities for discussion and collaboration. Particularly at this political moment, simply creating space for conversation about LGBT issues amongst these actors, which has been facilitated by HIV as an entry point, can be seen to constitute major progress. Importantly, the processes of policy reform can be faster than those of legal reform, and the opportunities worth exploring particularly as relevant to subsequent legal change. Key to the success of this work are: national ownership, informed stakeholders, civil society and government collaboration, a critical understanding of the political landscape, and key stakeholders' willingness to champion specific issues and existing opportunities for influencing laws, policies, budgets and actions.
Conclusions: Effecting legal change can take a very long time - often far longer than a project period or funding cycle. Interim successes can positively impact access to HIV services and the lives of women, girls and LGBT populations, and strengthen the rationale for positive legal change. Lessons from this review can support efforts to improve the legal environment for key populations in a variety of settings.

TUPEC589

A global analysis of the role of lay providers in national HIV testing and counseling policies

D. Flynn[1], C. Johnson[2], A. Sands[3], V. Wong[4], R. Baggaley[2]
[1]Griffith University, School of Medicine, Gold Coast, Australia, [2]WHO, HIV Department, Geneva, Switzerland, [3]WHO, Essential Medicines and Health Products, Geneva, Switzerland, [4]UNAID, Global Health Bureau, Office of HIV/AIDS, Washington DC, United States
Presenting author email: deflynn75@gmail.com

Background: HIV testing and counseling (HTC) is the first step toward accessing prevention, care and treatment. Only 45% of people living with HIV are aware of their serostatus; greater efforts are needed to achieve new UNAIDS "90-90-90" targets. WHO recommends lay providers support a variety of health services. However according to Global AIDS Response Progress Reporting (GAPR) 2014 data, 28/119 countries do not permit lay workers to support HTC services and 61 countries prohibit lay workers from performing HIV rapid diagnostic tests (RDTs).
Therefore, we conducted an in-depth analysis of national HTC policies, examining the role of lay providers in administering HTC services.
Methods: Between 1 November and 21 December 2014, electronic searches for national HTC policies were conducted, using Google, government and NGO websites and WHO databases. WHO and UNAIDS regional technical advisors, and key experts in the field were contacted. No geographic or language restrictions on the search; however, English language versions were sought when available. Policies were reviewed and data relating to lay providers was extracted and compared to GAPR data.
Results: 49/65 policies identified were analysed in this review. Nearly 60% of policies permit lay providers to administer counseling, but only 40% permit lay providers to perform HIV RDTs (with fingerstick whole blood) and one-third prohibit lay providers from performing HIV RDTs. A greater proportion of policies in the WHO African Region support lay providers to administer counseling (80%) and to perform HIV RDTs (58%); with only 12% prohibiting lay providers from such tasks. Nearly one-third of reviewed policies did not specify the role of lay providers. GAPR data mostly agreed with the policy data extracted and reviewed; but with considerably more policies analyzed that did not clearly specify the role of lay providers.

Conclusions: Lay providers are key in the scale-up of HTC services and reaching global targets. Supportive and clear policies which permit lay providers to administer both HIV RDTs and counseling are needed. The African region appears to have a very supportive policy environment for lay provider HTC. Countries in other regions should review these policies to enhance task-shifting in their context and better utilize lay providers.

TUPEC590

Criminalization of HIV transmission in France: knowledge of and concerns about HIV-related court-case verdicts in a representative sample of people living with HIV (ANRS VESPA2 survey)

M. Suzan-Monti[1,2,3], B. Demoulin[1,2,3], M. Celse[4], R. Dray-Spira[5,6], F. Lert[7], B. Spire[1,2,3], ANRS VESPA2 Study Group
[1]INSERM, UMR 912 (SESSTIM), Marseille, France, [2]Aix Marseille Université, UMR_S 912, IRD, Marseille, France, [3]ORS PACA, Observatoire Régional de la Santé Provence-Alpes-Côte d'Azur, Marseille, France, [4]French National AIDS Council, Paris, France, [5]INSERM, UMR_S 1136, Pierre Louis Institute of Epidemiology and Public Health, Team Research in Social Epidemiology, Paris, France, [6]Sorbonne Universités, UPMC Univ Paris 06, UMR_S 1136, Pierre Louis Institute of Epidemiology and Public Health, Team Research in Social Epidemiology, Paris, France, [7]Centre de Recherche en Épidémiologie et Santé des Populations, Inserm U 1018, Villejuif, France
Presenting author email: marie.suzan@inserm.fr

Background: In France, criminal prosecution for HIV transmission resulted in approximately 10 trials and sentences between the very first trial in 1998 and 2011. Prison terms were handed down in all but one case. Media coverage of most trials remained limited to local newspapers but a few major cases attracted the attention of the wider public. This may have had a negative impact on people living with HIV (PLWH) by reinforcing stigma and discrimination. The objective of the present analysis was to characterize, among a representative sample of PLWH followed-up in French hospitals, those aware of and concerned about HIV criminalization.
Methods: ANRS-VESPA2 was a cross-sectional survey conducted in 2011 on 3022 adult PLWH attending French hospitals HIV-diagnosed >6 months. Socio-behavioural (face-to-face patient interviews) and medical (provided by medical staff) data were collected. Participants were asked if they were aware of HIV-related court case verdicts and if they were concerned about them. Multivariate analyses were performed on weighted and calibrated data.
Results: Among the 3022 PLWH enrolled in the survey, 2141 (71.2%) were aware of the verdicts of whom 1207 (56.4%) reported they were concerned about them. Migrants from Sub-Saharan Africa (reference group) were the population with the greatest concerns compared with men who have sex with men (OR[95%CI] 0.73[0,59;0,97], p=0.047), intravenous drug users (0.55[0,37;0,83], p=0.005), and other PLWH (0.7[0,49;0,98], p=0.04). Living in precarious conditions (0.76[0,59;0,97], p=0.03) and having unprotected anal/vaginal sex with one's main partner (1.39[1,01;1,91], p=0.044) were also statistically associated with being concerned about the verdicts, while age, sex, educational level, disclosure to one's main partner, time since HIV diagnosis and viral load were not.
Conclusions: Publicity about HIV criminalization affects the most vulnerable PLWH, especially foreigners living in precarious conditions who find it difficult to negotiate prevention with their main partner. Despite their greater concern, migrants are under-represented among victims and those convicted in French HIV-related cases. Further analyses are needed to understand the reasons explaining their fear. However, the study suggests that criminal risk perception among PLWH reflects more the level of stigma and discrimination they globally experience than the actual risk of prosecution they are exposed to.

TUPEC591

Policy and legal challenges and opportunities for HIV and drug abuse prevention among migrant tourism workers in the Dominican Republic

M. Padilla[1], N. Varas-Diaz[2], J. Colon Burgos[3], A. Matiz-Reyes[4]
[1]Florida International University, Global and Sociocultural Studies, Miami, United States, [2]University of Puerto Rico, School of Social Work, San Juan, United States, [3]University of Puerto Rico, School of Public Health, San Juan, United States, [4]Florida International University, Latin American and Caribbean Center, Miami, United States
Presenting author email: marpadi@fiu.edu

Background: The presentation discusses results from a NIDA-funded mixed-method ethnographic study of the health vulnerabilities and social factors contributing to HIV/AIDS and drug abuse among migrant workers in two tourism areas in the Dominican Republic. Prior research by our team has demonstrated a behavioral and epidemiological connection between tourism zones and HIV and drug abuse risk.
This project represents the first large-scale mixed-method ethnographic and survey study to determine the social, structural, environmental, and demographic factors that may contribute to "ecologies of vulnerability" within Caribbean tourism zones.
Methods: In Phase 1, the study utilized ethnographic mapping with male tourism migrants, key informant interviews, and in-depth qualitative semi-structured interviews with a theoretically-sampled group of 36 migrant tourism workers (each interviewed twice).
Results: Our research has identified several key structural factors that contribute to vulnerability to HIV, drugs, and other health conditions. Our analysis focuses on understanding the distinct risks and vulnerabilities for deportees in comparison to internal migrants, and determines that the former group faces a unique and particularly traumatic set of circumstances contributing to drug abuse and HIV risk. Our research with institutional representatives provides some directions for policy and structural interventions to address current gaps in services and policies that would narrow the gap in providing much-needed support for this neglected, highly vulnerable population.
Conclusions: Our analysis provides several structural and policy suggestions that would begin to alleviate some of the health effects among the migrant population working in Dominican tourism areas including:
(1) public awareness of the damaging results of the stigmatization of deportees upon return "home";
(2) policy advocacy and community mobilization to change laws that criminalize clinical drug treatments (e.g., methadone);
(3) sensitivity training and accountability for authorities who are often known to abuse informal tourism laborers and drug users;
(4) greater awareness among policymakers in the US of the invisible linkages between the mass incarceration and deportation of young men in the United States and the vulnerabilities that exist in Caribbean tourism areas that receive millions of tourists annually.

TUPEC592

Gender differences in meeting legal obligations to disclose HIV status within a cohort of HIV-positive illicit drug users in Vancouver

S. Patterson[1,2], A. Kaida[1], P. Nguyen[2], J.S. Montaner[2,3], G. Ogilvie[3,4], R.S. Hogg[1,2], M.-J. Milloy[2,5]
[1]Simon Fraser University, Faculty of Health Sciences, Burnaby, Canada, [2]British Columbia Centre for Excellence in HIV/AIDS, Vancouver, Canada, [3]University of British Columbia, Faculty of Medicine, Vancouver, Canada, [4]British Columbia Centre for Disease Control, Vancouver, Canada, [5]University of British Columbia, Division of AIDS, Vancouver, Canada
Presenting author email: sophiep85@googlemail.com

Background: The Canadian legal position on HIV non-disclosure is among the strictest internationally. In October 2012, the Supreme Court of Canada (SCC) ruled that people living with HIV must disclose their HIV status to sexual partners prior to vaginal intercourse, unless they use a condom and have a low viral load, defined as < 1500 copies/ml.
Methods: Using cross-sectional data from the AIDS Care Cohort to Evaluate Access to Survival Services (ACCESS) a prospective cohort of HIV-positive illicit drug users in Vancouver, we estimated the proportion of participants who would be legally obligated to disclose their HIV status to sexual partners based on the 2012 SCC ruling. Interviewer-administered surveys collected socio-behavioural data, which were linked with clinical data and de-identified. ACCESS participants interviewed since October 2012 and self-reporting vaginal intercourse within six months before interview were included. Participants self-reporting 100% condom use and demonstrating viral load < 1500 copies/ml at every test within six months before the interview were deemed to satisfy the non-disclosure criteria. Multivariable logistic regression identified independent covariates of failing to satisfy the non-disclosure criteria.
Results: Our analytic sample included 176 participants, including 77 (44%) women. The median participant age was 45 (IQR: 40-51), and 42% were in a stable relationship at interview. Within six months before interview, 95% of participants had received ART for ≥1 day, 25% were employed, 12% were homeless, 16% had engaged in sex work, 66% had used injection drugs, and 6% had been incarcerated. Overall, 56% of participants satisfied the criteria for non-disclosure. Independent predictors of failing to satisfy the HIV non-disclosure criteria were female vs. male gender (aOR 0.43 [95% CI: 0.22-0.87]), having one recent sexual partner (vs. >1 partners) (aOR 0.35 [95% CI: 0.16-0.77]), recent incarceration (aOR 0.20 [95% CI: 0.05-0.99]), and being in a stable relationship (aOR 0.40 [95% CI: 0.20-0.80]).
Conclusions: Female and recently incarcerated participants were less likely to satisfy the Canadian legal criteria for non-disclosure, and as such are more likely to face a legal obligation to disclose HIV status to sexual partners, irrespective of the challenges to disclosure within the highly criminalized environment in which they seek care.

TUPEC593

Supporting policy-level action for improved health outcomes in Zimbabwe

C. Zinyemba[1], A. Mahomva[1], E. Tumbare[1], A. Mushavi[2]
[1]Elizabeth Glaser Pediatric AIDS Foundation, Technical Department - Communications & Advocacy, Harare, Zimbabwe, [2]Ministry of Health & Child Care, AIDS & TB, Harare, Zimbabwe
Presenting author email: czinyemba@pedaids.org

Background: Zimbabwe moved swiftly to adopt the 2013 WHO PMTCT regimen of initiating lifelong ART among all HIV-positive pregnant and breastfeeding women (Option B+) in November 2013. The new guidelines increase access to treatment, which requires increased human resource capacity in health systems. ART initiation in Zimbabwe has remained largely doctor-driven. Eighty percent of the country's pregnant women receive care from nurses, and as such, nurses are key to effective implementation of Option B+. The Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) engaged legislators to support policy reforms aimed at changing the scope of practice of nurses to allow them to initiate ART as a task sharing strategy in support of rapid transition to Option B+.
Methods: EGPAF provided technical and financial support to the Ministry of Health & Child Care (MOHCC) in developing a policy brief aimed at Parliamentary legislators. The policy brief simplified the technical narratives of the updated 2013 guidelines and highlighted policy-level reforms promoting nurse-led ART initiation and decentralization of ART to all health facilities. The MOHCC and EGPAF collaborated to hold dialogues with legislators in March and June 2014 using the policy brief to provide further guidance, generate discussion and keep up momentum on the importance of nurse-led and decentralized ART.
Results: Nearly 100 legislators and parliamentary staff attended the dialogues, held in March and June 2014. Elimination of mother-to-child transmission of HIV was prioritized on the legislative work plan. Legislators used the brief and dialogues to conduct fact-finding visits to selected central, provincial and district hospitals to review the progress in implementation of Option B+. Results from these findings were discussed in Parliament culminating in a motion - a critical first step towards policy change - moved through the House of Assembly. Members of Parliament used the information to hold community dialogues with their constituencies. The Parliamentarians appreciated the simplified policy brief and dialogues in understanding the policy-level action of the WHO 2013 guidelines.
Conclusions: Continued advocacy with legislators from varying backgrounds and with different levels of education is necessary to advance facilitative policy-level action for Option B+ and other HIV services.

Community involvement in biomedical prevention

TUPEC594

Facilitating community-led action for optimal uptake of prevention of mother to child transmission of HIV (PMTCT) services in vulnerable communities: the Elizabeth Glaser Pediatric AIDS Foundation-Zimbabwe community engagement program

C. Zinyemba[1], E. Tumbare[2], E. Chinake[2], W. Ushamba[3], T. Gutuza[4], A. Mahomva[2]
[1]Elizabeth Glaser Pediatric AIDS Foundation, Technical Department - Communications & Advocacy, Harare, Zimbabwe, [2]Elizabeth Glaser Pediatric AIDS Foundation, Technical Department, Harare, Zimbabwe, [3]Ministry of Health & Child Care, Mutasa District, Manicaland, Zimbabwe, [4]Ministry of Health & Child Care, Makoni District, Manicaland, Zimbabwe
Presenting author email: czinyemba@pedaids.org

Background: Zimbabwe's Demographic Health Survey (ZDHS) 2012 shows 65% of births occur in health facilities. The survey highlights strong relationship between uptake of antenatal care (ANC) and place of delivery. These high levels of home deliveries (35%) threaten Zimbabwe's efforts to eliminate pediatric AIDS, as opportunities are missed to test women and ensure enrollment in prophylaxes. Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) engaged communities in targeted regions to promote actions that address hindrances associated with suboptimal uptake of PMTCT services.
Methods: Manicaland Province was targeted for support due to high home delivery rates (35.7% of deliveries occur at home here). This rate is likely due to local beliefs that oppose biomedical interventions. In 2014, EGPAF facilitated community stakeholder dialogues in five districts in the province. Six Dialogues gathered community residents and leaders (religious and political) within a health facility catchment area to discuss PMTCT, build local understanding and promote ownership of the community's roles in supporting optimal uptake of PMTCT services including institutional delivery.
Partnering with other local health organizations, health services such as HIV testing and counseling, CD4 count testing, ANC, and well-baby checks were offered to residents during the dialogues. Aggregate PMTCT cascade data from local health facilities were presented, followed by discussions with different population groups (men, women, community leaders, youths, etc.) on their role to support PMTCT services.
Results: Nearly 4,000 people attended six community dialogues. Community leadership expressed appreciation of the platform to discuss local PMTCT aggregate data and understanding challenges associated with barriers to optimal service access. Local- led actions, based on decisions made during the dialogues included: community leaders in one district committed to building a shelter to provide temporary residence for expectant mothers to avoid the long distances; the local council in the same district allocated land for the shelter and a community business operator committed resources; In another district, the community raised its own resources and organized another community dialogue in a separate ward to address religious objections for facility deliveries.
Conclusions: Community dialogues promoted local-led action to addressing hindrances associated with sub-optimal uptake of PMTCT services.

TUPEC595

Engaging MSM key opinion leaders to create and sustain HIV and STIs services for a trusted community health centre Lagos, Nigeria

E. Shoyemi[1], J. Njab[2], S. Adebajo[2], D. Offie[1], P.L. Oladimeji[1], B. Keshinro[3]
[1]Population Council, HIV/AIDS, Lagos, Nigeria, [2]Population Council, HIV/AIDS, Abuja, Nigeria, [3]Walter Reed Programme-Nigeria, Abuja, Nigeria
Presenting author email: shoyemi.elizabeth@gmail.com

Background: Located in South west Nigeria with a population of 15million, Lagos State has HIV prevalence rate of MSM at 15.8%. Demand for HIV testing and counseling (HTC) services is low, condom use with both male and female partner is below 50% and self-reported STI symptoms are increasing (IBBSS 2010) with less than 10% of the population accessing such services due to their behaviours being stigmatized and criminalized making them hard to reach. A Trusted Community Health Centre (TCHC) is believed to have the capacity to reach the hard to reach MSM with HIV and STI services through the engagement of Key Opinion leaders (KOLs).
Methods: Within its 2 years of operation, 10 MSM volunteers were selected and trained in December 2012 from different Local Government areas in Lagos State based on their willingness to serve and having a large friend's network. Volunteers were trained for 5 days on HIV/AIDS basic facts, prevention, care and support for people living with HIV and benefits of counseling. Pre- and post- test questionnaires were used to assess change in knowledge. MSM specific Behaviour Change Communication (condoms, lubricants, leaflets, picture codes etc.) materials were given upon completion of training to commence work and act as Key Opinion Leaders (KOLs) to create HTC demand for the Community Health Centre using small group discussions, peer education and peer mentoring approach. Ongoing support from the TCHC was provided to the KOLs through regular visits to the mobilization sites and incentives.
Results: 100% volunteers completed the training. Pre and post- test questionnaire showed a 30% increase in knowledge. There was high level of active participation and contributions between the participants and facilitators. A total of 3,714 MSM above age 18 were tested and counselled and 3,221 cases of STIs were diagnosed and treated at the TCHC. There is an increased knowledge of HIV and increased uptake of condoms by the MSM who receive services at the TCHC.
Conclusions: MSM demonstrate higher knowledge acquisition after being trained. MSM as KOLs generate and sustain demand for HIV and STI services for stand- alone health facilities and promote positive health seeking behaviour of other MSM.

Integration of prevention interventions with care/treatment

TUPED761

Effective use of task shifting in strengthening 4 symptom screening for TB disease among PLHIV in rural clinics in Northern Nigeria

G. Egesimba, N. Nwokedi, E. Nwabueze, A. Abdulraheem, J. Kolin, A. Etsetowaghan
Management Sciences for Health, Clinical, Abuja, Nigeria
Presenting author email: gegesimba@msh.org

Background: To support seamless TB screening for the purpose of detecting TB suspects for further patient evaluation, including placing non-TB suspect on INH 300mg for prophylaxis against TB. WHO recommended 4 clinical symptom evaluation as follows: current cough, fever, weight loss, night sweat (adult patients parameters); and history of contact with persons with active TB, failure to thrive, fever, and cough (Pediatric specific) as a standard for clinical screening of TB. However, TB screening among PLHIV remains challenging. To address this, The USAID-funded Pro-ACT project implemented by MSH introduced non-clinicians to complement clinicians in screening PLHIV for TB.

There is a need to continue to evaluate the objectivity of this approach in the midst of current task shifting as emphasis is on more involvement of non-clinicians to take on minor non-complex clinical task.

Methods: HCWs of all cadres from 11 high volume facilities at all points of service provision were provided with the necessary skills through trainings, coaching, mentoring and use of TB screening SOPs to be able to screen PLHIV for TB. Patients who are TB suspects based on screening were referred to the laboratory for further evaluation while those found to be non- TB suspects were commenced on INH 300mg. TB screening data collected over a period of 15 months from June 2013 to September 2014 were reviewed.

Results: Findings from 11 high volume health facilities showed that 3,805 patients were screened for TB and found to be non-TB suspects before commencing INH 300mg for TB prophylaxis. Of this number, 1,019 have completed 6 months of IHN300mg. No patient has been reported to have developed TB following screening and commencement of IPT. This result demonstrates that with adequate capacity building and support, non-clinicians can support TB screening in health facilities, and TB prevention.

Conclusions: 4 symptom screening for TB has proven to be effective in excluding TB for patients declared non- TB suspect before commencement of IPT. The finding also supports TB screening by non-clinicians who are provided with adequate skills for TB screening.

TUPED762

Integrating direct provision of ART into TB services to increase ART uptake among TB-HIV co-infected clients in south west Uganda (2010-2014)

E. Natumanya Kajungu[1], M. Namubiru[1], C. Nerima[1], J. Seclen-Palacin[2], J. Asiimwe[3], E. Bitarakwate[1]
[1]Elizabeth Glaser Pediatric AIDS Foundation, USAID STAR-SW, Mbarara, Uganda, [2]Elizabeth Glaser Pediatric AIDS Foundation, Washington DC, United States, [3]Ministry of Health, Zonal TB and Leprosy Program Western Region, Mbarara, Uganda
Presenting author email: eknatumanya@gmail.com

Background: Despite mounting evidence suggesting better health outcomes among TB-HIV co-infected clients receiving antiretroviral therapy (ART), ART coverage among this group, globally, remains subpar. TB-HIV service integration is one strategy utilized to support uptake of ART among co-infected clients. Elizabeth Glaser Pediatric AIDS Foundation (EGPAF), in partnership with Uganda's Ministry of Health (MOH), supported the accreditation of TB sites to provide ART to co-infected clients in the 13 districts of SW Uganda.

Methods: EGPAF supported ART service delivery through facilitating accrediting of TB clinics to directly provide ART to co-infected clients at the TB clinic. Through onsite training, mentorship and coaching, we supported the integration of TB-HIV services into the TB diagnostic and treatment sites, including direct provision of ART. TB facilities received support in recording data in both TB and ART registers. Analysis of data from all the 203 supported-sites October 2010 to September 2014 was conducted in October 2014 to determine trends of ART initiation among TB-HIV co-infected clients. The percentage of TB-HIV co-infected clients receiving ART was calculated by dividing number of TB-HIV co-infected clients who had initiated ART by the total TB-HIV co-infected identified.

Results: During the analysis period, the percentage of TB-HIV co-infected clients initiated on ART increased three-fold. Despite the relatively constant number of TB-HIV co-infected clients identified in each one year period between October 2011 to September 2014, there was a progressive increment of TB-HIV co-infected clients that were initiated on ART in the same period, increasing from a low of 29.6% in 2010-11 to nearly 80% in 2013-14 (p value <0.001).

Analysis period	Number of TB sites providing ART	Number of TB-HIV co-infected clients identified	Number of TB-HIV co-infected clients started on ART	Percentage of TB-HIV co-infected clients started on ART
October 2010 - September 2011	20	1,664	493	29.6%
October 2011 - September 2012	36	1,860	1,032	55.5%
October 2012 - September 2013	50	1,632	1,109	68.0%
October 2014 - September 2014	94	1,489	1,175	78.9%

[Progress TB-HIV co-infected clients started on ART]

Conclusions: There has been a remarkable improvement in ART initiation among TB-HIV co-infected clients in SW Uganda from 2010 through 2014.This can be linked to improved TB-HIV service integration through the scale up of direct ART service provision at TB diagnostic and treatment facilities. Accreditation of TB service sites to provide ART to co-infected clients is an important way to increase the coverage of ART for the TB-HIV co-infected clients.

TUPED763

New strategies to increase HIV case finding in hard to reach populations

P. Smyrnov[1], A. Korobchuk[2], S. Muth[3], O. Denisiuk[1], D. Paraskevis[4], G. Nikolopoulos[5], J. Schneider[6], S. Friedman[7]
[1]International HIV/AIDS Alliance in Ukraine, Kyiv, Ukraine, [2]International HIV/AIDS Alliance in Ukraine, Odesa, Ukraine, [3]Quintus-ential Solutions, Colorado Springs, United States, [4]University of Athens Medical School, Athens, Greece, [5]National Development and Research Institutes, TRIP Office in Athens, Athens, Greece, [6]University of Chicago, Department of Medicine and Department of Health Studies, Chicago, United States, [7]National Development and Research Institutes, Institute for Infectious Disease Research, New York, United States
Presenting author email: smyrnov@aidsalliance.org.ua

Background: TRIP (transmission reduction intervention project) study in Odesa (Ukraine) began in November 2013 and aims to decrease HIV spread by the recently infected. TRIP is following risk networks of recent and other HIV-positive participants. At the same time in Odesa HIV screening of key populations is conducted within a GFATM (The Global Fund to Fight AIDS, Tuberculosis and Malaria) supported program. Here we compare percentage of positive cases found in TRIP and in HIV screening projects.

Methods: 604 TRIP participants were recruited through contact tracing and chain referral of sexual and injecting partners and others using the risk venues of HIV-positive participants. The GFATM HIV screening was conducted for 14,021 clients from various risk groups for all clients who were willing to test and had no prior positive test (self-reported) at 37 stationary and 2 mobile clinic sites (p by chi-square).

Results: In the screening project, 3.52% of clients were HIV-positive with higher % among sexual partners of PWID (10,53%). In TRIP, a higher proportion (23.7%; chi-squared = 566, p < 0.0001) of network participants were HIV-positive with similar HIV prevalence at one and two steps distance from the seed.

	Network of recently infected, HIV+		Network of long-term infected positive controls, HIV+		Total of HIV+	Total # of network participants who have been tested	Ratio (% HIV positive)
	HIV -	HIV +	HIV -	HIV +			
Screening/seeds*		21		17	38	38	
1 step from seeds	60	11	88	33	44	192	22.9%
2 steps from seeds	109	46	204	53	99	412	24.0%
Total (excluding seeds)	169	57	292	86	143	604	23.7%
*Many of the seeds were referred from the screening program and are not included as TRIP cases							

[Table. Participants in TRIP 1.11.13 till 31.1.14]

Conclusions: Focusing HIV screening on the risk networks of HIV-positive people significantly increases the percentage of HIV+ cases. TRIP, with only 4 staff members, found 143 HIV+ people while for the same time period screening project found only 493 cases with involvement of considerably higher number of staff at about 40 sites. The TRIP strategy, which uses a broader and deeper approach to network sampling than traditional contact tracing and routine on-site screening appears to be highly effective and resource efficient in HIV case finding and should be considered for HIV prevention projects among hard to reach populations.

Methods to improve provider quality, supply and tailoring of services

TUPED764

Are women enrolled in the PMTCT program breastfeeding their infants? Findings from a PMTCT electronic database in Zimbabwe

E.A.J. Tumbare Machakaire[1], E. Tachiwenyika[1], A. Mahomva[1], J. Mabuku[1], C. Muchuchuti[1], N. Mahachi[2]
[1]Elizabeth Glaser Pediatric AIDS Foundation, Technical Department, Harare, Zimbabwe, [2]Ministry of Health and Child Care, PMTCT, Harare, Zimbabwe
Presenting author email: etumbare@pedaids.org

Background: The WHO introduced infant feeding guidelines for HIV-infected women in 2010 and 2013 in the wake of global evidence demonstrating poor survival among HIV-exposed, non-breastfed infants. Zimbabwe adopted these guidelines; adapting them to include exclusive breastfeeding for newborns for the first six months with introduction of solids and continued breastfeeding for up to 24 months.

However, challenges exist in monitoring breastfeeding patterns among HIV-infected postnatal attendees in Zimbabwe. To inform Zimbabwe's Ministry of Health and Child Care (MOHCC) on

the status of implementation of the guidelines regarding breastfeeding, and program implementation, the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) captured and analyzed data from facility registers for women attending antenatal and postnatal care through an electronic database (EDB) available at 36 representative sites throughout Zimbabwe.

Methods: From January to December 2013, infant feeding data for 339 HIV-infected women (at birth, six weeks, three, nine and twelve months) were collected from registers at EDB sites. Analysis examined percentages of women exclusively breastfeeding, mixed feeding or formula feeding. The objective of the analysis was to assess to what extent women were adhering to infant feeding guidelines as set in the national PMTCT program. Data on HIV-retesting at 18 months for HIV exposed infants was also evaluated.

Results: From January to December 2013, six-week exclusive breastfeeding among HIV-infected women at these sites remained high at 94%. By three months, 75% were still exclusively breastfeeding; however, the proportion fell to about 21% at the six-month review (fig 1). Completeness of data captured in the registers covered by the EDB varied considerably from site-to-site and trends after the first six months were not collected. Infant 18-month HIV tests were only recorded in about 10% of cases; consequently, 18-month mother-to-child HIV transmission rates could not be analyzed.

Conclusions: Recommendations for six-month exclusive breastfeeding are only adhered to by a fifth of women attending EDB sites in Zimbabwe. There is a need to improve infant feeding counseling, better monitor long-term breastfeeding patterns; strengthen 18 month infant re-testing and improve completeness of data recording.

TUPED765

Quality of care and treatment for HIV-positive patients in two rural health districts in sub-Saharan Africa

S. Nahrgang[1,2], M. Sarker[2,3], A. Sié[4], H. Masanja[5], H.W.F. Neuhann[2], ARVMAC
[1]WHO Regional Office for Europe, DCE, Copenhagen, Denmark, [2]Heidelberg University, Institute of Public Health, Heidelberg, Germany, [3]BRAC University, Dhaka, Bangladesh, [4]Centre de Recherche en Santé de Nouna, Nouna, Burkina Faso, [5]Ifakara Health Institute, Ifakara, Tanzania, United Republic of
Presenting author email: sa.nahrgang@gmail.com

Background: Quality of care is a determinant for access to care, adherence to treatment as well as retention in care and is essential to ensure good health outcomes and to minimize transmission, morbidity and mortality. Nevertheless, providing good quality care and treatment is specifically challenging in health districts with scarce resources. This study assessed the quality of care and treatment for PLHIV during the phase of rapid scale-up of ART in resource-limited health districts in Tanzania and Burkina Faso in diverse epidemiological context focusing on interpersonal, service delivery and process of care related quality.

Methods: A cross-sectional study design was adopted with mixed-methods approach, that included
(i) key informant interviews;
(ii) client survey;
(iii) checklist for patient-provider encounter, health facility infrastructure, medical files; and
(iv) participatory observations.
Demographic information was collected from Demographic Surveillance Systems data. All ART providing health facilities in the respective districts were included. A quality score with a maximum score of 5 was constructed to compare performance across facilities in both countries.

Results: None of the health facilities received performance scores higher than 3.5 (3.2-3.5) indicating an average level of quality. The difference between facilities was not statistically significant. Four main areas of weakness were:
(a) inappropriate care delivery processes, including lack of adequate physical examinations and laboratory testing;
(b) incomplete assessment of patient's readiness for ART eligibility;
(c) insufficient provision of information on ART implications; and
(d) incomplete and unsystematic health record and referral systems.

Conclusions: During the crucial phase of rapid scale up all health facilities included in this study reported difficulties in coping with an increased demand for ART and 70% of the health facilities did not meet the World Health Organization's "four minimum requirements" for ART provision.
Main challenges encountered included the number and capacity of health workers. Nurses often provided the largest share of ART consultations, however were less likely to receive appropriate training and capacity building opportunities. Any further expansion of ART provision requires innovative models of care delivery and sustained capacity building for HCWs.

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TUPED766

Determinants of forecast accuracy for paediatric antiretroviral drugs in Kenya

S. Njogo[1], G. Osanjo[2], E. Guantai[2]
[1]National AIDS/STI Control Program, HIV Commodities, Nairobi, Kenya, [2]University of Nairobi, School of Pharmacy, Nairobi, Kenya
Presenting author email: smnjogo2012@gmail.com

Background: To ensure uninterrupted supply for antiretroviral drugs, the Ministry of Health in Kenya conducts annual forecasting and supply planning. This has been a laborious and costly exercise. Monthly review of available stock at national store and quantities under procurement have revealed existing and/or potential overstocking and/or under stocking of various paediatric antiretroviral drugs. Dosing of antiretroviral drugs among children is weight dependent. Demand forecast for paediatric antiretroviral drugs has been challenging due to lack of data on proportion of children on various weight categories. As such, assumptions are made that children below age of 15 years weigh < 25Kg and use paediatric formulations. This study aimed to establish forecast accuracy for paediatric antiretroviral drugs in Kenya, and determine factors affecting forecast accuracy.

Methods: Mean Absolute Percentage Error (MAPE) was calculated for seven paediatric antiretroviral drugs for periods 2010/11, 2011/12 and 2012/13. Randomness of forecast errors was tested using Augmented Dickey Fuller and Run tests. Retrospective longitudinal cohort design was used to determine effect of age, weight and sex on antiretroviral formulations dispensed to children at a selected public health facility. Univariate, bivariate, within-subject effects and population-averaged logistic regression data analysis were done on longitudinal data.

Results: There were 311, 306 and 285 children studied for periods 2010/11, 2011/12 and 2012/13, respectively.

Characteristics	July 2010	July 2011	July 2012
Sex: Male n(%)	171 (55.0)	171 (55.9)	169 (55.8)
Female n (%)	140 (45.0)	135 (44.1)	126 (44.2)
Age(years) Median(IQR)	9.2 (6.8,12.0)	9.6 (7.3, 12.0)	10.3 (7.5,12.5)
Weight(Kg) Median(IQR)	26 (20,32)	27 (21, 32)	28 (21, 34)
Weight category (Kg)			
<25Kg n(%)	140 (45.0)	118 (38.5)	100 (35.1)
≥25Kg n(%)	171 (55.0)	188 (61.5)	185 (64.9)

[Demographic characteristics]

Forecasts for six paediatric formulations namely abacavir/lamivudine-60/30mg; zidovudine/lamivudine-60/30mg; zidovudine/lamivudine/nevirapine-60/30/50mg; efavirenz-200mg; Lopinavir/ritonavir-80/20mg and zidovudine-10mg/ml were found to be inaccurate. Only nevirapine-10mg/ml recorded reasonable forecasts with MAPE < 50% for the three periods studied. Forecast errors were non-random for all products. More than 50% of children weighed ≥25Kg for the three periods. Children were likely to turn 25Kg at age of 8 years as opposed to the assumed 15 years. Only 19.0%, 30.3% and 32.6% of children used paediatric formulations in 2010/11, 2011/12 and 2012/13 respectively.

Conclusions: Considerable forecast inaccuracies were found for six of the seven products. Only nevirapine-10mg/ml had reasonably accurate forecasts. Forecast errors for all products exhibited non-randomness. Assumptions that children aged < 15 years weigh < 25Kg and use paediatric formulations were incorrect. Weight was found to be an important determinant of formulation selection.

TUPED767

HIV-infected adolescent and caregiver experiences of HIV stigma and discrimination in Kenya

L. Fischer[1,2], W. Nyandiko[2,3], M. Scanlon[1,2], M. McHenry[1,2], V. Naayu[2,4], R. Vreeman[1,2,3]
[1]Indiana University School of Medicine, Department of Pediatrics, Indianapolis, United States, [2]Academic Model Providing Access to Healthcare (AMPATH), Eldoret, Kenya, [3]Moi University, College of Health Sciences, School of Medicine, Department of Child Health and Paediatrics, Eldoret, Kenya, [4]Moi University, College of Health Sciences, School of Medicine, Department of Behavioural Sciences,, Eldoret, Kenya
Presenting author email: lydfisch@iupui.edu

Background: There are few data exploring how HIV stigma affects the lives and HIV care of those infected or affected by HIV. We sought to better understand how HIV stigma is experienced by HIV-infected adolescents and caregivers in Kenya.

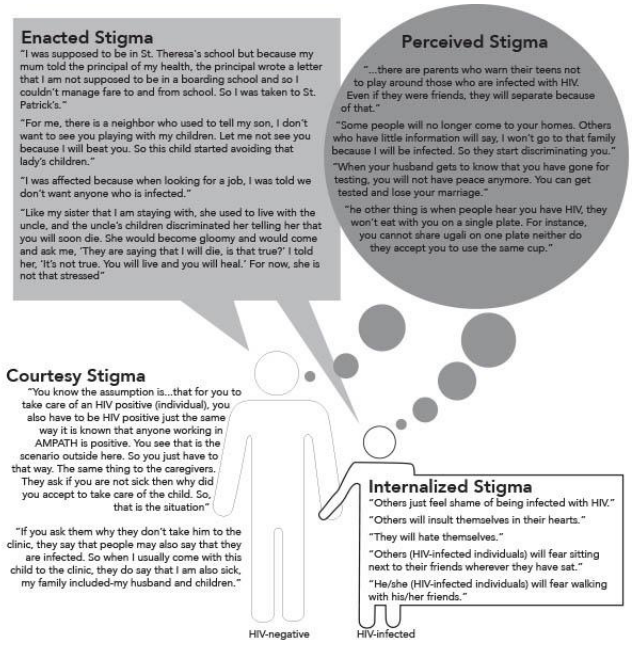
Methods: We conducted a qualitative study using focus group discussions (FGD) at 3 HIV clinics in western Kenya. Separate FGDs were held for HIV-infected adolescents (aged 10-14 years) and for caregivers of HIV-infected children. A trained facilitator led FGD in Kiswahili using a semi-structured interview guide based in grounded theory and covering multiple aspects of HIV-related stigma. FGD recordings were translated into English, transcribed, and analyzed using constant comparison, progressive coding, and triangulation to arrive at a contextualized understanding of adolescent and caregiver experiences of HIV stigma.

Results: Forty adolescents (mean age: 13 years) participated in 5 FGD and 53 caregivers (mean age: 40 years) participated in 6 FGD. Most caregivers were the biological mother of an HIV-infected child (51%), aunt or uncle (19%) or biological father (13%). Participants described 4 types of HIV stigma: perceived, internalized, enacted, and courtesy (Table 1, Figure 1). Perceived stigma was the most common type of stigma identified by both adolescents and caregivers and was described as a deep fear of discrimination, specifically in the form of facing isolation and gossip within the community. Fears of loss of social support or damage to relationships were more common than fears of physical forms of stigma (e.g., fear of losing jobs, bullying/abuse, or losing community resources.) Fear of stigma motivated a number of treatment-related behaviors including secrecy about HIV status, not taking medicines in front of others, and hiding medicines, although caregivers alone reported attending distant clinics to avoid recognition. Reports of instances of enacted stigma were rarer than these prominent fears would suggest, and were less common with adolescents than with caregivers.

Conclusions: HIV-infected adolescents and caregivers described an environment characterized by fear of HIV stigma and discrimination in western Kenya. These perspectives offer valuable insight into the experiences of living with HIV in this setting and may inform interventions.

Courtesy Stigma	Stigma experienced by an HIV negative individual based on their relationship with an HIV-infected individual
Internalized Stigma	Stigma directed at oneself
Enacted Stigma	Accounts of stigma lived in real time
Perceived Stigma	Fear of future stigma

[Table 1: Types of Stigma Described by HIV-Infected]



[Figure 1: Illustrative Descriptions HIV Stigma]

TUPED768

What factors are critical in improving client satisfaction with PMTCT services in Zimbabwe? Findings from a client satisfaction survey

B. Mutede[1], E. Tachiwenyika[1], R. Musarandega[1], B. Khabo[2], M. Mhangara[3], E. Tumbare[4]
[1]Elizabeth Glaser Pediatric AIDS Foundation, Technical Department, Harare, Zimbabwe, [2]Ministry of Health and Child Care Zimbabwe, AIDS and TB Unit, Harare, Zimbabwe, [3]Ministry of Health and Child Care, AIDS and TB Unit, Harare, Zimbabwe, [4]Elizabeth Glaser Pediatric AIDS Foundation, AIDS and TB Unit, Harare, Zimbabwe
Presenting author email: bmutede@pedaids.org

Background: Quality improvement (QI) in health care aims to improve quality of care by modifying service delivery processes to optimize health services and client satisfaction. In Zimbabwe, client satisfaction with PMTCT services is not well-documented. Through support to the Ministry of Health and Child Care (MOHCC), the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) conducted a survey to assess client satisfaction with PMTCT services.

Methods: EGPAF conducted a descriptive cross-sectional survey on client satisfaction with services at 43 rural and urban health facilities across 6 provinces in November 2014. Interviews and focus group discussions were conducted with pregnant and breastfeeding women attending antenatal care (ANC) and postnatal care (PNC) clinics after receiving care. Client satisfaction with PMTCT services was assessed through 2-5 point bipolar Likert scales on care experiences and perceptions such as waiting time and confidentiality during consultation. Availability and functionality of client involvement systems was also assessed. Logistic regression was conducted to determine independent factors associated with client satisfaction. Ethical approval was granted by Medical Research Council of Zimbabwe.

Results: Five hundred and sixty six, (300 ANC and 266, PNC) women were interviewed. Eighty two percent lived within 10km of the health facility. Eighty nine percent of the respondents were satisfied with PMTCT services received on the assessment day. Having had a physical health assessment by a clinician was independently associated with client satisfaction (AOR=2.12, p=0.04). Perceived long waiting periods before receiving services was associated with client dissatisfaction (AOR=0.36, p=0.008). Although not statistically significant, giving out clear instructions to clients was associated with client satisfaction (AOR=2.40, p= 0.07). Systems to gather client views and comments (health center committees, comments books and suggestion boxes) were present; however client awareness of the platforms was low (43%, 5% and 29% respectively).

Variable	Adjusted Odds Ratio	95% Confidence Interval	Coefficient	P- value
Long client waiting time	0.37	0.17- 0.78	-1.01	0.0087
Being physically examined during consultations	2.12	1.01- 4.46	0.75	0.047
Being given clear instructions on how to take medication	2.40	0.92- 6.22	0.87	0.073

[Determinants of satisfaction with PMTCT services]

Conclusions: Client satisfaction with PMTCT services in Zimbabwe is high. Efforts to further improve client satisfaction should target shortening client waiting time and promoting good medical practice that involves physical examination of clients during consultations. This requires more health staff time, which could be accomplished through task shifting. Clients should be continuously engaged by promoting use of available client feedback systems.

TUPED769

Congestion in urban HIV treatment clinics in Lusaka, Zambia: an assessment of factors to inform decongestion solutions

S. Moberley[1], A. Mwango[2], F. Mpasela[3], H. Subramaniam[4], M. Prust[5], M. Prescott[4], G. Kadimba[6], C. Mbewe[7], B. Chibuye[3], J.W. Van den Broek[3], E. McCarthy[8]
[1]Clinton Health Access Initiative, Applied Analytics Team, Melbourne, Australia, [2]Ministry of Health, Zambia, Lusaka, Zambia, [3]Clinton Health Access Initiative, Lusaka, Zambia, [4]Clinton Health Access Initiative, Applied Analytics Team, New York, United States, [5]Clinton Health Access Initiative, Applied Analytics Team, Boston, United States, [6]Ministry of Community Development Mother and Child Health, Lusaka District Health Office, Lusaka, Zambia, [7]Ministry of Health, Pharmacy, Lusaka, Zambia, [8]Clinton Health Access Initiative, Applied Analytics Team, Lusaka, Zambia
Presenting author email: emccarthy@clintonhealthaccess.org

Background: In 2013, Zambia adopted national antiretroviral therapy (ART) guidelines that increased the number of treatment-eligible patients. Concern over the impact of crowding and congestion in Lusaka's ART clinics on retention rates prompted an assessment to gather evidence on the critical factors contributing to and possible solutions for facility congestion, with particular attention focused on barriers to 3-month refills for stable patients.

Methods: In November 2014, eight of the eligible ART clinics were randomly selected to participate in the assessment. ART registry records for 80 stable patients were reviewed and 84 patient exit interviews and 16 key informant interviews with clinicians were conducted. We obtained stockout history from medical store registers and observed patient time spent waiting for and receiving care at each clinic station.

Results: Across sites, between 8% and 70% of stable patients received a 3-month supply of antiretroviral drugs (average 46%). Key informant interviews suggested shortages of staff and poor filing systems as causes of congestion, and inconsistent supply of drugs and the need to frequently return for lab results owing to lab systems challenges as barriers to 3-month prescriptions. From January to October 2014, 3 of 8 facilities experienced at least one stockout of the recommended first-line ART regimen (TDF+3TC+EFV). Average stockout duration was 2.5 days (1-4.5 range). Most (77.4%) patients reported that long wait times were the primary reason for difficulty receiving care. Patients who only attended the clinic to refill their ARVs from the pharmacy (47.5%) spent an average of 1 hour 34 minutes from triage to departure, while patients coming for a clinical visit spent on average 2 hours 10 minutes. Actual consultation time with a clinician was 5 minutes on average.

Conclusions: A large percentage of patients attended the facilities only to collect a refill from the pharmacy. Although Zambia's national ART guidelines recommend that stable ART patients receive 3-month prescriptions, we found wide variation in refill practices across sites. We have tailored an intervention using quality improvement officers to troubleshoot challenges and improve refill practices. This work is expected to contribute to clinic decongestion and pave the way for additional service delivery improvements.

TUPED770

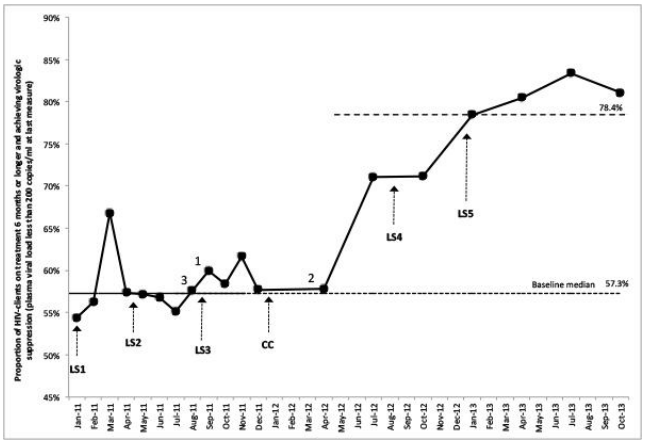
Descriptive case study of a quality improvement intervention to implement evidence-based HIV care and improve HIV care and treatment outcomes in 17 British Columbia sites

C. Clarke[1], T. Cheng[1], K. Reims[2], C. Steinbock[3], S. Milligan[4], M. Thumath[5], D. Hall[6], E. Kanigan[7], J. Postnikoff[8], J. Toy[9], R. Undi[8], R. Barrios[1]
[1]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada, [2]CSI Solutions, Lafayette, United States, [3]National Quality Center, New York, United States, [4]Northern Health, Prince George, Canada, [5]BC Centre for Disease Control, Vancouver, Canada, [6]Vancouver Coastal Health, Vancouver, Canada, [7]First Nations Health Authority, Victoria, Canada, [8]Living Positive BC, Vancouver, Canada, [9]St. Paul's Hospital Pharmacy, Vancouver, Canada
Presenting author email: cclarke@cfenet.ubc.ca

Background: In high-income countries where highly active antiretroviral therapy (HAART) may be more widely available via established healthcare systems, gaps persist across the HIV continuum of care. In the intervention setting of British Columbia (BC), Canada, only 46.6% of the HIV-diagnosed population were adherent to treatment and achieving virologic suppression in 2010. In December 2010, a quality improvement (QI) initiative was launched to disseminate and implement evidence-based practices for improving HIV care and treatment outcomes.
Methods: HIV care sites across BC were recruited to participate in a quality initiative using Breakthrough Series Collaborative methodology. Between December 2010 and October 2013, sites learned about and applied evidence for improving HIV care and reported monthly qualitative descriptions of their changes with four numerical care quality indicators. From January 2011 to 2012, two reviewers analyzed reports and assigned implementation scores based on objective criteria (Table 1). Quality indicators were pooled and interpreted using accepted probability-based run charts rules (RCR).

0.5	No Changes
1.0	Forming Team: Team has been formed; HIV-population has been identified; Aim has been determined.
1.5	Project planning underway: Team is meeting, discussion is occurring, plans for the project have been made and measures defined.
2.0	Activity, but no changes: Team actively engaged in development, learning, and discussion about the Chronic Care Model (CCM), but no changes have been tested. Team aim is consistent with the Collaborative charter.
2.5	Changes tested: a) Data on all key quality measures are reported in run charts; and, b) Tests have been initiated in at least two components of the CCM
3.0	Modest improvement: Initial test cycles have been completed in at least four components of the CCM. Implementation has begun for at least one component of the CCM. Evidence of modest improvement1 in one or more required measures.
3.5	Improvement in outcomes: At least one required outcome measure must show modest improvement. The required measure used to achieve modest improvement has held the gain or improved (gotten closer to goal) and at least one other required measure meets the criteria for modest improvement. Changes have been implemented in at least three components of the CCM and test cycles have been completed on all components of the CCM.
4.0	Significant improvement: The CCM has been implemented, with at least one change implemented in each component of the CCM. Evidence of significant improvement in required outcome measures. All required process measures are at least 50% of the way to goal. Plans for spread of improvement are in place.
4.5	Sustainable improvement: Sustained improvement in required outcomes measures. All required process measures are at least 75% of the way to goal. Spread to a larger population has begun.
5.0	Outstanding sustainable results: All components of the CCM are integrated into system of care. All goals have been accomplished. Spread to another area is well underway.

[Table 1: Objective criteria for assigning monthly]



[Proportion on treatment and suppressed]

Results: A total of seventeen teams with a pooled median population of 2,296 HIV-patients in 2011 joined the initiative. In year one, median implementation scores increased from 1.0 (SD=0.38) to 3.3 (SD=0.85) on a scale ranging from 0.5 (no activity) to 5.0 (full implementation of the Chronic Care Model (CCM), all quality indicators at 95%, and spread of changes beyond the initial population). A total of 29% of sites achieved an implementation score of 4.0 or greater, indicative of comprehensive CCM implementation and evidence of improvements, signaled by RCR, in quality indicators. Analysis of pooled quality indicators using RCR signaled evidence of improvement for patient engagement in care (median 88.8% to 90.4%), and the proportion of patients on treatment for six months or more and achieving virologic suppression (median 57.3% to 78.4%) (both $p < 0.05$).
Conclusions: This multi-site QI intervention successfully increased implementation of evidence-based practices to improve HIV care quality outcomes. The overall success of the intervention points to opportunities for spreading this methodology to improve HIV care and treatment outcomes. Scaling-up time-limited interventions such as this have potential to maximize the efficacy and efficiency of publicly-funded healthcare systems across Canada and in other high-income countries.

TUPED771

Forecasted demand for ARV medicines in low and middle income countries up to the end of 2018

V. Habiyambere, J. Perriens, B. Dongmo-Nguimfack
WHO, Dept of HIV, Geneva, Switzerland
Presenting author email: perriensj@who.int

Background: With increasing momentum for the 90-90-90 objectives of UNAIDS, it is critical that global supply of antiretroviral drugs be forecasted and their production planned. To ensure that enough ARVs are produced globally, WHO convenes a global ARV Forecasting Technical Working Group, with UNAIDS, the Clinton Foundation Health Access Initiative (CHAI), the Global Fund, the Futures Institute, PEPFAR, and UNICEF which annually develops 3-year forecasts of the demand of ARVs. The forecasts for 2014 to the end of 2018 are presented.
Methods: The demand forecast is based on
1) the annual WHO survey on ARV use,
2) volume of individual ARVs in the global procurement reporting mechanism,
3) CHAI projections for 22 high volume countries,
4) quantification data from the Global Fund and PEPFAR, and
5) the projected evolution of ART needs from UNAIDS and the Futures Institute.
Three forecast scenarios were used and averaged arithmetically to generate the projected demand. Forecasts were broken down by active pharmaceutical ingredient and adults vs children.
Results: The preliminary forecasted demand for ART will increase from 13.7 million person-years (PYR) by mid- 2014 to 24 million PYR by end 2018, comprising 22.8 million PYR of adult and 1.375 M PYR of paediatric ART. The market share of tenofovir will increase from 50% of treated patients in 2013 to 68% in 2018, that of AZT will decrease from 43% to 28 %, and that of d4T from 8% in 2013 to less than 1% in 2018. That of EFV will increase from 48% in 2013 to 72%, and NVP will reduce to 28% in 2018. Second line ART uptake will increase slowly from 4.4% in 2013 to 6.0% in 2018. Insufficient data were available to project the uptake of third line drugs. The above forecasts and their margins of uncertainty will be refined in the next few months.
Conclusions: While there continues to be uncertainty on the exact number of people who will be able to access ART in the future, our preliminary forecasts suggest that close to 24 million people will be on ART by the end of 2018.

TUPED772

The demand for CD4 testing, viral load and early infant diagnostic testing in low and middle income countries will grow strongly between now and 2018

V. Habiyambere[1], J. Perriens[2], M. Perez-Gonzales[2], B. Dongmo-Nguimfack[2], Diagnostic Access Initiative Forecasting Technical Working Group
[1]WHO, HIV Department, Geneva, Switzerland, [2]WHO, Geneva, Switzerland
Presenting author email: habiyamberev@who.int

Background: The 90-90-90 targets require more access to diagnostic testing, in particular for viral load (VL). In addition, if VL is increasingly used, there will be less need for CD4 testing to monitor treatment. To clarify how much demand there will be for CD4, VL and EID testing in low and middle income countries, and ensure the timely production of diagnostic tests, WHO convened, as part the Diagnostics Access Initiative, a Technical Working Group comprised of UNAIDS, CHAI, UNICEF, Global Fund, CDC, PEPFAR, and Futures Institute.
Methods: The preliminary demand forecast by the workng group are at present based on 1) WHO surveys on diagnostics use in 2012, 2013 and 2014, 2) volume of CD4, VL and EID tests recorded in WHO and Global Fund databases, 3) projections by the Clinton Foundation Health Access Initiative for 22 high volume countries, 4) PEPFAR/SCMS quantification data, and 5) projected evolution of HIV diagnostics based on country targets. Four forecast scenarios were used and averaged arithmetically to generate the preliminary point estimates

of the projected demand. These estimates are being refined and more refined estimates will be presented.

Results: The preliminary forecasts indicate that, from 2014 to 2018, the demand for CD4 tests will increase from 16.6 to 25.8 million CD4 tests (1.5 times); that of VL tests from 5.8 to 17.1 million tests (3 times) and that of EID tests from 0.9 to 1.7 million tests (double). Per person on treatment, CD4 tests will in the future be used less often than now, but the uptake of VL will be insufficient to document viral suppression in all people expected to be receiving treatment in 2018.

Conclusions: The availability of data limits the ability to forecast the future use of HIV-related diagnostics, the demand of all of CD4, VL and EID will increase between now and 2018. This increasing demand should enable the introduction of new - including point of care - technologies.

Healthcare workers and volunteers: training, mentoring, retaining, task shifting, safety

TUPED773

Community Lay Cadres' contributions and over task-shifting in expansion of antiretroviral therapy to rural health centres in Zambia

K. Komada[1,2], M. Chirwa[3], C. Msiska[3], V. Chipeta[4], K. Chibwe[4], P. Nambara[5], P. Mwaba[5], N. Kayama[6], C. Dube[6], A. Mwango[7]
[1]Japan International Cooperation Agency, Project for Scaling up of Quality HIV/AIDS Care Service Management (SHIMA), Lusaka, Zambia, [2]National Center for Global Health and Medicine, Bureau of International Medical Cooperation, Tokyo, Japan, [3]Chongwe District Community Medical Office, Chongwe, Zambia, [4]Kalomo District Community Medical Office, Kalomo, Zambia, [5]Kazungula District Community Medical Office, Kazungula, Zambia, [6]Mumbwa District Community Medical Office, Mumbwa, Zambia, [7]Ministry of Health, Clinical Care and Diagnostic Services, Lusaka, Zambia
Presenting author email: shimaproject@gmail.com

Background: The Government of Zambia has committed to bringing antiretroviral therapy (ART) as close to the family as possible. However, limited human resource for health services especially in the rural health centres (RHCs) is one of the major challenges and the expansion of ART services has brought substantial workload to health workers. In this situation, community lay cadres (CLCs) are performing important roles to support the services at RHCs, but over task-shifting to CLCs was sometimes observed such as drug dispensing and blood collection. The study aims to understand their working volumes and roles in ART services.

Methods: Self-administered working records were distributed to CLCs who were particularly and actively involved in ART services in 16 RHCs in 4 districts namely Chongwe, Kalomo, Kazungula and Mumbwa, in Zambia. Their three-month working records from September to November 2012 were collected. Descriptive analysis was done to assess their working volumes and roles. Chi-square test was used to examine the relationship between over task-shifting to CLCs and client burden in RHCs.

Results: The working records were collected from 128 CLCs. The median of average working hours per week during observation period was 22.9 [IQR:16.4-29.8] hours. 93.8% of CLCs were involved in health education and prevention, 78.1% in ART-related record keeping, 77.3% in checking body temperature and 56.3% in checking blood pressure. Some experienced over task-shifting such as drug dispensing (22.7%) and blood collection (6.3%). Out of 16 rural health centres, 9 centres handled more than 20 clients per health worker on ART service day while 7 centres handled less 20 clients. 37.7% (95%CI: 26.0-49.4) of CLCs in RHCs with high client burden experienced over task-shifting, compared to 11.9% (95%CI: 3.4-20.4) in RHCs with lower burden. (p=0.001).

Conclusions: CLCs are essential manpower to implement the health services at RHCs. However, carrying out clinical procedures such as blood drawing and drug dispensing are beyond CLCs' capacities. Such over task-shifting to CLCs should be carefully monitored. The sufficient allocation of the human resources to RHCs and the adequate system to supervise CLCs are urgently required for sustainable and quality ART service at rural area.

TUPED774

Reductions in annual ART costs in Uganda: implications for future ART resource needs and task-shifting

L. Vu[1], L. Ssali[2], L. Buzaalirwa[3], S. Waliggo[4], B. Zieman[1], N. Jani[1], S. Okoboi[2], M. Etukoit[2], P. Kiyingi[3], J. Nsamba[4], S. Kalibala[1]
[1]Population Council, Washington DC, United States, [2]The AIDS Support Organization, Kampala, Uganda, [3]Uganda Cares, Kampala, Uganda, [4]Kitovu Mobile, Kampala, Uganda
Presenting author email: lvu@popcouncil.org

Background: Data on per-patient ART costs provide information for budgeting, planning, and modeling cost and cost-effectiveness. We estimated the cost per ART visit for three large AIDS treatment organizations in Uganda. Kitovu Mobile (KM) uses a community outreach approach and services are delivered at the community level; Uganda Cares (UC) has a mixed model: Standard (UC-S) and Task-Shifted (UC-TS); and TASO uses a hierarchical structure with one headquarter, four regional offices, and 11 service delivery centers all associated with community drug distribution points (CDDPs). Of these three models, KM is considered highly task-shifted, while UC and TASO have a mixture of highly- and minimally- task shifted models.

Methods: Retrospective costs directly incurred by the providers in 2012 were collected. Provider costing data reflected both financial costs of services for ART treatment such as drug and personnel costs; and economic costs such as equipment, training, and construction. The cost per client visit was estimated, as provider records did not account for numbers of unique patients.

Results: The average estimated cost per client visit was $21 for KM; $26 for UC; and $39 for TASO clients. For TASO and UC, personnel and operational costs accounted for approximately 50% of total costs; while drugs and laboratory account for the rest. For KM, drugs and laboratory account for over 60% of the total costs. Given that each patient makes an average of four visits per year, the annual provider ART cost per client ranges from $100 to $160.

Conclusions: Outreach or more task-shifted models cost less to service providers. The analysis also revealed a reduction in annual ART cost compared to findings from previous studies in Uganda and similar contexts. This might be due to increases in number of clients, reductions in drug costs, and the fact that these three organizations are mature. In addition, these three task-shifting models did not compromise service quality (80% reported satisfied) and retention rate (80% at 18 months) based on our separate analysis. Further studies are needed to identify and understand the quality and effectiveness of each model, as well as the economic costs to the clients who receive their services.

TUPED775

The effectiveness of men who have sex with men (MSM) sensitivity training for Nigerian health care providers (HCPs)

C. Ifekandu, S. Sangowawa, A. Oginni, D. Iriaye, I. Suleiman, J. Njab, B. Abdullahi, S. Adebajo
Population Council, Nigeria Office, HIV Department, Lagos, Nigeria
Presenting author email: cifekandu@popcouncil.org

Background: Health care providers (HCPs) in Nigeria receive little or no training of the healthcare needs of men who have sex with men (MSM) limiting the quality and effectiveness of comprehensive HIV prevention and treatment services. Consequently, most MSM disguise themselves to access services which limit the quality of care provided partly due to challenges related to stigma and discrimination, and breach of confidentiality.

Objective: To assess the knowledge of healthcare providers on effective intervention for MSM.

Methods: We trained 122 HIV focal persons drawn from 60 health facilities from twelve Nigerian states, the participants were requested to complete a pre-training questionnaire to assess their level of working experience with key populations as a baseline. Participants included male and female doctors, nurses and counselors/testers. A test was administered to measure their knowledge on MSM sexual risk practices, HIV prevention and healthcare needs and also to assess their attitudes (including homophobia) and beliefs and how it affects service uptake by key populations particularly MSM prior and immediately after the training to ascertain the impact of the training.

Results: The mean age of the HCP was 38years +/- SD Of the 122 HCPs (45% female, 55% male;85% counsellor/testers; 15% doctors and nurses; 92% working in government facilities) from 42 health facilities were trained, of which 105 attempted the test questions. At the baseline, few HCPs reported any prior sensitivity training on MSM. Most of the HCPs had limited knowledge of MSM sexual health needs. Over 90% of the HCPs believed that homosexuality is a mental illness. 85% do not consider MSM, FSW and PWID as key populations for HIV infection. 45% lacked knowledge on MSM anal sexual practices. The post-test showed that homophobic attitudes had decreased significantly by the end of the training; the health care providers have acquired basic knowledge compared to the pre-test.

Conclusions: Scaling up MSM sensitivity training for Nigerian HCPs is likely to be a timely and effective means to improve their understanding of MSM-related health issues, reduce homophobic sentiments and enhance their capacity to provide responsive HIV prevention, treatment and care services in a supportive and non-stigmatizing environment.

TUPED776

HIV training program is effective to increase HIV knowledge among health care workers in Georgia

O. Chokoshvili[1], N. Gulua[2], N. Chkhartishvili[3], M. Tsintsadze[1], N. Chokoshvili[1], T. Tsertsvadze[4]
[1]Infectious Diseases, AIDS and Clinical Immunology Research Center, Epidemiology, Tbilisi, Georgia, [2]International Academy for Continuing Medical Education, Diretor Executive, Tbilisi, Georgia, [3]Infectious Diseases, AIDS and Clinical Immunology Research Center, Sceintific Diretor, Tbilisi, Georgia, [4]Infectious Diseases, AIDS and Clinical Immunology Research Center, Diretor General, Tbilisi, Georgia
Presenting author email: ochokoshvili@gmail.com

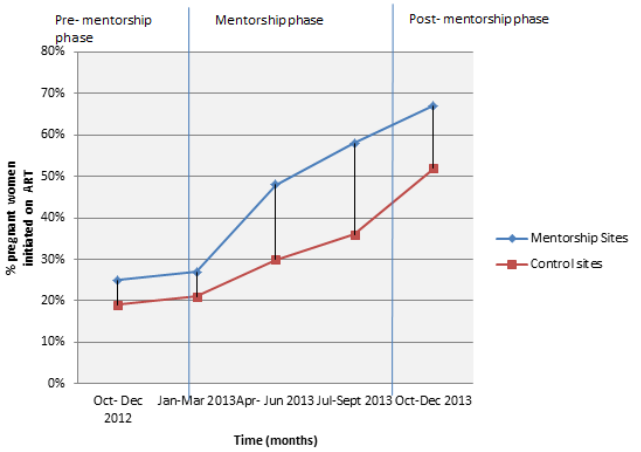
Background: Increasing HIV related knowledge to reduce HIV associated stigma is crucial intervention to fight against HIV epidemic. We proposed a study to asses the improvement of HIV knowledge and to reveal its associated factors, among healthcare workers participating in HIV training program. The program provided HIV trainings for healthcare workers to increase HIV knowledge and reduce stigma in Eastern European country of Georgia.
Methods: A total of 1880 health professionals participated in HIV trainings during 2012-2013 years. HIV trainings were provided in 5 regions of Georgia. HIV knowledge was assessed using identical self administered pretest-posttest survey questionnaires before and after training. Questionnaire included demographic and professional information, as well as multiple choice questions about HIV: diagnostic, transmission, ART treatment and care. We applied "R for windows" statistical package to produce descriptive statistics, paired t test and multiple linear regression models.
Results: From 1880 health professionals participating 84 % (1575) were females; median age was 41, IQR 20(31, 51). Participants with high medical education and nurses represented 83.1 % (1562) and 16.9% (318) consecutively. The mean percent of correct answer at pre-test was 50.0%, which was increased to 85.7% after HIV training in post-test. The difference between mean scores tested with paired t test was statistically significant (p< 0.0001). Multiple linear regression models suggests that age, experience and HIV training sometimes before pretest are significant (p< 0.0001) predictors to increase HIV knowledge after participating in HIV training program.
Conclusions: In conclusion HIV training program among health care workers was effective to increase HIV knowledge. We recommend more training and/or retraining of health professionals, as well as to include HIV training course into Continuing Medical Education for health workers.

TUPED777

Taking lessons learned in the implementation of a clinical mentorship program to increase the confidence of nurses to initiate ART, in support of the roll out of Option B+

T. Moga, T. Ncomanzi, B. Mutede, T. Nyamundaya, E. Tumbare
Elizabeth Glaser Pediatric AIDS Foundation, Technical Department, Harare, Zimbabwe
Presenting author email: etumbare@pedaids.org

Background: Since inception of the anti-retroviral therapy (ART) program in Zimbabwe in 2004, ART initiation among pregnant women and children has been doctor-led. There is a shortage of doctors in Zimbabwe, particularly in rural settings. Despite decentralization efforts, only 25% (401/1560) of antenatal care (ANC) facilities in Zimbabwe dispensed ART by December 2013. The majority of ANC nurses trained in HIV management working at these sites cited lack of confidence as a key barrier to ART initiation. EGPAF sought to address this gap through implementation of a clinical mentorship program for nurses.
Methods: EGPAF supported clinical mentorship in seven provinces of Zimbabwe from March to September 2013, involving 230 nurses from 103 sites. The trained nurses completed a one-week, practical training on ART initiation and care of HIV and opportunistic infections at ART sites. Following this internship, a multidisciplinary team of mentors (a doctor, nurse, and pharmacy technician) from each district hospital provided onsite mentorship bimonthly for three months. Mentorship included observation of case management and reinforcement of skills, and review of patient monitoring cards and registers. These mentors would also check in with nurses over the phone between visits to answer questions. To compare data, 447 control sites were selected - frequency matched to mentorship sites by number of ANC bookings per quarter, geographic location and availability of CD4 testing. Quarterly mean uptake of ART in ANC was compared between mentorship and control sites for before, during and after mentorship using EGPAF program data.
Results: There was a significant increase in ART initiation among pregnant women at the mentorship sites compared to control sites (p value = 0.048) (Figure1). A total of 168 children less than 2 years of age were initiated on ART at mentorship sites. Before mentorship all infants and young children were referred to district and central hospitals for ART initiation by doctors.
Conclusions: Clinical mentorship is an effective way of building the confidence of trained nurses to initiate pregnant women and children on ART and can be used to support decentralization and expedite the rollout of Option B+ as recommended in WHO's 2013 guidelines.



[Figure 1. Comparison of trends in the uptake of ART initiation in ANC between mentorship sites and control sites]

TUPED778

Cryptococcal antigen screening by lay cadres using a rapid test at the point of care: a feasibility study in rural Lesotho

K. Luzinda[1], V. Buard[1], I. Damiani[1], S. Sedlimaier Ouattara[1], M. Kuleile[1], T. Mots'oane[2], M. Leqheka[3], G. Van Cutsem[4], A. Shroufi[4]
[1]Médecins Sans Frontières, Roma, Lesotho, [2]Ministry of Health Laboratory Services, Maseru, Lesotho, [3]Ministry of Health Quality Assurance Unit, Maseru, Lesotho, [4]Médecins Sans Frontières, Cape Town, South Africa
Presenting author email: amir.shroufi@doctors.org.uk

Background: Cryptococcal meningitis causes over 600,000 deaths per year, an impact not matched by preventative and curative resources. In Lesotho; limited access to diagnostics and treatment mean most cases go unidentified resulting in high mortality. Screening at risk patients for Cryptococcal Antigens (CrAg) and pre-emptive treatment with fluconazole, a less toxic and more widely available drug than used for treatment, has the potential to reduce mortality. Although recommended by the World Health Organization this is rarely implemented in resource-limited settings; including Lesotho, despite recent inclusion in national guidelines. This study describes feasibility of screening with a recently available Lateral Flow Assay (LFA) rapid test used at the point of care and performed by lay counselors in rural clinics in Lesotho.
Methods: All HIV-infected patients presenting at 3 rural clinics in Roma, Lesotho, between May and December 2014 had a CD4 count done by a lay counsellor (finger prick with PIMA, Alere), with a CD4< 100 prompting CrAg LFA (Immy diagnostics) testing, performed by a lay counsellor. Positive asymptomatic patients received Fluconazole from a nurse while symptomatic patients were referred to hospital for lumbar puncture and further management. All results were entered into Epi Info.
We trained lay counselors by conducting laboratory technician led training visits reinforced through the use of visual support aids. Lab technician and a counselor supervisor visited the clinics monthly to ensure correct use of the test. In parallel nurses were trained in treating pre-symptomatic disease and in referring Cryptococcal Meningitis.
Results: During the study period, 114 patients presented with CD4 below 100 and all were screened with CRAG LFA; 5/114 (4.4%) tested positive; 3 were asymptomatic and 2 symptomatic. Asymptomatic patients were treated with Fluconazole and remained well after 3 months of follow up; the 2 symptomatic patients were referred to hospital where they died.
Conclusions: Point of care screening for cryptococcal antigen by lay counselors using CrAg LFA and pre-emptive treatment or referral by nurses in remote rural clinics proved feasible, with modest implications for overall clinic workload. These early results support the wider use of CRAG LFA screening in remote primary care settings.

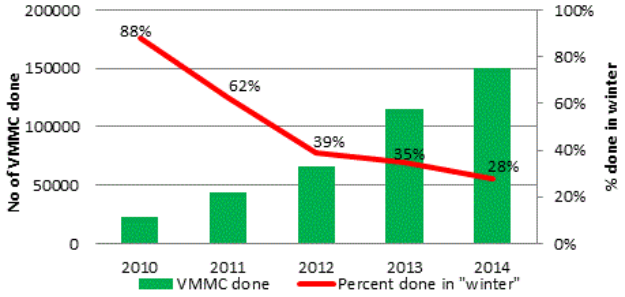
Demand generation for HIV services

TUPED779

Overcoming burden of seasonality in scaling up voluntary medical male circumcision: a case study from Tanzania

H.R. Mahler[1], E. Gold[2], D. Boyee[1], A. Hellar[1], J. Lija[3], E. Mlanga[4], E. Njeuhmeli[5], K. Curran[6,7]
[1]Jhpiego - an affiliate of Johns Hopkins University, Dar es Salaam, Tanzania, United Republic of, [2]Johns Hopkins University, Center for Communications Programs, Baltimore, United States, [3]Ministry of Health and Social Welfare, National AIDS Control Programme, Dar es Salaam, Tanzania, United Republic of, [4]USAID Tanzania, Dar es Salaam, Tanzania, United Republic of, [5]USAID, Washington, DC, United States, [6]Jhpiego - an affiliate of Johns Hopkins University, Baltimore, United States, [7]Johns Hopkins University, Bloomberg School of Public Health, Baltimore, United States
Presenting author email: hally.mahler@jhpiego.org

Background: Local beliefs about healing, agricultural and school traditions, and widespread preferences for VMMC during "cold" months have plagued the VMMC scale- up and is a major barrier to the target of serving 20 million adults in 14 priority countries. Seasonality causes inefficient use of health workforce and infrastructure. Cost analyses suggest low service utilization in "off seasons" results in the greatest increase in unit price among all factors examined. Research conducted in 2010 in Iringa region of Tanzania indicated very strong client preferences for circumcision during the 3-month long "cool" season, and in the first year of the program 88% of VMMCs were performed during these months. To become more efficient the VMMC program, led by the Government of Tanzania with support from Jhpiego (funding from PEPFAR through USAID), endeavored to overcome the constraints of seasonality.
Methods: Routine VMMC client data in de-identified individual records is collected during clinical services and entered into a database. Data from October 2009 to September 2014 was exported into Excel and analyzed. Programmatic experiences were collected by project staff and documented in annual reports. Key informant interviews were held with eight VMMC providers.
Results: Approaches used to overcome seasonality were:
(1) Focus on rural areas where VMMC services would not be otherwise available during the preferred season,
(2) Collaborate with district and local school officials and parents to allow students to be released for services,
(3) Use media and peers to expose potential clients to satisfied clients circumcised off-season and promote positive benefits such as shorter lines/more privacy,
(4) Train providers to change their attitudes and also to address issue of healing and seasonality with clients.
As a result of these efforts, the percentage of clients served in the winter season decreased from 88% in 2010 to 28% in 2014, while the number of clients served overall increased each year.



[Figure. Percent of VMMCs in "Winter"]

Conclusions: Tanzania has provided a pathway of low cost solutions that can be used by other countries faced with the challenge of seasonality. Breaking seasonality will decrease the VMMC unit cost while increasing productivity with similar resources - making the VMMC programs more efficient overall.

Strategies to increase linkage to HIV care

TUPED780

Implementing access to care interventions: structural, organizational and personnel barriers and facilitators

S. Kinsky[1], C. Maulsby[2], K. Jain[2], V. Charles[3], M. Riordan[3], D. Holtgrave[2]
[1]University of Pittsburgh, Department of Behavioral and Community Health Sciences, Pittsburgh, United States, [2]Johns Hopkins Bloomberg School of Public Health, Health, Behavior, and Society, Baltimore, United States, [3]AIDS United, Washington, United States
Presenting author email: mriordan@aidsunited.org

Background: Early connection to and retention in HIV care is critical to reaching and maintaining viral load suppression but current information indicates that only 19.0% - 43.4% of people who live with HIV (PLWH) are undetectable. Given the recent findings that viral load suppression dramatically reduces the transmissibility of HIV, finding and linking PLWH to care is critical. Yet, we know relatively little about how to effectively implement linkage interventions to reach PLWH who are not in care.
Methods: AIDS United's Positive Charge (PC) initiative funded five U.S. sites from 2010-2013 to implement linkage to care interventions. Each site implemented evidence-based strategies, including care navigation, case management, motivational interviewing, and addressing structural barriers to care (such as providing transportation or providing same-day appointments). Because the interventions aimed to both engage the individual and increase coordination among service providers to facilitate access to care, each lead agency had at least two local collaborating agencies. Qualitative interviews about the experiences of implementation, including barriers and facilitators, were conducted with 37 staff members from 20 implementing agencies.
Results: Descriptions of implementation barriers and facilitators fell into four major categories: environmental factors; collaboration; staffing; and, role confusion. Environmental factors included organization readiness to implement and lack of service infrastructure in the community. Collaborative factors included the necessity of smooth integration among different programs to enable "warm" handoffs. Ensuring confidentiality of patient information within the service network was of particular concern. Adequate leadership support and staff training were other factors that impacted implementation. Finally, differentiating roles of linkage staff and case managers was critical. Successful implementation strategies included developing early relationships with collaborating partners, finding ways to share key information among agencies, and using evaluation data to build support among leadership staff.
Conclusions: Given the increased interest in engaging PLWH in care, the findings from this study have potential to greatly inform community-based interventions in the U.S., as linkage and retention in HIV care is now understood to be critical to stemming the epidemic. Ensuring there is a culturally competent system of care that is responsive to PLWH's needs is a crucial task for the public health system.

TUPED781

Peer navigation in South Africa: addressing stigma and psychosocial barriers to engagement in HIV services

W.T. Steward[1], J. Sumitani[2], J. Morris[2], M.-J. Ratlhagana[2], M.E. Moran[1], J. Grignon[3], S. Barnhart[3], J. Tumbo[4], J. Gilvydis[3], S.A. Lippman[1]
[1]University of California San Francisco, Center for AIDS Prevention Studies, San Francisco, United States, [2]International Training and Education Center for Health (ITECH), Pretoria, South Africa, [3]University of Washington, International Training and Education Center for Health (ITECH), Seattle, United States, [4]University of Limpopo, Medical University of South Africa Campus, Department of Family Medicine and Primary Health Care, Medunsa, South Africa
Presenting author email: wsteward@gmail.com

Background: Engaging patients in medical care and supportive services is essential to HIV treatment and prevention goals. In higher resource settings, peer navigation (PN), the use of HIV-positive individuals to help optimize patients' utilization of clinical resources, has been effective at improving retention in care. The feasibility of implementing PN in lower resource settings with widespread epidemics is not well understood. In South Africa, prior research has shown that social support enhances medication adherence, but it is unknown whether PN can address barriers to engaging in clinical services.
Methods: We conducted a five-month pilot PN program at four primary health clinics in North West Province, South Africa to promote retention in care, medication adherence, and secondary prevention behaviors (e.g., disclosure, condom use). Upon completion of the program, in-depth interviews were conducted with five healthcare providers, four HIV-positive peer navigators, and nine patients who were newly diagnosed when PN services were introduced. Interviews explored experiences receiving and providing navigation, program acceptability, and challenges and successes in engaging patients. Interviews were recorded, translated and transcribed, and coded and analyzed using Atlas.ti.

Results: Participants felt that PN was valuable in improving retention in care, adherence, and prevention. Its impact was most evident around helping patients disclose, elicit social support, and make prevention decisions. The primary barriers that newly diagnosed patients faced were stigma-related (e.g., difficulty accepting their status, fears about telling others of their infection). Whereas other healthcare providers had little time to address such barriers, navigators helped patients overcome them by adopting multiple roles, including mentor and confidante. Challenges faced by navigators included stigma-related concerns about their own HIV status disclosure and difficulties helping patients become self-sufficient problem solvers. A programmatic challenge is training PNs to engage in dynamic interactions and creative problem solving.
Conclusions: In this setting, a PN model is feasible and acceptable for providers, navigators, and clients. It is critical that peer navigators receive psychosocial support to accept and disclose their own HIV status, and ongoing training to manage patients' stigma-related barriers and to teach safe disclosure and problem-solving skills. Larger studies are needed to test the approach's efficacy over the long term.

TUPED782

Implementation of a rapid referral pathway to HIV treatment for gay men and MSM diagnosed with acute HIV-infection in sexual health clinics in British Columbia

M. Thumath[1,2], D. Moore[1,3], M. Hull[3], B. Brownrigg[1], I. Sandstra[1], G. Ogilvie[1]
[1]BC Centre for Disease Control, Clinical Prevention Services, Vancouver, Canada, [2]University of British Columbia, School of Nursing, Vancouver, Canada, [3]BC Centre for Excellence in HIV/AIDS, University of British Columbia, Vancouver, Canada
Presenting author email: meaghanthumath@gmail.com

Background: During acute HIV infection (AHI), there is a high risk of onward transmission due to significantly elevated HIV viral load. This intervention was designed to facilitate immediate linkage for acutely infected individuals detected with pooled nucleic acid amplification (NAAT) HIV testing from STI clinics to HIV treatment and support. The objectives of the pilot were to improve retention and engagement in HIV care by linking MSM to care within 48 hours and potentially impact onward transmission.
Methods: Patients were offered the choice of standard of care (passive linkage) or the offer of an immediate same-day linkage and accompaniment to an HIV specialist. Patients were also offered referrals to peer navigation, primary care and social work as appropriate. A retrospective evaluation using quality improvement methods was conducted. This included a chart review to assess linkage to care and qualitative interviews with providers and patients to assess patient satisfaction. Linkage to care was defined as having an HIV viral load by an HIV treating physician.
Results: Prior to pilot implementation, out of 45 patients diagnosed with HIV, the median linkage to care in 2013 was 21.5 days. After applying the intervention, a total of 19 clients were diagnosed with acute HIV from Jan 1 to Sept 1, 2014 at the STI clinics. Of these, 16 (84%) chose immediate referral and were linked to care in a median of 1.0 days. The median linkage to care for non-acute patients (n15) was 14.0 days during the same time ($p < 0.05$). The majority of acute patients using the immediate referral pathway expressed a high degree of satisfaction with immediate linkage to care. Clinicians reported high patient interest in immediate treatment.
Conclusions: Immediate linkage from STI services to HIV specialist care, with comprehensive social supports, appears to be highly acceptable to MSM diagnosed with acute HIV infection in Vancouver. Important implications exist for partner notification including the offer of post exposure prophylaxis for contacts. Further research is needed to assess the potential impact on HIV prevention and the long-term implications of earlier treatment including adherence.

TUPED783

Factors associated with ART initiation among HIV-infected participants in the Bangkok men who have sex with men cohort study, 2006-2014

W. Wimonsate[1], A. Sriporn[1], P. Luechai[1], K. Pancharoen[1], S. Lertpruek[1], S. Yafant[1], S. Winaitham[1], T. Holtz[1,2], A. Chitwarakorn[3], E. Dunne[1,2], T. Chemnasiri[1]
[1]Thailand MOPH - U.S. CDC Collaboration, HIV/STD Research Program, Nonthaburi, Thailand, [2]Centers for Disease Control and Prevention, Division of HIV/AIDS Prevention, Atlanta, United States, [3]Ministry of Public Health, Department of Disease Control and Prevention, Nonthaburi, Thailand

Background: In 2014 Thailand released new antiretroviral treatment (ART) guidelines stating that persons with HIV should initiate ART regardless of CD4+ cell count. We investigated the factors associated with initiating ART among HIV-infected participants in the Bangkok Men Who Have Sex with Men Cohort Study (BMCS).
Methods: Between 2006-2010, we enrolled men into the BMCS and followed them every 4 months for 3-5 years. At every visit, we conducted HIV testing, and collected behavioral data using computer-assisted self-interview. For HIV-infected participants, we provided post-test and ART counselling, follow-up visits with CD4+ cell count monitoring from HIV diagnosis until the last study visit, and referral to a specialized ART service when they were eligible for ART according to Thailand's ART guidelines at the time of assessment (contemporary guidelines). Participants were asked about ART initiation during follow-up visits. We used logistic multivariate regression to identify factors associated with ART initiation, adjusting for demographics, risk behaviors, and syphilis infection.
Results: As of 16 December 2014, we detected HIV infection in 614 (35.2%) of 1744 participants. Of these, 482 (78.5%) had follow-up with CD4+ cell count monitoring. During follow-up, 90 (18.7%) became eligible for ART, according to contemporary guidelines. In total, 271 (56.2%) initiated ART, with a mean of 11 visits prior to ART initiation. Among the 482 men, the following factors were significantly and independently associated with ART initiation: being eligible for ART according to contemporary guidelines (Adjusted Odds Ratio [AOR] 4.6, 95% Confidence Interval [CI] 2.3-9.0), being 25 years or older at time of enrollment (AOR 1.7, 95% CI 1.1-2.6), self-reporting not paying for sex in the 4 months prior to current visit (AOR 3.9, 95% CI 1.5-10.2), and number of study visits prior to ART initiation
(AOR 0.8, 95% CI 0.8-0.9).
Conclusions: Only half of HIV-infected participants who were followed-up with CD4+ cell counts initiated ART. Under current guidelines, immediate referral of HIV-infected men who have sex with men to ART services should be a priority, especially among those who were not previously eligible for ART, young men, and those with a history of paying for sex.

TUPED785

Factors associated with disclosure of HIV status following testing HIV-positive at mobile HIV counselling and testing units in South Africa

T. Mabuto[1,2], S. Charalambous[1,2], K. Fielding[3], G. Churchyard[1,2], M. Hlongwane[1], G. Kubeka[1], C. Hoffmann[1,4]
[1]Aurum Institute, Epidemiology Research, Johannesburg, South Africa, [2]University of the Witwatersrand, School of Public Health, Johannesburg, South Africa, [3]London School of Hygiene and Tropical Medicine, London, United Kingdom, [4]Johns Hopkins, School of Medicine, Baltimore, United States
Presenting author email: tmabuto@auruminstitute.org

Background: Disclosure of HIV status may result in increased social support and subsequent increased engagement in HIV care. Timely entry-into-care following HIV diagnosis is a point of loss from the care continuum for 40-60% of individuals requiring HIV care. Here we describe HIV disclosure among participants with ≥ 3 months follow-up in a trial of improved entry-into-care.
Methods: Participants in this trial were recruited in two districts (rural and urban) in South Africa immediately after testing HIV-positive at mobile HIV counseling & testing (HCT) units. Data are shown combined across all four study arms: point-of-care CD4 testing (POC-CD4) and multi-session counselling, POC-CD4 and transport assistance, POC-CD4 only, and standard of care. Disclosure was defined as voluntary release of HIV status information to at least one person within 3 months of enrolment. Analysis was restricted to participants who had both ≥3 month's follow-up and disclosure data. We describe proportion reporting HIV disclosure and assess factors associated with disclosure using logistic regression.
Results: Between March 2012 and December 2014, 2,474 participants were enrolled, 1,241 had ≥ 3 months follow-up and of these; 1,133 had disclosure data, with a median CD4 count of 419 cell/μL (interquartile range [IQR]: 275, 576), median age of 34 years (IQR: 27, 41), 38% were men, and 33% were rural residents. 771 out of 1,133 participants (68%) disclosed their status, of which 44% first disclosed to their partners. Factors associated with disclosure were seeking HCT due to suspected HIV exposure from partner (odds ratio (OR) 2.0, 95% CI: 1.0, 3.7), and ART eligibility at the time of HCT (OR ≤ 350 compared to >350, 1.5; 95% CI: 1.1, 2.2). There were no differences in disclosure by age or sex.
Conclusions: This study has the advantage of evaluating the role of disclosure on the early stages of the HIV care continuum compared to prior studies of individuals already in care. Within the context of high stigma, HIV disclosure is a difficult decision, but one that should continue to be targeted to reduce the delay between testing and initiation of HIV care.

TUPED786

Preliminary findings from a care facilitation approach to accelerate entry into care after HIV diagnosis from mobile HIV counselling and testing units in South Africa

T. Mabuto[1], S. Charalambous[1,2], K. Fielding[3], G. Churchyard[1,2], M. Nathane-Taulela[4], C. Hoffmann[1,5]
[1]Aurum Institute, Epidemiology Research, Johannesburg, South Africa, [2]University of the Witwatersrand, School of Public Health, Johannesburg, South Africa, [3]London School of Hygiene and Tropical Medicine, London, United Kingdom, [4]University of the Witwatersrand, Social Work Department, Johannesburg, South Africa, [5]Johns Hopkins, School of Medicine, Baltimore, United States
Presenting author email: tmabuto@auruminstitute.org

Background: Individuals recently diagnosed with HIV need to overcome several individual- and system-level barriers in order to benefit from both the health and prevention goals of early HIV care. Participation in motivational and strengths-based counselling support may assist individuals in developing self-efficacy to overcome these barriers. Here we describe the uptake of a multi-session strengths-based care facilitation programme by participants diagnosed through mobile HIV counselling and testing (HCT) units.
Methods: A prospective study in a pragmatic trial in which participants are recruited in two districts in South Africa immediately after testing HIV-positive at mobile HCT units. Participants in this analysis were limited to those randomized to the care facilitation arm. Care facilitation was offered; after diagnosis, at individual-level, within 90 days of HCT and a maximum of five sessions were provided in person at a venue accessible to the participant or telephonically. Uptake was defined as attending at least one session. We describe the proportion of intervention uptake and factors associated with uptake using logistic regression.
Results: Between March 2012 and October 2014, 603 participants were assigned to care facilitation. 40% were male, 40% were rural residents, with a median age of 33 years (interquartile range [IQR]: 27, 40) and CD4 cell count of 435cells/μL (IQR: 280, 600). Overall 366 (61%) attended at least one session. The median time to the first session was 21 days (IQR; 8, 45), and this was lower among rural compared to urban residents (15 vs. 25days). 246 (67%) of the first sessions were conducted in-person. Place of residence was the only factor associated with uptake (rural compared to urban OR, 2.3; 95%CI 1.7, 3.4). No associations were found between uptake and sex, age, employment status, education level or CD4 count. We did not observe any interaction between place of residence and these factors.
Conclusions: These findings suggest the feasibility of a multi-session counselling approach in non-traditional HCT settings to accelerate entry into HIV care. Uptake was lower than desired, more especially among urban participants and additional approaches may be needed to increase uptake for strengths-based counselling to be an effective component of connecting people with HIV to care.

TUPED787

TB/HIV Care Association's model to increase linkage to care for sex workers: a peer linked mobile service with point of care CD4 testing and STI syndromic management

H. Hausler[1,2], A. Lambert[1], H. Mhlope[3], M. Greeves[3], W. Joyce[3], R. Ogle[3]
[1]TB/HIV Care Association, Cape Town, South Africa, [2]University of the Western Cape, School of Public Health, Cape Town, South Africa, [3]TB/HIV Care Association, Ethekwini, South Africa
Presenting author email: hhausler@tbhivcare.org

Background: Linkage to care and treatment is crucial for public health impact. Referral challenges exist for all clients, but for sex workers (SW) , who are criminalized and stigmatized, this path to health services is a more difficult journey.
Methods: TB/HIV Care Association (THCA) is providing a SW peer linked mobile health programme in Ethekwini (Durban), in South Africa. The services include screening for HIV, tuberculosis(TB), and sexually transmitted infections(STIs) with referral into care and support. HIV positive SWs are provided with point of care CD4 testing and WHO staging, TB suspects have sputum collected and GeneXpert-positive clients are referred and STI clients received on site STI syndromic management. Referred clients are linked to a SW peer navigator and sensitized THCA clinic staff member and provided a referral letter to the clinic. Referred SWs benefit from our algorithm to ensure linkage to care (phone calls, peer visits and navigation/verification with clinic). Successful referral was measured as the proportion of clients with confirmed clinic attendance or who received STI syndromic management. Service delivery data was analysed from July 2012 to June 2013 (Y1), July 2013 to June 2014 (Y2) and July to September 2014 (Y3).
Results: Successful referral for all HIV-positive SWs increased from 33% (247/751) in Y1 to 49% (352/717) in Y2 to 68%% (145/213) in Y3. In Y3, only 27% (10/27) of clients who refused point of care CD4 testing were successfully referred compared to 72% (91/127) of clients CD4 tested not eligible for ART and 75% (44/59) of clients CD4 tested eligible for ART. Successful referral for TB increased from 39% (94/244) in Y1 to 60% (34/57) in Y2 and for STIs increased from 39% (104/269) in Y1 to 89% (277/310) in Y2.
Conclusions: A peer linked, sensitized mobile clinic staff, point of care CD4 testing and STI syndromic management and strengthened referral improved linkage to care for HIV ,TB and STIs. This may have an important impact on decreased transmission in the community.

TUPED788

Delays in antiretroviral therapy initiation among HIV-positive individuals: results of a community-based positive living with HIV (POLH) study in Kathmandu, Nepal

K.C. Poudel[1], D.R. Buchanan[1,2], K. Poudel-Tandukar[1]
[1]School of Public Health and Health Sciences, University of Massachusetts Amherst, Department of Health Promotion and Policy, Amherst, United States, [2]University of Massachusetts Amherst, The Institute for Global Health, Amherst, United States
Presenting author email: krishna@schoolph.umass.edu

Background: Approximately 5.3 million people living with HIV/AIDS (PLWHA) needing antiretroviral therapy (ART) in low-and middle-income countries had not received it by 2012. Among those who initiated the treatment, high rates of ART initiation during the advanced stages of the disease remain a concern because of increased risk of early mortality and further HIV transmission. Although treatment eligibility has been monitoring during pre-ART care, many PLWHA fail to access regular care after HIV diagnosis or obtaining CD4+ count results. Yet studies exploring ART eligibility among PLWHA at the community level are sparse. This community-based study explored ART eligibility and correlates among PLWHA in Kathmandu, Nepal, where ART coverage was only 23.7% in 2011.
Methods: This cross-sectional study was conducted among 322 PLWHA (20-60 years) recruited through the networks of five non-governmental organizations working with PLWHA. Participants' CD4+ cell counts were tested by the National Public Health Laboratory. Potential correlates included perceived family support (measured with 10-item scale), depression (measured with Nepali version Beck Depression Inventory-I), illicit drug use, and HIV symptom burden. Correlates of ART eligibility were examined using multivariable logistic regression analysis.
Results: We obtained CD4+ count results of 289 participants; 72 of them were ART-naïve. Half of the ART-naïve participants were eligible for ART with CD4+ counts of < 350 cells/mm^3; 33.3% of these participants had CD4+ count result < 200 cells/mm^3. In multivariate analysis, low levels of perceived family support was associated with ART eligibility (AOR=6.05; 95% CI=1.95-18.73).
Conclusions: High proportion of ART-eligible individuals and strong association between low levels of perceived family support and ART-eligibility among our participants suggest that, to improve ART initiation among treatment-eligible individuals, thereby ART coverage in the country, HIV service providers should consider the role and impact of family support in influencing individual decision.

Engagement of community in service delivery

TUPED789

Enhancing community engagement through involvement of community members in delivery of antiretroviral drugs (ARV) to fellow community members: TASO Rukungiri experience

B. Kizito Joseph
The AIDS Support Organisation (TASO), Information Management, Kampala, Uganda
Presenting author email: bennetjoe@yahoo.com

Background: The AIDS Support Organization (TASO) is the biggest HIV/AIDS care organization caring for PLHIV in Uganda since 1987. To date over 150,000 PLHIV have been supported with psychosocial, medical and social support services. In Uganda the HIV prevalence rate is over 7.3% meaning that the demand for HIV services is enormously higher yet resources especially human resources for health are limited. TASO employed a strategy of engaging community members mostly those living with HIV (commonly known as **Expert clients**) to support in service delivery, empower fellow clients in management of own health and reduce frequent clinic visits, and community HIV/AIDS sensitisation.
Methods: In one of the 11 branches of TASO, Rukungiri recruited and trained 107 Expert Clients (ECs) in 2010 covering a radius of 100kms from the branch offices, caring for atleast 8,000 PLHIV. In addition over 25,000 family members of PLHIV are also supported with routine psychosocial services, economic strengthening and education support for OVCs, support fellow community member in delivery of drugs (ARVs), HIV sensitization, ART and TB adher-

ence monitoring through Directly Observed Therapy (DOTs) and pill count, follow through with behavioral change management strategies within the same communities and act as referral or contact agents between the health facility (TASO) and community. At quarterly basis all PLHIV in a given area converge and interface with technical staff and also give account of the quality of service provided by their Expert clients.

Results:

1. On average each EC reaches 50 PLHIV per month which has increased reach of HIV/AIDS services to would be hard to reach areas in Uganda.
2. Engagement of ECs has reduced operational cost for HIV service delivery in TASO as technical staff interface with PLHIV only on quarterly basis other than monthly basis.
3. ECs have improved HIV/AIDS awareness levels in their communities since they are always within the community moving home to home, counseling and offering paramedical services to fellow members.

Conclusions: Engaging communities in service delivery is not only a key driver to achieving community ownership and accountability but also a way to reduce operational cost and demand for human resources for health.

TUPED790

Bringing community to cure

L. Sylla[1], M. Louella[2], E. Seelbach[1], T. Andrus[2]
[1]Fred Hutchinson Cancer Research Center, defeatHIV Martin Delaney Collaboratory Community Advisory Board, Seattle, United States, [2]Fred Hutchinson Cancer Research Center, defeatHIV Martin Delaney Collaboratory, Seattle, United States
Presenting author email: mlouella@fredhutch.org

Background: Community engagement is essential for successful HIV Cure Research. Individuals with HIV will need to be aware of the potential and risks of HIV cure research in order to make informed decisions about participating in clinical trials. Those with and affected by HIV are needed for advocacy, ethics discussions, and messaging feedback. The *defeatHIV Community Advisory Board* (*dHCAB*) is an effective catalyst for community engagement and feedback between HIV cure researchers and the community, as well as for collaboration among different local HIV-related CABs, such as those for CFAR, ACTU, and HVTU. The *dHCAB* is the local CAB for the *defeatHIV Martin Delaney Collaboratory* based at Fred Hutchinson Cancer Research Center in Seattle, WA, one of three NIH-supported cure collaboratories.

Methods: The *dHCAB* has employed multiple strategies for community engagement, including: community forums with HIV cure research leaders; opportunities to meet Timothy Ray Brown; providing multi-cultural food and music at education events; holding community events at different community organizations and venues; visiting agencies to engage them in cure research; tabling at events such as the annual AIDS walk and pride festivals, theater productions, etc; webinars; active use of social media, including Facebook, Twitter and Youtube. Those on the *dHCAB* have had the opportunity to attend and present at scientific meetings and to provide input to researchers on protocols, informed consent documents, and recruitment.

Results: Over 1000 community members have participated in *dHCAB* events and we have reached thousands more through outreach. The *dHCAB* currently consists of 12 members. Members range in age from high school to senior citizens and include women, gay and straight men, individuals in recovery, newly diagnosed individuals and long term survivors, African-Americans, Asians, Latinos, and Native Americans. Programs typically bring in dozens to hundreds of participants. The *defeatHIV* investigators consider the *dHCAB* a valuable asset and partner and have taken feedback to heart. We have learned about community concerns and provided meaningful pathways for education and dialogue.

Conclusions: With creativity, perseverance and respect it is possible to engage the community and researchers in meaningful ways that will advance HIV cure research.

TUPED791

Implementation of community-based adherence clubs for stable antiretroviral therapy patients

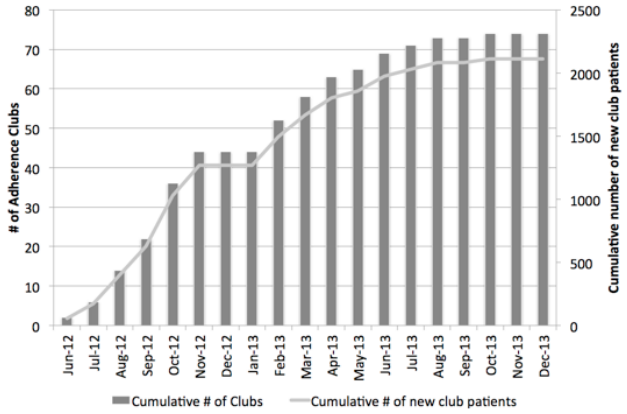
A. Grimsrud[1], J. Sharp[2], C. Kalombo[3], L.-G. Bekker[2,4], L. Myer[1]
[1]Division of Epidemiology & Biostatistics, University of Cape Town, Cape Town, South Africa, [2]The Desmond Tutu HIV Centre, University of Cape Town, Cape Town, South Africa, [3]Gugulethu Community Health Centre, Provincial Government of the Western Cape, Cape Town, South Africa, [4]University of Cape Town, Department of Medicine, Cape Town, South Africa
Presenting author email: landon.myer@uct.ac.za

Background: Community-based models of antiretroviral therapy (ART) delivery have been recommended to support ART expansion and retention in resource-limited settings. However the evidence base for community-based models of care is limited. We describe the implementation of community-based Adherence Clubs (CACs) at a large, public-sector facility in peri-urban Cape Town, South Africa.

Methods: Starting in May 2012, stable ART patients were down-referred to CACs. Eligibility was based on self-reported adherence, >12 months on ART, and viral suppression. CACs were facilitated by 4 community health workers (CHWs) and met every 8 weeks for group counselling, a brief symptom screen and distribution of pre-packed ART. The CACs met in community venues for all visits including annual blood collection and clinical consultations. CAC patients could send a patient-nominated treatment supporter ("buddy") to collect their ART at alternate CAC visits. Patient outcomes during the first 18-months of the programme are described using Kaplan-Meier methods.

Results: From June 2012 to December 2013, 74 CACs were established, each with 25-30 patients, providing ART to 2,133 patients (Figure 1). CAC patients were predominantly female (71%) and lived within 3km of the facility (70%). During the analysis period, 9 patients in a CAC died (< 0.1%), 53 were up-referred for clinical complications (0.3%) and 573 CAC patients sent a "buddy" to at least one CAC visit (27%). After 12 months in a CAC, 6% of patients were lost to follow-up and fewer than 2% of retained patients experienced viral rebound (>1000 copies/ml).

Conclusions: Over a period of 18 months, a community-based model of care was rapidly implemented decentralizing more than 2,000 patients in a high prevalence, resource-limited setting. Key factors contributing to the implementation success were a cohesive multidisciplinary team, policies supporting out-of-facility ART distribution by CHWs and a reliable supply of ART. The primary challenge for this out-of-facility model was ensuring that patients receiving ART within a CAC were viewed as an extension of the facility and part of the responsibility of CHC staff. Further operational research is needed to optimise timing of down-referral after ART initiation and to examine patients' experiences of community-based ART delivery.



[Figure 1. Implementation of community-based adherence clubs between June 2012 - December 2013]

TUPED792

"Health care workers have changed their bad language": When the patient's voice is heard

G. Mbita[1], T. Kiwale[2], R. Ally[2], E. Mshana[3], A. Shirima[4], C. Kimario[5], J. Macha[6], A.B. Ntogwisangu[7], T. Mtambalike[8], G. Antelman[1], R. Van den Ven[8]
[1]Elizabeth Glaser Pediatric AIDS Foundation, Public Health Evaluation, Dar es Salaam, Tanzania, United Republic of, [2]Elizabeth Glaser Pediatric AIDS Foundation, Quality Improvement, Dar es Salaam, Tanzania, United Republic of, [3]Moshi District Council Health Management Team Kilimanjaro, CHMT Member, Moshi, Tanzania, United Republic of, [4]Hai District Council Health Management Team Kilimanjaro, CHMT, Moshi, Tanzania, United Republic of, [5]Kibosho Hospital, CHMT, Moshi, Tanzania, United Republic of, [6]Hai District Hospital, CHMT, Moshi, Tanzania, United Republic of, [7]Elizabeth Glaser Pediatric AIDS Foundation, Program, Moshi, Tanzania, United Republic of, [8]Elizabeth Glaser Pediatric AIDS Foundation, Program, Dar es Salaam, Tanzania, United Republic of
Presenting author email: gmbita@pedaids.org

Background: Elizabeth Glaser Pediatric AIDS Foundation, in collaboration with facility-based and district quality improvement teams (QIT), introduced the Patient's Voice program to solicit community-level feedback on clinical services in Kilimanjaro Tanzania.

Methods: : Two high-volume hospitals providing HIV treatment services, who utilize community resource persons (CORPS), and QITs, introduced quarterly assessments, including patient satisfaction exit surveys (PSS) administered by district-level QIT members to about 25 patients, and *Community Dialogues* attended by up to 50 community members, led by the CORPs. For transparent data review and action planning, the program incorporated consumer representation on the facility QIT. These teams were then responsible for implementing improvement projects in response to the issues identified.

Results: Since 2013, each site completed four rounds of assessments resulting in 363 community participants and seven completed QIT meetings. The PSS and dialogues revealed different issues at each round and in each facility. In one facility, the main finding from the first round was long waiting time at various service delivery points. Mean waiting time reported on PSS was significantly reduced in subsequent rounds (R1=3.8 hrs, R2=2.4, R3=2.6, R4=3.0; p=.005) after the QIT implemented the following changes: appointment time blocks, two additional drug dispensing windows/stations, and a clock placed in the staff meeting room to encourage timeliness of meetings and breaks. The other facility's dialogue highlighted poor quality of care at the labor ward, namely that women were required to wash hospital linens after delivery and staff spoke rudely.

The district management addressed the issue with hospital staff, and patients reported in the next round an improvement: *"Health care workers have changed their bad language."* Later

rounds showed both sites reporting issues related to misperceptions of medical care costs or triage/referral policies. Action points focused on community sensitization and posting information about eligibility for free medical care and other policies at the facility.
Conclusions: Involving patients in a collaborative QI approach using both qualitative and quantitative assessment approaches can reveal quality gaps that providers are either not aware of, or are not actively addressing, and positively engage community members, providers and local government leaders in holding public services accountable.

TUPED793

A community-led health campaign in a low-resource rural setting in Western Uganda

J. Kabami[1], D. Kwarisiima[2], G. Chamie[3], E. Biira[1], P. Ssebutinde[4], M. Petersen[5], E.D. Charlebois[3], M.R. Kamya[1,6], D.V. Havlir[3], T.D. Clark[3]
[1]Infectious Diseases Research Collaboration, Kampala, Uganda, [2]Makerere University Joint AIDS Program (MJAP), Kampala, Uganda, [3]University of California, San Francisco, United States, [4]Uganda Ministry of Health, Mbarara, Uganda, [5]University of California, Berkeley, United States, [6]Makerere University, Kampala, Uganda
Presenting author email: jkabami@idrc-uganda.org

Background: Universal HIV testing and counseling is critical for comprehensive test and treat strategies in prevention and reduction of new infections. Community health campaigns have been proved effective in providing HIV and multi-disease screening in a research setting (SEARCH; NCT01864603). We sought to evaluate the feasibility and cost of a community-led approach to carrying out a multi-disease health campaign using local political and health leadership, in a rural Uganda community.
Methods: In September 2014, community leaders within the geo-political area of the Rwebishekye health center, initiated and led a village-level census and mobilization activities including organized meetings and poster distribution, in advance of implementing a 6-day health campaign conducted in 3 different locations. Local leaders from a neighboring SEARCH community volunteered in an advisory capacity during the planning stages. During the campaign, healthcare staff provided counseling, diagnostic, treatment and referral services to all campaign participants. Lab services included point-of-care screening for HIV, malaria, hypertension and diabetes. Referral for all further care, safe male circumcision, and family planning services was offered. Costing of all supplies purchased and donated was conducted after the health campaign.
Results: 5194 persons were enumerated prior to and 2468 persons attended the health campaign. The mean age in attendance was 25 years with 41.8% male participation. HIV tests were performed in 2119 (85.9%) participants and in 1537 adults (>15 years); 114 (7.42%) tested positive. The community expended $7584 to implement mobilization and campaign activities. The Uganda Ministry of Health (MOH) provided HIV and malaria test kits, some drugs and condoms at a cost of $4031. The SEARCH program provided limited administrative support and one-time capital goods (e.g. tents, chairs, photocopier) at $4738. The total cost per person in attendance was $6.63. Excluding MOH- and SEARCH- provided goods; the cost of conducting this health campaign to the community was $3.07/person.
Conclusions: Rural political and health leaders successfully conducted a health campaign with high HIV testing uptake. The per person cost of a multi-disease health campaign conducted under a research setting in an adjacent community was approximately $13/person compared to $6.63/person for similar services in this community-led health campaign.

TUPED794

Engaging the community to improve delivery and uptake of TB HIV collaborative services at health facilities: experience from public health facilities in Northern Nigeria

A. Inedu, F. Oronsaye, C. Imarhiagbe, B. Oyeledun, P. Jwanle, E. Medina, A. Olaitan, B. Uguge, G. Agada
Center for Integrated Health Program (CIHP), Abuja, Nigeria

Background: Nigeria ranks 10th among the 22 high TB burden countries in the world and it is estimated that 210,000 new cases of all forms of TB occurred in the country in 2010, equivalent to 133/100,000 population. 90,447 TB cases were notified in 2010 with 41, 416 new smear positive cases. Globally Nigeria has the highest number of new HIV infections reported each year, and an estimated 3.7% of the population is living with HIV . Delivery and uptake of TB HIV collaborative services had remained low in Nigeria due to poor community awareness, poor access to health facilities and human resources gaps. The Center for Integrated Health Program (CIHP) with funding from the United States Government implemented and evaluated "community involvement in TB HIV care" in Benue, Gombe, Kaduna, and Kogi states to address these gaps.
Methods: 60 staff and volunteers of 7 community based organizations selected from the 2 states were trained on community TB care and then supported to provide TB HIV services in the health facilities in addition to the community with community-health facility linkages from January to December 2013. Service areas covered were community TB awareness creation, HIV testing and counselling(HTC) for TB cases and suspects, TB screening for persons living with HIV (PLHIV) and TB suspect referral, community-facility and intra-facility referrals and service documentation. After a period of 12 months, routine pre and post intervention secondary data from health care facilities on TB screening for PLHIV, HTC for TB cases and suspect and new TB HIV co-infected cases identified, as measures of service delivery and uptake, were analyzed.
Results:

Variable	Pre-intervention (January-December 2012)	Post-intervention (January-December 2013)	Percentage increase over same period
Number of new PLHIV screened for TB at enrollment	22,703	32,884	44.8%
Number of TB patients and suspects visiting facility counseled and tested for HIV	15,196	19,917	31.1%
Number of TB patients and suspect positive for HIV	2,249	2,147	-4.5%

[Table of Results]

TB screening for PLHIV and HTC for TB patients and suspects increased post-intervention while TB HIV co-infected cases identified and treated remained about the same, as shown in the table.
Conclusions: Community involvement in TB HIV care has the potential to address barriers such as awareness, access and human resources gaps in order to improve delivery and uptake of TB HIV collaborative services at health facilities. This should be promoted in control of TB and HIV.

TUPED795

Early diagnosis of HIV infections and detection of asymptomatic STI in a community-based organization addressed to MSM

P. Coll[1], A. Leon[2], F. Garcia[2], A. Carrillo[3], E. Fernandez[2], I. Bravo[4], J. Saz[3], M. Meulbroek[3], F. Pujol[3], V. Gonzalez[5], J. Casabona[5], L. Ferrer[5], J.L. Blanco[2], M. Piñol[6], F. Garcia-Cuyas[6], G. Sirera[4], A. Chamorro[4], B. Revollo[4], J.M. Gatell[2], B. Clotet[1,4], C. Brander[1,7]
[1]IrsiCaixa, Badalona, Spain, [2]Fundacio Hospital Clinic, Barcelona, Spain, [3]BCN Checkpoint, Barcelona, Spain, [4]Fundacio Lluita contra la Sida, Badalona, Spain, [5]CEEISCAT, Barcelona, Spain, [6]Hospital Germans Trias i Pujol, Badalona, Spain, [7]ICREA, Barcelona, Spain
Presenting author email: pcoll@irsicaixa.es

Background: HIV prevalence and incidence are still increasing in men who have sex with men (MSM). An important factor contributing to this increase are HIV infections not detected, mainly acute infections with high viral loads. Another contributing factor are Sexually Transmitted Infections (STI), which can increase the risk of HIV transmission, being sometimes asymptomatic. A shared project between the HIV vaccine research programme in Catalonia (HIVACAT) and a community centre for the detection of HIV in MSM (BCN Checkpoint), was set up. The objectives were: 1. Early diagnosis of HIV infections and referral to HIV Units; 2. Detection and treatment of asymptomatic STI.
Methods: A cohort of MSM at higher risk of infection was set up. Individuals were selected through a risk-assessment questionnaire. The participants were screened on a quarterly basis for HIV infection, and once a year for other STI: serologies for syphilis, hepatitis A, B and C. PCR for *C. trachomatis* and *N. gonorrhoeae* in penis and rectum. In addition, HPV in anus and mouth was screened by PCR, together with an anal cytology. A High Resolution Anuscopy was performed if a dysplasia was detected.
Results: Between December 2009 and October 2012, 267 MSM were recruited, 44 were lost to follow up, and 19 acute HIV infections were diagnosed (incidence: 3,5 per 100 persons/year). Prevalence of STI at baseline visit were: syphilis 8,2%, *C. trachomatis* in penis 3,1% (95% CI: 1,5-3,2), in rectum 6,3% (95% CI: 3,9-10), *N. gonorrhoeae* in penis 2% (95% CI: 0,7-4,7), in rectum 6% (95% CI: 3,6-9,7), HPV in anus 76,2% (95% CI: 69,6-81,8), in mouth 4% (95% CI: 1,9-7,8). Cytological abnormalities were detected in 41,7% (95% CI: 35,8-47,9). 1 acute hepatitis C was diagnosed. All individuals with HIV infection were referred to an HIV Unit, within 10 days.
Conclusions: The active collaboration between a community centre and HIV researchers in this project, allows identifying early HIV infections and asymptomatic STI among MSM, ensuring an adequate linkage to health care. The high incidence and prevalence of HIV and STI supports the recommendation of periodical screenings among MSM with sexual activity.

TUPED796

How can involving women living with HIV strengthen the evidence base of our policies and programmes? A methodological analysis

A. Welbourn[1], L. Orza[2], E. Tremlett[1], S. Dilmitis[1], J. Stevenson[3], C. Kenkem[4], E. Bell[3], E.T. Crone[5], T. Atsbeha[6], N. Damji[6], E. Bass[7], N. Aidarus[7], K. Fisher[7]
[1]Salamander Trust, London, United Kingdom, [2]ATHENA Network, Bridport, United Kingdom, [3]ATHENA Network, London, United Kingdom, [4]ATHENA Network, Yaounde, Cameroon, [5]ATHENA Network, Seattle, United States, [6]United Nations Entity for Gender Equality and the Empowerment of Women, New York, United States, [7]AVAC: Global Advocacy for HIV Prevention, New York, United States

Background: Few examples exist of peer-led and -governed analyses of treatment access where women with HIV are central to study design and implementation. A multi-phase global review, to explore barriers and enablers to women accessing HIV care and treatment sought to address this gap, ensuring experiences, realities, needs and priorities of women with HIV in relation to treatment access are better understood, and create a robust model for meaningful involvement.
Methods: The study (literature review; global consultation; and country case studies) was informed by a Global Reference Group (GRG) made up of 14 women with HIV from 11 countries worldwide. The global consultation was designed and implemented by the GRG which comprised women from diverse key populations and age-groups. GRG members conducted a "pre-consultation" among small groups of HIV-positive women, utilising a holistic well-being approach to define key themes informing focus group discussion (FGD) and interview guides. The GRG coordinator established a closed international email listserv for 19 women with HIV, and moderated an extensive e-discussion. The GRG then contributed to a literature review; led the global consultation (pre-consultation, e-discussion, FGDs and one-to-one interviews); and provided guidance for country case studies run by GRG members. Each review phase built on and was informed by preceding phase(s).
Results: The above methodology resulted in a Community Dialogue questionnaire framework which expanded traditional questions regarding treatment access (focusing on initial uptake), towards a more holistic, women-centred and rights-based "continuity of care" approach. This included attention to quality of care, basic needs including nutrition, peer support and treatment literacy, decision-making and choice around treatment initiation, care and treatment for side-effects and treatment monitoring. The 175 women living with HIV who participated in peer-led FGDs and interviews in Tunisia, Bolivia, Nepal and Cameroon appreciated this holistic focus on women's health and rights, compared with traditional questions.
Conclusions: Meaningful involvement of women with HIV (where they are intended beneficiaries), in implementation science reviewing service delivery, creates enhanced contextually-specific evidence to inform treatment uptake and utilization. The GRG model presents a framework for involving women with HIV, which emphasises critical contributions of women's agency, quality of care, rights and choice.

TUPED797

Engaging frontline community health workers to provide oral rapid HIV testing to pregnant women in rural India

S. Mehra[1], A. Sarkar[1], G. Mburu[2], P. Sharma[1], J. Behara[1], S.K. Mishra[1]
[1]MAMTA Health Institute for Mother and Child, Research Department, New Delhi, India, [2]International HIV/AIDS Alliance, Brighton, United Kingdom
Presenting author email: archanas@mamtahimc.org

Background: Early screening of HIV among pregnant women is an important component of PMTCT. Currently in India, only 20% of the 27 million pregnant women are annually tested for HIV, partly due to shortage of trained health workers and partly due to lack of testing kits. Therefore, training frontline community health workers to provide HIV testing with a non-invasive oral rapid fluid testing such as using FDA-approved OraQuick®could enable significant task shifting and increase early screening of pregnant women in rural areas.
The aim of this study was to test the feasibility of structured training of frontline health workers on OraQuick® for HIV screening.
Methods: The frontline community health workers also known as Auxiliary Nurse Midwives (ANM) of all Primary Health Centres, from one block each of Nagpur and Adilabad districts were identified. A two-day training session was used to build their capacity to conduct effective oral rapid HIV testing, and build their knowledge and counselling skills on HIV. Participants were also trained on completing a questionnaire for assessing the feasibility of the kit for its accurate usage in field setting. After training, application of the kit by the health workers and its use in screening was assessed within the maternal health care services.
Results: From May to December 2014, 89 ANMs were trained in Nagpur (40) and Adilabad (49) respectively on oral rapid testing, pre and post-test counselling skills, universal precautions and the need to have a confirmatory HIV test irrespective of the screening results. The training also refreshed their knowledge on obstetric care and HIV prevention. Following this, the frontline workers have performed HIV testing of 363 pregnant women using OraQuick®. All test results were confirmed at government run Integrated Testing and Treatment Centres (ICTC), with 100% conformity rate.
Conclusions: Oral fluid rapid HIV testing by community workers for HIV could improve the uptake of HIV testing services among pregnant women in rural India. Our findings provide a foundation for policy advocacy to allow task-shifting of oral fluid rapid HIV testing to frontline community health workers based on further implementation and research outcomes.

Operational challenges in implementing test and treat strategies

TUPED798

Feasibility of supervised self-testing using an oral fluid-based HIV rapid testing method among pregnant women in rural India

A. Sarkar[1], G. Mburu[2], J. Behara[1], P. Sharma[1], S.K. Mishra[1], S. Mehra[1]
[1]MAMTA Health Institute for Mother and Child, Research Department, New Delhi, India, [2]International HIV/AIDS Alliance, Brighton, United Kingdom
Presenting author email: archanas@mamtahimc.org

Background: Access and utilization of HIV screening among pregnant women in rural India is prevented by inaccessibility of health facilities, lack of point-of-care HIV testing services, HIV-related stigma and discrimination. In addition, invasiveness of HIV testing could be a contributing factor. The aim of this study was to assess the feasibility of a supervised self-testing using FDA-approved OraQuick® a non-invasive Oral Fluid-based HIV Rapid Test. The study was conducted by MAMTA Health Institute for Mother and Child in collaboration with Mahatma Gandhi Institute of Medical Sciences at Kasturba Hospital in Wardha, Nagpur.
Methods: Between October and December, 2014, a random sample of consenting 200 pregnant women were oriented on test procedure, provided with pre-test counselling, and subsequently asked to perform the test by themselves under observation of a trained medical doctor. Post-test counselling and linkage to appropriate care were provided to all participants. All test results were conformed through method at government-run Integrated HIV testing centers. Participants also completed a self-administered semi-structured questionnaire to assess acceptability and feasibility of self-testing.
Results: Of the 200 participants, 71.5% had never been tested for HIV before. 84% preferred oral-based tests to blood-based HIV testing mainly because it was very easy to use (43%), gave results quickly (27.5%), non-invasive (22%), among others. In addition, 92.5% participants reported that the instructions given for the test were easy to understand while 7.5% found them difficult. After completion of test, 95.5% were confident that they had performed the test correctly. 96% of participants recommended that the OraQuick® kits should be made available publicly. The HIV test status obtained through oral testing concurred 100% with the ICTC results. Two women were detected HIV positive. However, the band forming (T-line) for HIV positive was not very dark.
Conclusions: Self-testing using oral fluid-based HIV Rapid Test could potentially improve access to HIV testing among pregnant women in rural India. Policy advocacy and further research related to different high-risk groups that could benefit them with preferred supply channels (private, public, community-based) of HIV testing is required in coming days.

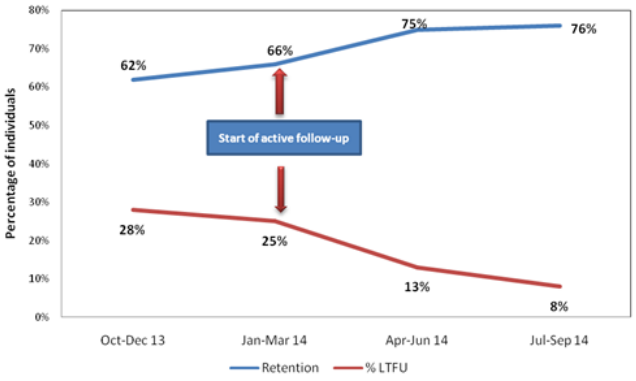
TUPED799

Increasing ART retention in Cote d'Ivoire through active monitoring and follow-up

B.C.J. Diby[1], K.M. N'goran[1], N.J.P. N'da[1], J. Essombo[2], A. Angel[3], S. Howard[4], A. Kouamé[5]
[1]Elizabeth Glaser Pediatric AIDS Foundation, SI&E, Abidjan, Cote D'Ivoire, [2]Elizabeth Glaser Pediatric AIDS Foundation, Country Director, Abidjan, Cote D'Ivoire, [3]Elizabeth Glaser Pediatric AIDS Foundation DC, PRC, Washington, United States, [4]CDC, Departement of Science, Abidjan, Cote D'Ivoire, [5]Ministry of Health and Figth against AIDS, HIV Programm, Abidjan, Cote D'Ivoire
Presenting author email: dcharlesjoseph@pedaids.org

Background: Ensuring HIV-positive clients are retained in ART care programs is a significant challenge for HIV program implementers. Within Elizabeth Glaser Pediatric AIDS Foundation-Cote d'Ivoire (EGPAF-CDI) supported sites, the 12-month ART retention rate was 62% in October -December 2013. Factors that influence patient retention include health systems challenges and the patient's own perceptions and experiences of ART. EGPAF-CDI's care and treatment program has been working to address the myriad factors associated with poor adherence. Strategies were implemented to improve patient retention including active monitoring of patients on ART and community follow-up.
Methods: A strategy to monitor and reach out to ART patients was implemented in 27 sites in January 2014 in 4 health regions and 16 health districts. This strategy involved EGPAF-CDI working with sites to develop an electronic list of patients ever initiated on ART. EGPAF field program officers would update this electronic list weekly to insert data on new clients enrolled, clients who had been retained for 6 months and clients who had been retained for 12 months

post-ART initiation. Outcomes of each patient were recorded; patients were listed as either active, transferred, dead, stopped ART or lost to follow-up (LTFU).
The facility community counselors would use the electronic list from EGPAF computers of those who had not returned to the clinics to refill their ART prescription. Community counselors would contact clients through phone calls or home visits to confirm client outcome and if applicable, encourage clients to resume treatment as soon as possible.
Results: Overall, 12-month retention increased from 62% (N=734) in 2013 to 76% (N=1565) in July-September 2014 in the 27 sites. This increase was observed along with a decrease in the LTFU rate from 28% (N=734) in October -December 2013 to 8% (N=1565) in July-September 2014.



[Figure: Retention and LTFU rates in 27 sites]

Conclusions: Active monitoring and follow-up of ART patients resulted in increased retention and decreased LTFU in select sites in Cote d'Ivoire, but requires strong human resource commitment and community counselor participation. Next steps include scale-up of this approach in all ART sites supported by EGPAF-CDI and greater engagement from health care workers at facilities.

TUPED801

Using the new ART guidelines to overcome the challenges of paediatric and adolescent ART enrollment in resource-limited settings: The AIDS Support Organization (TASO) Gulu experience

P. Ijotre
The AIDS Support Organisation (TASO) Uganda Ltd., Medical Department, Kampala, Uganda
Presenting author email: ijotrepeter@yahoo.com

Background: In Uganda, children constitute 16% of new HIV infections. Without early diagnosis, care and treatment, 50% of HIV positive infants die at 2 years and 75% at 5 years; and between 2005 and 2012, HIV related deaths among adolescents increased by 50%, while the global number of Adult HIV- related deaths fell by 30%. Antiretroviral therapy (ART) for HIV infected children has lagged behind that of adults for several reasons, including lack of identification of infected children and healthcare providers not being comfortable treating children. The new Global and national ART guidelines (2014) which recommend initiation of all children less than 15 years irrespective of their clinical or immunological staging was implemented by TASO Gulu from April 2014.
Methods: Clinicians and counselors were oriented in the new ART guidelines. Children and adolescents were identified from the general clinics by the expert clients at registration and linked to PMTCT-EID and adolescent clinics respectively for specialized care and treatment. A master list of children and adolescents eligible but not started on ART was printed out, followed up and were started on ART. 2 focal point persons ensured that all children were monitored for growth and development and started on ART during the specialized clinics.
Results: 679 children and adolescents were enrolled on ART within one year. 67% (452/679) enrolled in the period April to September 2014(when implementation of the new ART guidelines were started) which is twice the enrolment for the period October 2013 to march 2014(227). Similarly in the adult clinic, 499 were enrolled compared with 211 for the respective periods. 85% were offered psychosocial support. 98% had good adherence (>95%).
Conclusions: Using simplified Guidelines can overcome the challenges of Paediatric and adolescent ART enrollment.

TUPED802

Peer-provided HIV counselling and testing for key populations in Cambodia: lessons learnt and implications for service delivery

T. Sovannary[1], Y. Siyan[1], J. Willem van Wijngaarden[2], M. Srey[1], G. Mburu[3]
[1]KHANA, Phnom Penh, Cambodia, [2]Independent Consultant, New York, United States, [3]International HIV/AIDS Alliance, Hove, United Kingdom
Presenting author email: gmburu@aidsalliance.org

Background: Peer-provided testing can potentially increase uptake of HIV testing at the community level. However, this approach has not been widely implemented in Cambodia. In April 2013, KHANA, a local Cambodian organization began the implementation of peer-provided finger-prick testing for key populations. This study explores early outcome and lessons learnt.
Methods: Programmatic data related to the intervention was collected. This was complemented by semi-structured interviews (n= 29) and focus group discussions (5 sessions; n=27) conducted among beneficiaries, peer providers of finger-prick testing, and key population representatives from implementing organizations.
Results: By June 2014, peer-provided testing had been expanded to 18 municipality and provinces, and 391 trained peer providers of testing had conducted 15,000 HIV tests among entertainment workers (EW), men who have sex with men (MSM), transgender people (TG), and people who use or inject drugs (PWUD/PWID). Of the 15,000 HIV tests conducted, 75 were positive. Qualitative findings suggested that key population beneficiaries found that the experience of being counselled and tested by a peer was acceptable and, in some cases, preferable to professional counsellors at VCT centres. Peer providers of HIV testing reported that the training that occurred as part of the project was beneficial in terms of capacity building. No incidents of undue pressure to test were reported.
Conclusions: Peer-provided finger-prick testing is acceptable among key populations in our study setting, and may contribute to early identification of HIV infection and linkage to care as well as capacity building of community-based peer health workers. However, given that only 75 new HIV cases, that is 0.005%, were found out of the 15,000 tests conducted between March 2013 and March 2014 a better understanding of the HIV prevalence and geographic dynamics is required. This will inform subsequent strategies for reaching key populations.

Integration of HIV services with other health programmes

TUPED803

Integration and utilization of family planning services in a HIV clinic in Nairobi, Kenya

E. Njuguna[1], S. Ilovi[2], K. Mutai[2], P. Njoroge[2], P. Muiruri[1], J. Kinuthia[2]
[1]Kenyatta National Hospital, Nairobi, Kenya, [2]University of Nairobi, Nairobi, Kenya
Presenting author email: kinuthia@u.washington.edu

Background: Women's knowledge and access to reproductive health services improves their ability to safely achieve their required fertility, thus reducing maternal and infant morbidity and mortality. In HIV infected women the levels of unintended pregnancies range from 51-90%, with 90% of all HIV transmission among children less than 15 years being attributed to Mother to Child Transmission. Integrated Family Planning (FP) services and HIV services have been recommended as a cost effective strategy to prevent mother to child transmission.
We aimed to determine the utilization of FP services among HIV Infected women visiting the HIV clinic.
Methods: A cross-sectional quantitative study involving randomly selected HIV positive females was conducted in Kenyatta National Hospital, Nairobi, Kenya. The outcome variable was the utilization of family planning services. Data were acquired by one to one interviewer administered structured questionnaires and entered into Access data base. Analysis was done using Stata version 11.1.
Results: We enrolled a total of 387 patients, median age (IQ range) 40 years (36-44). The contraceptive prevalence was 53% with an unmet need of family planning of 38.5%. Patients were more likely to use family planning if they were married, (OR 12.9, 95% CI 6.5-25.7, p-value <0.01), if condoms were offered at the clinic (OR 3.2, 95% CI 1.9-5.4, p-value <0.001), if they discussed contraception with the clinic staff (OR 3.4, 95%CI 2.2-5.4, p-value <0.001) and their partners (OR 2.6, 95%CI 1.7-4.0, p<0.001). They were less likely to use FP if they had expressed fertility desire (OR 3.0, 95%CI 1.8-4.8, p-value < 0.001). Widows were less likely to use any form of FP than married couples despite having sexual partners (OR 0.1, 95% CI 0.04-0.2, p-value <0.001). Similarly, single and divorced women were less likely to use FP than married women (OR 0.1, 95% CI 0.03-0.3, p-value <0.001) and (OR 0.4, 95% CI 0.02-0.1, p-value <0.001) respectively.

Conclusions: The unmet need of family planning was high. Staff and partner involvement increased utilization of family planning while particular groups such as sexually active widows, single and divorced women were identified as being in need of targeted interventions.

TUPED804

Missed opportunities to reduce the risk of cardiovascular disease amongst people living with HIV: high prevalence of untreated cardiovascular disease risk factors at an HIV clinic in South Africa

M. Rabkin[1], A. Mutiti[2], C. Chung[3], Y. Zhang[4], Y. Wei[4], W. El-Sadr[5]
[1]Columbia University Mailman School of Public Health, ICAP Columbia, New York, United States, [2]ICAP Columbia, Pretoria, South Africa, [3]ICAP Columbia, Lilongwe, Malawi, [4]Columbia University Mailman School of Public Health, Biostatistics, New York, United States, [5]Columbia University Mailman School of Public Health, ICAP, Epidemiology and Medicine, New York, United States
Presenting author email: mr84@columbia.edu

Background: In South Africa (SA), both HIV and cardiovascular disease (CVD) are prevalent health threats. As people living with HIV (PLWH) live longer on antiretroviral therapy (ART), identifying and managing those with CVD risk factors (CVDRF) and providing prevention services to others will optimize health outcomes. However, there is insufficient information about CVDRF amongst PLWH on ART in SA, and optimal screening strategies have not been identified.
Methods: We conducted a cross-sectional study at an urban HIV clinic in Free State, SA. 175 PLWH ≥ 30 years, on ART, were screened for CVDRF via questionnaire, physical examination, chart review, total cholesterol and HbA1c. High blood pressure (HBP) was defined as average systolic BP > 140 mmHg and/or diastolic BP > 90 mmHg. Obesity was defined as body mass index > 29. Diabetes was defined as HbA1c > 6.5%. 10-year WHO/ISH risk stratification was used to define ten-year CVD risk in participants ≥ 40 years.

		All (N=175)	Female (N=130)	Male (N=45)
Demographic and Socioeconomic				
Sex, female		130 (74.2%)		
Age, mean (SD)		45.4 (8.8)	44.7 (9.0)	47.6 (7.9)
Population group	*Black/African*	173 (98.9%)	128 (98.5%)	45 (100%)
Marital status	*Currently married or living with partner*	56 (32.0%)	34 (26.2%)	22 (48.9%)
Educational attainment	*Any secondary*	66 (37.9%)	41 (31.5%)	25 (55.6%)
	Completed secondary	75 (43.1%)	61 (46.9%)	14 (31.1%)
Primary occupation	*Not employed*	103 (58.9%)	80 (61.5%)	23 (51.1%)
Average household monthly income, mean (SD) in $USD		226 (187)	196 (156)	289 (231)
Household has electricity		158 (90.3%)	121 (93.1%)	37 (82.2%)
Household has piped water		175 (100%)	130 (100%)	45 (100%)
Health - HIV history				
# years at this clinic, mean (SD)		3.98 (2.2)	4.07 (2.3)	3.73 (1.9)
Most recent CD4, mean (SD)		411 (184)	395 (213)	322 (175)
Most recent viral load	*missing*	32 (18.9%)	30 (23.1%)	2 (4.4%)
	undetectable	94/143 (65.7%)	67/100 (67.0%)	27/45 (60.0%)
	detectable	49/143 (34.3%)	33/100 (33.0%)	16/45 (40.0%)
	mean (SD) for those with detectable results	8,693 (26,454)	4,326 (9,028)	17,700 (44,012)
On nevirapine or efavirenz		159 (90.9%)	119 (90%)	42 (93.3%)
On protease inhibitor-containing regimen		0	0	0
Health - NCD history				
Prior diagnosis of hypertension (HTN) documented in chart		52 (29.9%)	46 (35.6%)	6 (13.3%)
Prior diagnosis of diabetes (DM) documented in chart		7 (4%)	5 (3.9%)	2 (4.4%)
Prior diagnosis of high cholesterol/hyperlipidemia documented in chart		14 (8%)	13 (10.1%)	1 (2.2%)
Prior documentation of cigarette smoking (ever documented)		1 (0.6%)	0	1
Prior documentation of weight (ever documented)		173 (99.4%)	129 (100%)	44 (97.8%)
Prior diagnosis of obesity documented in chart		0	0	0
High BP documented at most recent visit	Any high BP (SBP >140 and/or DBP ≥ 90)	61 (34.9%)	46 (35.4%)	15 (33.3%)
	Grade 1 (SBP 140-159 and/or DBP 90-99)	41 (23.4%)	32 (24.6%)	9 (20%)
	Grade 2 (SBP ≥ 160 and/or DBP ≥ 100)	20 (11.4%)	14 (10.8%)	6 (13.3%)
Of participants with diagnosis of HTN, percent with high BP when last documented		63.5%	61%	83%
Findings at study visit				
High BP	Any high BP (SBP >140 and/or DBP ≥ 90)	66 (37.7%)	50 (38.5%)	16 (35.6%)
	Grade 1 (SBP 140-159 and/or DBP 90-99)	41 (23.4%)	31 (23.8%)	10 (22.2%)
	Grade 2 (SBP ≥ 160 and/or DBP ≥ 100)	25 (14.3%)	19 (14.6%)	6 (13.3%)
BMI	*underweight (BMI <18.5)*	17 (9.8%)	8 (6.2%)	9 (20%)
	normal weight (BMI 18.5-24.9)	70 (40%)	44 (34%)	26 (57.8%)
	Overweight (BMI 25-29)	31 (17.8%)	25 (19.4%)	6 (13.3%)
	Obese (BMI > 29)	56 (32.2%)	52 (40%)	4 (8.9%)
HbA1c	*Diabetes (HbA1c > 6.5%)*	7 (4.1%)	6 (4.7%)	1 (2.2%)
Total Cholesterol, mean (SD) in mg/dL		184.8 (41.38)	188.2 (40.85)	175.4 (41.65)
	Hypercholesterolemia (TC > 240 mg/dL)	18 (10.4%)	15 (11.7%)	3 (6.6%)
Ever smoked tobacco products (cigarette, cigar, pipe)?		54 (30.9%)	16 (12.3%)	38 (84.4%)
Currently smokes tobacco products (in past 30 days)		27 (15.4%)	4 (3.1%)	23 (51.1%)
Currently smokes tobacco daily		23 (13%)	3 (2.3%)	20 (44.4%)
Self-describes as physically active		155 (88.6%)	116 (89.2%)	39 (86.7%)
Did vigorous activity on 3+ days in past week		76 (43.4%)	51 (43.6%)	25 (61.0%)
# days eats fruit in a typical week, mean (SD)		3.1 (1.6)	3.07 (1.53)	3.03 (1.8)
# days eats vegetables in a typical week, mean (SD)		4.3 (2.0)	4.2 (1.95)	4.46 (2.29)

[Table 1. Participant demographics, health history, and CVD RF prevalence]

Results: Table 1 shows participant demographics, medical history, and CVDRF prevalence. Average CD4$^+$ count was 411/mm^3 (SD±184); 65.7% of 143 participants with documented viral load had undetectable levels. Most (90.9%) were taking ART regimens containing nevirapine or efavirenz; none took protease inhibitors. At the study visit, 37.7% of participants had HBP, which was generally not well controlled. Only 64.9% of those with HBP had a prior diagnosis of hypertension, and their previous BP control had been poor, with nearly two-thirds (63.5%) having HBP at their last HIV clinic visit. Cigarette smoking was documented in <1% of charts, while on interview 15.4% were current tobacco smokers (3.1% women, 51.1% men, p <0.001). Of all participants, 10.4% had random total cholesterol >240 mg/dL, 4.1% had diabetes, and 32.2% were obese (40% women, 8.9% men, p <0.001). Of 110 participants eligible for CVD risk stratification, 96.4% had <10% ten-year risk of a cardiovascular event.
Conclusions: CVDRF were common amongst PLWH on ART. Despite their engagement in continuity care, many participants had not been previously diagnosed with CVDRF. Systematic CVDRF screening and effective preventive and therapeutic management are necessary to maximize health and longevity of PLWH.

TUPED805

Caries experience in HIV-infected, HIV-perinatally exposed but uninfected and HIV unexposed, uninfected Nigerian children: a comparative study

M. Coker[1], S. El-Kamary[2], P. Akhigbe[3], O. Obuekwe[3], E. Mongodin[4], M. Charurat[1], W. Blattner[1]
[1]Institute of Human Virology, University of Maryland, Division of Epidemiology, Baltimore, United States, [2]University of Maryland, Baltimore, United States, [3]University of Benin Teaching Hospital, Benin, Nigeria, [4]Institute of Genomic Sciences, University of Maryland, Baltimore, United States

Background: Oral health is one of the highest unmet needs of HIV infected children in the developing world. Studies have shown that HIV-infected subjects experience more dental caries and other oral diseases compared to their uninfected counterparts, suggesting a compromised bacterial environment. HIV exposed but uninfected children might also be at a higher risk for such infections. Although HIV infection is associated with well-known oral pathologies, there remains a dearth of comparative studies aimed at determining the association between HIV infection/exposure and early childhood caries.
This information will help understand the extent to which the oral microbiome is disrupted with HIV infection or perinatal exposure.
Methods: A cross-sectional study of 3 groups of age-matched children receiving care and treatment at a Nigerian tertiary hospital. The groups comprise of 100 each: - HIV infected (HI), HIV exposed but uninfected (HEU), and HIV unexposed and uninfected (HUU) children aged between 6 and 72 months. Standardized clinical oral examinations were performed by trained dentist-examiners in conjunction with saliva and plaque sample collection to determine microbiome diversity using 16S DNA sequencing.
Results: Overall, the prevalence of caries was 10%. Compared with HUU children, HI children presented with more oral diseases (34% vs.17%) and a higher mean caries index (1.8 vs 1.2), however there were no significant differences in caries prevalence (16% vs. 11% p=0.31). HIV exposure was not associated with dental caries or oral diseases. Caries was associated with age, CD4 counts, socioeconomic status and sugar intake. Preliminary data from the analysis of 10 saliva samples per group suggest that the HI group had a higher diversity index compared to the HUU group.
Conclusions: HIV infected children present with more dental caries than HIV unexposed and uninfected children. Our data suggests that HIV infection might be associated with caries severity. Our study adds to the body of knowledge regarding the association between caries, the oral microbiome and HIV. Further comparative longitudinal studies are required to examine this relationship particularly at advanced stages of HIV infection. This knowledge will help inform the integration of oral health services to the care of pediatric HIV patients particularly in the developing world.

TUPED806

An unannounced standardized patient actor assessment of STI services in public health facilities in South Africa

P. Kohler[1,2], S. Jed[3], E. Pillay[3], G. Mema[3], S. Galagan[1], J. DeKadt[3], J. Dombrowski[4], M. Golden[4], K. Tapia[1], E. Naidoo[3], K. Holmes[1,4,5], E. Marumo[6]
[1]University of Washington, Global Health, Seattle, United States, [2]University of Washington, Psychosocial and Community Health, Seattle, United States, [3]University of Washington, International Training and Education Center for Health, Pretoria, South Africa, [4]University of Washington, Medicine, Seattle, United States, [5]University of Washington, Epidemiology, Seattle, United States, [6]National Department of Health, STI and HIV Prevention, Pretoria, South Africa
Presenting author email: pkohler2@uw.edu

Background: Sexually transmitted infections (STIs) are associated with increased HIV acquisition and transmission. Health systems barriers can prevent implementation of high quality, integrated STI/HIV care. This study aimed to evaluate STI service delivery on behalf of the National Department of Health in South Africa.
Methods: A cross-sectional assessment of 50 public health facilities in nine provinces in South Africa was conducted. Clinics were randomly sampled from clinical sentinel surveillance sites, facilities selected by the government for enhanced monitoring of STIs, and were sampled proportional to population size at the province level. Each clinic participated in a survey and an unannounced standardized patient (SP) assessment: two male and two female actors per

clinic. SPs reported checklist items to a research assistant. Unweighted proportions of SPs receiving STI services were calculated, and standard errors were adjusted for clustering at the clinic level.

Results: Professional nurses provided the majority of care; a median of four nurses per clinic. 198 SPs saw a health provider, although three were initially turned away due to high client volume. Nine visits ended prematurely due to clinician refusal to continue after SP declined physical examination or detection of the SP. Overall, 58% of 186 SPs were offered correct treatment regimens, 38% were offered condoms, 69% received counseling on partner notification, and 73% were offered an HIV test; however only 22% of SPs received all of these services. Female clients were significantly less likely to receive condoms (p=0.002), partner notification counseling (p=0.023), counseling about safer sex (p=0.047), or referral to HIV testing (p=0.016). Discussion of or referral to family planning and circumcision services was less frequent (32% and 11% respectively). SPs perceived their care to be compassionate and non-judgmental, however reported concerns over privacy in waiting areas and treatment rooms.

	Total (N=186)		Men (N=93)		Women (N=93)		
	N	*% (SE)*	*N*	*% (SE)*	*N*	*% (SE)*	*p-value*
Appropriate treatment regimen*	108	58.1 (4.7)	60	64.5 (5.5)	48	51.6 (6.0)	0.057
Received 1 or more condoms*	70	37.6 (4.7)	45	48.4 (6.2)	35	26.9 (5.2)	0.002
Partner notification counseling*	129	69.4 (3.8)	72	77.4 (4.4)	57	61.3 (5.8)	0.023
Safer sex counseling	125	67.2 (4.2)	68	73.2 (4.6)	57	61.3 (5.6)	0.047
Offered HIV test*	135	72.6 (4.2)	74	79.6 (4.4)	61	65.6 (5.7)	0.016
Discussed male circumcision (males only)	10	10.8 (3.5)	10	10.8 (3.5)			
Discussed family planning (females only)	30	32.3 (4.8)			30	32.3 (4.8)	
All key services provided (*above)	40	21.5 (4.1)	27	29.0 (5.5)	13	14.0 (4.5)	0.014

[STI services received by standardized patients]

Conclusions: The majority of clinicians provided correct treatment regimens, counseling, and HIV testing. Referrals to other services and condom provision continue to be challenges, especially among female clients. Current findings represent improved care when compared to a similar 2002 national evaluation, in which 8.1% were offered HIV testing, 7.7% were offered contraception, and 36% reported partner notification counseling.

TUPED807

Does the patient experience of healthcare change following the implementation of the integration of HIV care into primary health care clinics? Perspectives from patient surveys in Free State South Africa

A. Rawat[1], K.E. Uebel[2], D. Moore[3], L. Cingl[4], J. Spiegel[5], A. Yassi[1]
[1]University of British Columbia, School of Population and Public Health, Vancouver, Canada, [2]Free State Department of Health, Bloemfontien, South Africa, [3]British Columbia Centre for Excellence in HIV/AIDS, Vancouver, Canada, [4]Charles University, Institute of Economic Studies, Faculty of Social Sciences, Prague, Czech Republic, [5]University of British Columbia, Liu Institute of Global Issues and the School of Population and Public Health, Vancouver, Canada
Presenting author email: angelirawat@gmail.com

Background: Integration of HIV-care into primary health care (PHC) clinics is a strategy used in South Africa to expand access to antiretroviral therapy (ART) while maximising health system resources. However, how patients at PHC clinics perceive changes in their healthcare after integration is unknown.

Methods: In Free State, South Africa, we administered surveys in two cross-sectional waves ten months apart to patients attending four PHC clinics that were at various stages after PHC clinics began offering ART as part of their PHC services. We measured Quality of Care (QoC) and Satisfaction with Staff (SwS) using validated instruments. We used T-tests, Pearson's χ^2 and multiple linear regression to understand changes in QoC and SwS between years of administration. Qualitative questions were collected and thematically coded for dominant themes.

Results: 910 patients/caregivers (2012:n=487, 2013:n =423) participated. Adjusted regression estimates showed no differences in QoC and SwS from 2012 to 2013. QoC was 1.63 points higher (CI:0.16,3.10)(p< 0.05) for those age 36-45 compared to 18-25. Those attending clinics for >10 years reported 1.44 points lower QoC (CI:-2.79,0.09)(p< 0.05) than those coming for 6 months to 1 year. Those coming every 3 months reported a 2.76 point higher QoC (CI: 0.13,5.39)(p< 0.05) than those coming at least twice a month. Compared to chronic disease patients, child health attendees reported 2.69 points lower QoC (CI:-4.49,-0.89)(p< 0.01), ART patients reported 1.67 points lower QoC (CI:-3.08,-0.26)(p< 0.05) and tuberculosis patients reported 3.53 points higher QoC (CI:0.83,6.23)(p< 0.05). Compared to chronic disease attendees, child health attendees reported a 1.77 points lower SwS (CI,-2.71,-0.83)(p< 0.01) while tuberculosis attendees reported a 2.13 higher SwS (CI:0.74,3.52(p< 0.05). The most common complaint and compliment for staff was long wait time and respectful/friendly staff, respectively.

Conclusions: While the implementation of integration of HIV-care into PHC clinics progressed, we identified no changes to QoC and SwS and conclude that integration was done with concerns for providing high-quality healthcare. However, we observed variations in QoC and SwS reported by participants' purpose of visit. Further research is needed to understand these disparities in patient QoC and SwS to ensure excellent healthcare for patients attending PHC clinics with integrated HIV-care.

TUPED808

Who doesn't disclose their HIV-positive status? Patterns of disclosure and factors associated with not disclosing to a spouse or primary sexual partner among TB-HIV patients initiating antiretroviral therapy in Lesotho

E. Hayes-Larson[1,2], S. Saito[1,2], Y. Hirsch-Moverman[1], L.B. Maama[3], K. Frederix[1], B. Pitt[1], A.A. Howard[1,2]
[1]Columbia University Mailman School of Public Health, ICAP, New York, United States, [2]Columbia University Mailman School of Public Health, Department of Epidemiology, New York, United States, [3]Lesotho Ministry of Health, National Tuberculosis Control Programme, Maseru, Lesotho
Presenting author email: elh2167@cumc.columbia.edu

Background: Disclosure of HIV-positive status has important implications for antiretroviral adherence and preventing transmission to sexual partners, but some TB-HIV patients preferentially disclose only their TB diagnosis. We assessed patterns of HIV disclosure and factors associated with non-disclosure among adult TB-HIV patients initiating ART within 8 weeks of TB treatment initiation who enrolled in the **S**tart **T**B patients on **A**RT and **R**etain on **T**reatment (START) Study.

Methods: START is an ongoing cluster-randomized implementation science trial in 12 health facilities in Berea district, Lesotho, evaluating the effectiveness, cost-effectiveness, and acceptability of a combination intervention package (CIP) vs. standard of care to improve early ART initiation, retention, and TB treatment success among TB-HIV patients. Interviewer-administered baseline questionnaires (collected 4/2013-12/2014) were analyzed to describe patterns of HIV disclosure. Factors were assessed for associations with non-disclosure to a spouse/primary partner among married/cohabitating participants using Chi-square, Fisher's exact, and Wilcoxon rank-sum tests. Variables associated at p< 0.2 were included in an initial multivariate logistic regression model; the final model was selected using manual backward stepwise selection.

Results: Among 300 participants with available data, 285 (95%) had disclosed to someone other than healthcare workers. Participants had most commonly disclosed to a spouse/primary partner (74.3%), parent (70.5%) or sibling (61.9%). Among 156 married/cohabitating participants, 128 (82.1%) had disclosed to their spouse/primary partner and 33 (21.2%) knew their partner was HIV-positive. The median age was 37y, 35.9% were female, 55.8% were sole/shared heads-of-household, and 32.0% reported hazardous/harmful alcohol use. In bivariate analyses, not knowing if a partner was HIV-positive was associated with non-disclosure (p=0.045). On multivariate analysis controlling for age and knowledge of partner HIV-positive status, factors associated with not disclosing to a spouse/primary partner included female sex (AOR 3.32, 95% CI 1.10-10.07), and self-reported hazardous/harmful alcohol use (AOR 3.64, 95% CI 1.27-10.42).

	Overall (N=156)		*HIV status disclosed (N=128)*		*HIV status not disclosed (N=28)*		*Unadjusted p-value*	*Adjusted analysis (N=150), AOR (95% CI)*	
Age, median (IQR)	37	(31-45)	36	(31-44)	41	(34-48)	0.150	1.03	(0.98-1.08)
Female, n (%)	56	(35.9%)	43	(33.6%)	13	(46.4%)	0.200	**3.32**	**(1.10-10.07)**
Any electricity in home, n (%)	80	(51.3%)	70	(54.7%)	10	(35.7%)	0.069		
Hazardous or harmful alcohol use (AUDIT), n (%)	48	(32.0%)	36	(28.8%)	12	(48.0%)	0.060	**3.64**	**(1.27-10.42)**
Other person in home with HIV, n (%)	62	(42.2%)	54	(44.6%)	8	(30.8%)	0.194		
Does not know if sexual partner is HIV-positive, n (%)	123	(78.8%)	97	(75.8%)	26	(92.9%)	0.045	3.97	(0.85-18.44)
HIV knowledge (# correct out of 7), median (IQR)	5	(4-6)	5	(4-6)	5	(4-6)	0.318		
TB knowledge (# correct out of 7), median (IQR)	6	(5-6)	6	(5-6)	5	(4-6)	0.112		
CIP study arm, n (%)	84	(53.8%)	71	(55.5%)	13	(46.4%)	0.385		

[Associations with non-disclosure of HIV to partner]

Conclusions: Although nearly all TB-HIV patients reported disclosing their HIV status to someone other than a healthcare worker by the time of ART initiation, 17.9% of married/cohabitating participants had not disclosed to their partner. Interventions supporting TB-HIV patients with disclosure to their partners are urgently needed, particularly for women and those with hazardous/harmful alcohol use.

TUPED809

Incorporating non-communicable disease screening into community-based HIV counselling and testing in Cape Town, South Africa

M. van Niekerk, H. Draper, S.-A. Meehan
Stellenbosch University, Desmond Tutu TB Centre, Pediatrics, Faculty of Medicine & Health Sciences, Cape Town, South Africa
Presenting author email: mbunting@sun.ac.za

Background: Non-communicable diseases (NCD`s) account for 80% of deaths in low and middle income countries. In South Africa hypertension, diabetes mellitus, obesity and hyperlipidaemia are increasing due to on-going lifestyle transition as a consequence of economic development. Prevalence of NCD`s amongst the HIV-infected has increased due to premature aging effects of HIV infection on the immune system. The HIV epidemic in South Africa is huge with 12% prevalence. HIV counselling and testing (HCT) is a vital step in HIV prevention and care and is an entry point for NCD screening. This study used routine data to determine whether HIV status, age and gender are associated with NCDs in a population who self-initiate for community-based HCT.
Methods: Five Community HCT sites were established in partnership with non-government organizations, in high disease burden areas around Cape Town. Clients access HCT services at stand-alone centres (fixed sites) or (mobile sites), where services are provided from a mobile van and tents. HIV rapid testing was conducted according to national guidelines. Non-communicable disease screenings include; BMI (≥24 vs < 24), hypertension (high BP vs not high BP) and random blood glucose (≥11.0mmol vs < 11.0mmol). Comparisons were made using either Chi-square or Fisher's Exact and multivariable logistic regression.
Results: 11 210 clients were screened for HIV (October 2013 to June 2014). 443 clients were diagnosed with HIV (4%); of which 61% were diagnosed at mobile services. A higher proportion of clients with a high BMI(≥24) attended the fixed sites (69% vs 62%;p=< 0.001). A higher proportion of clients with a high BP(≤140/90 - ≤190/100)attended at the mobile site (73% vs 64%;p< 0.001). Elevated glucose (>11.0mmol) was associated with HIV status (0.28 vs 1.86%; p< 0.022). Females were more likely than males to have higher BMIs and lower BPs when controlling for age (OR: 5.6; 95% CI:(5.1 - 6.2), p<0.001 and OR:0.7; 95% CI:(0.6-0.8), p<0.001, respectively).

	Mobile		Stand-alone (fixed sites)	
	HIV uninfected (n=8,405)	HIV infected (n=271)	HIV uninfected (n=2,351)	HIV infected (n=172)
Median age in yrs (IQR)	30 (24-39)	30 (25-36)	28 (23-34)	28 (24-33)
Male(%)	4,481(53)	102 (38)	722 (31)	26 (15)
Female(%)	3,924(47)	169 (62)	1,629(69)	146 (85)
BMI Low[<18](%) % calculation excludes missing data	134(2)	7(3)	36(1.5)	1(0.5)
BMI Normal[18-24](%) % calculation excludes missing data	2,240(27)	78(29)	599(25)	47(27)
BMI High [>24](%) % calculation excludes missing data	3,820(45)	111(41)	1,435(61)	103(60)
Missing (%)	2,211(26)	75(28)	281(12)	21(12)

[BMI values for HIV status by clinic type]

Conclusions: Incorporating chronic health screening into a community HCT model can potentially allow for multiple disease screening in a single visit.This model is effective in resource constrained settings by providing an entry point for NCD screening and early case-finding.

TUPED810

Estimating the need for integrated management of hypertension and diabetes mellitus in HIV patients, Zomba District, Malawi

O. Divala[1], S. Sodhi[1,2], N. Kayange[3], M. Nyirenda[4], Z. Ismail[5], M. Joshua[6], G.S. Chinomba[7], T. Beyene[1], A. Kwekwesa[1], H. Akello[1], J. Bourgeois[1], G. Sankhulani[1], A. Matengeni[1], G. Mateyu[1], A. Chan[1], R. Bedell[1], T.J. Allain[3], J. Mallewa[3], J.J. van Oosterhout[1,3]
[1]Dignitas International, Zomba, Malawi, [2]University Health Network, Toronto Western Hospital, Toronto, Canada, [3]College of Medicine, Department of Medicine, Blantyre, Malawi, [4]Malawi Epidemiology and Intervention Research Unit, Lilongwe, Malawi, [5]Pirimiti Rural Hospital, Zomba, Malawi, [6]Ministry of Health, Zomba Central Hospital, Zomba, Malawi, [7]Ministry of Health, Zomba District Health Office, Zomba, Malawi
Presenting author email: o.divala@dignitasinternational.org

Background: Integrated care for HIV and non-communicable diseases can benefit patients for several reasons. Planning integrated care in busy, understaffed HIV clinics requires insight into the expected additional burden of care. However, prevalence rates of hypertension and diabetes in African HIV patients have been studied infrequently and no data exist about the anticipated burden of pharmacological hypertension treatment based on hypertension stage and cardiovascular disease (CVD) risk scores.
Methods: We conducted a cross-sectional study among adults at HIV clinics in Zomba Central Hospital (urban) and Pirimiti Hospital (rural), southern Malawi. Hypertension was diagnosed according to WHO criteria, using the average of 3 measurements and confirmed at two follow-up visits. Diabetes was diagnosed following WHO criteria and lipodystrophy with a validated questionnaire. Non-fasting samples were taken for point-of-care determination of total- and HDL-cholesterol. CVD risk was determined using WHO/International Society of Hypertension (ISH) and Framingham risk scores. Without means to diagnose end-organ damage, hypertension pharmacological treatment indication was determined by systolic-BP≥160mmHg or 10-year CVD risk >20%.
Results: 952 patients were enrolled, mean age 43 years, 72% female; 96% were on ART (85% tenofovir/lamivudine/efavirenz), mean duration 48 months.15% were overweight or obese, 27% had elevated waist/hip ratio and 43% lipodystrophy; 4% smoked, 16% had elevated total cholesterol. Women had significantly lower age, alcohol and tobacco consumption, higher education, BMI, waist/hip ratio, and ART duration. Rural patients had significantly lower education, BMI and ART duration.
Prevalence of hypertension was 24% (95%-CI 21-26), with no significant differences between men/women and rural/urban. 39% of hypertensives had systolic-BP≥160mmHg. Among those with hypertension stage I (systolic-BP< 160), 10-year CVD risk >20% was very uncommon (0% WHO/ISH score; 4% Framingham score), without significant differences between men/women and urban/rural. Diabetes prevalence was 3% (95%-CI 2-4), urban 5% vs. rural 2%, p=0.02; no significant difference between men/women.
Conclusions: The prevalence of diabetes and hypertension among Malawian adults in HIV care was lower than in previous surveys. According to criteria validated in western patients, around 40% of hypertensive patients require pharmacological treatment. The expected burden of integrated pharmacological treatment for HIV/hypertension was 10% and for HIV/diabetes 3% among patients in HIV care.

TUPED811

Lipid abnormalities in urban and rural patients on ART in Zomba district

O. Divala[1], S. Sodhi[1,2], N. Kayange[3], M. Nyirenda[4], Z. Ismail[5], M. Joshua[6], G.S. Chinomba[7], T. Beyene[1], A. Kwekwesa[1], H. Akello[1], J. Bourgeois[1], G. Sankhulani[1], A. Matengeni[1], G. Mateyu[1], A. Chan[1], T.J. Allain[3], J. Mallewa[3], J.J. van Oosterhout[1,3]
[1]Dignitas International, Zomba, Malawi, [2]University Health Network, Toronto Western Hospital, Toronto, Canada, [3]College of Medicine, Department of Medicine, Blantyre, Malawi, [4]Malawi Epidemiology and Intervention Research Unit, Lilongwe, Malawi, [5]Pirimiti Rural Hospital, Zomba, Malawi, [6]Ministry of Health, Zomba Central Hospital, Zomba, Malawi, [7]Ministry of Health, Zomba District Health Office, Zomba, Malawi
Presenting author email: o.divala@dignitasinternational.org

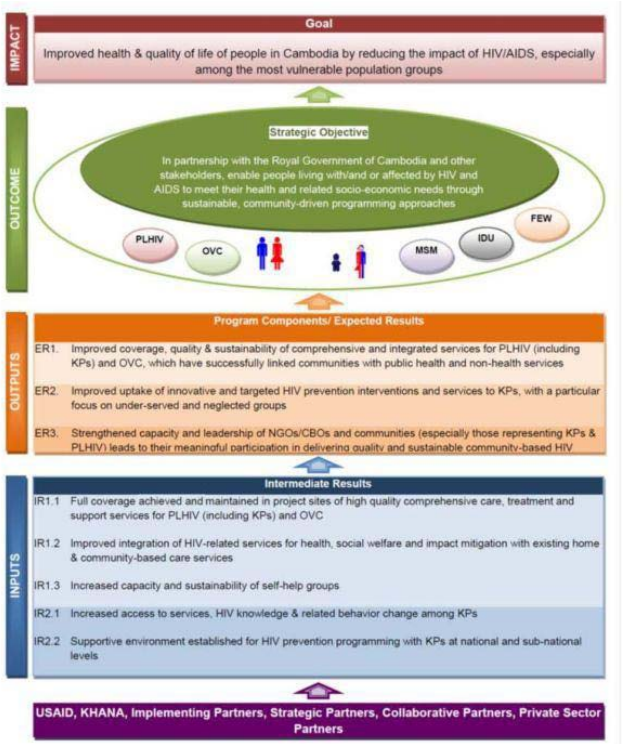
Background: In Africa large populations are ageing with long-term exposure to ART. Antiretroviral drugs may increase risk for cardiovascular conditions, for instance by affecting lipid profiles. Cardiovascular risk factors have therefore become a research priority, but few data about lipid abnormalities from HIV infected Malawians exist.
Methods: Adult patients were enrolled into a cross-sectional study from the HIV clinics at Zomba Central Hospital (urban) and Pirimiti Hospital (rural), both in southern Malawi. Lipodystrophy was diagnosed with a validated questionnaire. Non-fasting samples were taken for point-of-care determination of total cholesterol (TC), triglyceride (Tg) and HDL-cholesterol (HDL-c) levels. We used elevated TC/HDL-c ratio to signify increased cardiovascular risk.
Results: 554 patients were enrolled, 73% were female, mean age was 43 years; 97% were on ART, with a mean duration of 51 months, 84% were on tenofovir/lamivudine/efavirenz and 69% had previous exposure to stavudine or zidovudine. 16% were overweight (BMI≥25), 28% had elevated waist/hip ratio, 2% had a previous diabetes diagnosis and 44% had lipodystrophy. Previous exposure to stavudine and/or zidovudine was higher in those with lipodystrophy (78% vs. 62%; p< 0.001). Women were younger and had significantly higher BMI, waist/hip ratio and ART duration. Rural patients had significantly lower BMI and ART duration.
16% had elevated TC, 16% reduced HDL-c and 29% had elevated Tg. These abnormalities were generally mild, more common in women and similar in rural and urban patients. Elevated TC/HDL-c ratio was rare (4%). Elevated waist/hip ratio, but not age, gender, BMI, lipodystrophy diagnosis, duration of ART or urban/rural location, was significantly associated with elevated TC/HDL-c ratio in multivariable analysis.
Conclusions: Lipid abnormalities in ART patients in southern Malawi were generally mild and lipid profiles indicative of increased cardiovascular risk were rare. Prospective studies in ART populations are required to place lipid profiles into context with other cardiovascular risk factors and correlate them with clinical events. Similar to western populations, the waist/hip ratio may be an easily obtainable proxy for increased cardiovascular risk in Malawians on ART.

TUPED812

The impact of integrating HIV and sexual reproductive health services on health and healthcare-seeking behavior of female entertainment workers in Cambodia

S. Yi[1], P. Chhoun[1], S. Suong[1], K. Thin[1], K. Tith[2], S. Tuot[1]
[1]KHANA, Center for Population Health, Phnom Penh, Cambodia, [2]KHANA, Programs, Phnom Penh, Cambodia
Presenting author email: siyan@doctor.com

Background: In Cambodia, despite great successes in the fight against HIV and AIDS, challenges remain to eliminating new HIV infections and addressing sexual reproductive health (SRH) issues in key populations including female entertainment workers (FEWs). To address these issues, the Sustainable Action against HIV and AIDS in Communities (SAHACOM) project has been implemented since late 2009 using a community-based approach to integrate HIV and SRH services. This study evaluates the impacts of the SAHACOM project on SRH risks and care seeking behaviors among FEWs in Cambodia.
Methods: A midterm and end-line comparison design was used. Midterm data were collected in April 2012, and end-line data were collected in March 2014. A two-stage cluster sampling method was used to randomly select 595 women at midterm and 667 women at end line for face-to-face interviews.



[Figure. Logical framework for the SAHACOM]

Sexual reproductive health and care seeking behavior	Midterm (n, %)	End line (n, %)	OR (95% CI)
Had an STI symptom in the past 3 months	235 (39.6)	150 (22.5)	2.2 (1.8-2.8)
Sought care and treatment for the STI symptoms	103 (43.6)	103 (69.6)	2.8 (1.8-4.3)
Always used condom with regular partners	75 (34.1)	64 (31.4)	1.1 (0.8-1.7)
Had sex with clients in (past 3 months)	167 (28.1)	124 (22.5)	2.1 (1.6-2.7)
Always used condom with commercial partners (past 3 months)	103 (85.8)	100 (80.6)	2.6 (1.5-4.5)
Currently using a contraceptive method	188 (31.6)	253 (45.5)	1.3 (1.1-1.7)
Had at least an induced abortion in lifetime	302 (50.8)	359 (53.8)	1.1 (0.9-1.4)
Had at least one abortion during working as a FEW	122 (40.3)	119 (33.1)	1.6 (1.1-1.9)
More than one abortion during working as a FEW	80 (65.6)	55 (46.2)	2.2 (1.3-3.7)

[Comparisons of sexual reproductive health]

Results: Compared to women at midterm, women at end line were significantly less likely to report having sexual intercourse in exchange for money or gifts in the past three months (OR= 2.1, 95% CI= 1.6-2.7). The average number of commercial sexual partners in the past three months also decreased significantly from 5.5 (SD= 13.3) at midterm to 3.6 (SD= 13.9) at end line (p= 0.03). However, women at end line were significantly less likely to report always using condom when having sexual intercourse with clients in exchange for money or gifts (OR= 2.6, 95% CI= 1.5-4.5). Regarding sexually transmitted infections (STIs), women at end line were significantly less likely to report having an STI symptom in the past three months (OR= 2.2, 95% CI= 1.8-2.8) and more likely to seek treatment for the most recent symptom (OR= 2.8, 95% CI= 1.8-4.3). Furthermore, women at end line were significantly more likely to be currently using a contraceptive method (OR= 1.3, 95% CI= 1.1-1.7) and less likely to report having an induced abortion (OR= 1.6, 95% CI= 1.1-1.9) during the time working as a FEW.
Conclusions: The overall findings indicate that the SAHACOM is effective in reducing SRH risks and improving access to SRH care services among FEWs in Cambodia. However, several unfavorable findings merit attention.

TUPED813

A cost-finding study of cervical cancer screening methods integrated into HIV care in Nairobi, Kenya

E. Vodicka[1], J.B. Babigumira[1], M. Mann[1], R.J. Kosgei[2,3], F. Lee[1], N. Mugo[4], T. Okech[5,6], S. Sakr[7], L.P. Garrison, Jr.[1], M.H. Chung[1]
[1]University of Washington, Seattle, United States, [2]University of Nairobi, Department of Obstetrics and Gynecology, Nairobi, Kenya, [3]Kenyatta National Hospital, Department of Research and Special Programs, Nairobi, Kenya, [4]Kenya Medical Research Institute, Nairobi, Kenya, [5]University of Nairobi, Nairobi, Kenya, [6]United States International University, Nairobi, Kenya, [7]Coptic Hope Center for Infectious Diseases, Nairobi, Kenya
Presenting author email: evodicka@uw.edu

Background: Integration of cervical cancer screening into HIV clinics may be an efficient method for decreasing the burden of cervical cancer in low- and middle-income countries. As countries contemplate adopting this practice, choice of screening method - Papanicolaou (Pap) smear, visual inspection with acetic acid (VIA), human papillomavirus (HPV) testing - will be of key importance, and costs should be considered in the decision-making process. The purpose of this study was to determine per screening costs of each method in an integrated setting.
Methods: A micro-costing study was conducted at Coptic Hope Center for Infectious Diseases and Kenyatta National Hospital in Nairobi, Kenya from August to October 2014. We assessed direct medical costs (e.g., supplies, provider visits) and direct non-medical costs (e.g., transportation) of each testing method via interviews with administrative, clinical, and laboratory staff. To determine indirect costs (e.g., patient time, caregiver costs), we conducted a time-and-motion survey and patient interviews with 148 women receiving cervical cancer screening (Pap or VIA), and supplementary interviews with patients receiving treatment for pre-cancerous lesions and cervical cancer. As HPV testing is not frequently used, indirect costs for HPV testing were extrapolated from Pap smear data and direct costs were calculated based on clinical and administrative interviews, and on standard operating procedures for processing HPV laboratory tests.
Results: VIA was the least expensive method ($11.17 per screen), followed by Pap smear ($16.32 per screen) and HPV testing ($25.19 per screen). Per-screen direct medical costs - particularly supplies, equipment and lab costs - were the main cost drivers (VIA: $5.87; Pap: $11.28; HPV testing: $20.16). Direct non-medical costs and indirect costs were similar across methods (direct non-medical: $2.65-$2.84 per screen; indirect: $2.19-$2.65 per screen).
Conclusions: These findings provide estimates of cervical cancer screening costs integrated into care in an HIV clinic in Kenya that are more comprehensive and more up-to-date than currently exist in the literature. In addition to informing policy makers on the costs of different cervical cancer screening methods, these findings may also be used in future cost-effectiveness analyses to assess the incremental cost per clinical outcome (e.g., in terms of reduced of morbidity and mortality).

TUPED814

Integrating HIV care and treatment services within a methadone clinic in Dar es Salaam, Tanzania: a formative research study

H. Saleem[1], D. Mushi[2], J. Mbwambo[2], O. Chang[1], B.H. Lambdin[1]
[1]Pangaea Global AIDS, Oakland, United States, [2]Muhimbili University of Health and Allied Sciences, Department of Psychiatry and Mental Health, Dar es Salaam, Tanzania, United Republic of
Presenting author email: blambdin@panageaglobal.org

Background: Timely antiretroviral therapy (ART) initiation is a vital component of effective HIV prevention, care and treatment. Yet people who inject drugs (PWID) are less likely to receive ART than non-drug users. Methadone clinics provide a unique setting to deliver comprehensive HIV care and treatment to PWID disproportionately burdened by HIV. This formative research will inform the development of an implementation model for the effective integration of HIV care and treatment within methadone services in Dar es Salaam, Tanzania.
Methods: Semi-structured in-depth interviews were conducted with 12 providers and 20 HIV-positive clients (10 women, 10 men) at a methadone clinic in Dar es Salaam in January 2015. We used a grounded theory approach to identify barriers to ART initiation among eligible methadone clients and examine perceptions of integrating HIV care and treatment within methadone services.

Results: Participants identified several factors that impede timely ART initiation for methadone clients: delays in receiving CD4 results from the off-site laboratory, inconsistent ARV availability, and stigma, which operates at three levels: individual, social/familial, and institutional. At the individual level, internalized stigma was perceived as a barrier to following up on CD4 results and taking prescribed ARVs. Due to the double stigma of illicit drug use and HIV, methadone clients often lack social and family support to start treatment. At the institutional level, participants reported that methadone clients face discrimination at off-site HIV clinics. Participants favored integrating HIV care and treatment services within the methadone clinic with on-site point-of-care (POC) CD4 screening and HIV treatment specialists. Perceived benefits of an integrated model included: reduced stigma; lower burden on existing HIV clinics; less time spent by providers escorting clients to off-site HIV clinics and obtaining CD4 results; and more timely ART initiation. Perceived challenges included: added provider workload; lack of HIV training; limited staff capacity; and limited space at the methadone clinic to house a CD4 machine.
Conclusions: Using a human-centered design framework, we seek to develop a functional model of methadone and ART integration. On-site POC CD4 screening coupled with trained HIV specialists can help reduce barriers to timely initiation of ART for HIV-positive methadone clients.

TUPED815

Early exits from the opioid substitution treatment (OST) in Ukraine: reasons and possible explanation

A. Mazhnaya[1], A. Shost[1], S. Filippovych[1], Z. Islam[1], F.L. Altice[2]
[1]ICF, International HIV/AIDS Alliance in Ukraine, Treatment, Kyiv, Ukraine, [2]Yale University School of Medicine, AIDS Program, New Haven, United States
Presenting author email: mazhnaya@aidsalliance.org.ua

Background: Retention in OST is essential individual and population levels indicator. Those who leave the program early in treatment (< 30 days) may require specific attention to prevent treatment drop out.
Methods: Using uniquely coded individual level monitoring data from OST program in Ukraine (157 sites in all regions), reasons for discharge were investigated among those who enrolled (N = 4,239) end discharged (N=1,098, 26%) during July 1st, 2012 - September 30th, 2013 (14 months). Discharge reasons of those left OST site during first 30 days - early exits (N= 460, 42%), were compared to those who left later - exits (N= 638, 58 %) using bivariate analysis. Poisson regression, with robust variance estimates was utilized for identifying associations between program indicators and type of exit.
Results: Among early exits such reasons as death (6,3% vs 9,9%), own will (17,8% vs 39,2%) imprisonment (3% vs 9,9%) and administrative discharge (10,4% vs 16,5%) have been less prevalent at $p < 0.001$. However, change of OST site has been more prevalent among early exits (58,9% vs 19,6%, p< 0.001). Multivariate analysis showed that recommended WHO dosages (PR 0.26, 95%CI 0.12 -0.41) and being at integrated care sites (PR 0.39, 95% CI 0.21-0.57) were associated with less chances of leaving the program within first 30 days of treatment adjusted for type of treatment drug and HIV status.
Conclusions: At initial stages of OST comprehensive services and dosages play an important role in early retention of patients, possibly preventing patients from changing the treatment site.

TUPED816

Accelerated HIV/TB service integration into primary care clinics and programmatic outcomes in rural Swaziland

B. Kerschberger[1], I. Zabsonre[1], W. Sikhondze[2], S. Mazibuko[3], L. Rusike-Pasipamire[1], A.H. Bakri[1], S.M. Kabore[1], I. Ciglenecki[4]
[1]Medecins Sans Frontieres (Operational Centre Geneva), Mbabane, Swaziland, [2]Ministry of Health, NTCP, Manzini, Swaziland, [3]Ministry of Health, SNAP, Mbabane, Swaziland, [4]Medecins Sans Frontieres (Operational Centre Geneva), Geneva, Switzerland
Presenting author email: msfch-nhlangano-research@geneva.msf.org

Background: Swaziland is hardest hit by the dual HIV/TB epidemic. HIV and TB services were vertical and constrained by a human resource crisis. In 2007, the Ministry of Health and Medecins Sans Frontieres (MSF) launched an HIV/TB integration and decentralization project. HIV/TB care were integrated to primary health care clinics (PHC): ART initiation/follow-up were task-shifted to nurses, and HIV testing and counselling (HTC), pre-TB and HIV treatment and follow-up counselling to trained laypersons. We compare program outcomes before and after service integration.
Methods: We reviewed available programme records and analysed routine HIV and TB programme data from the rural Shiselweni region between 2008/2009 and 2012. Frequency statistics and proportions were used to assess level of scale-up, integration and outcomes.
Results: Within 2 years (2009-2010), HIV/TB care was integrated and decentralized from 3 secondary facilities to 22 nurse-led PHC. Annual HTC increased from 17,567 in 2009 to 36,977 in 2012, and HIV positivity decreased from 26% to 13%; PHC performed 46% of all HTC in 2009 and 57% in 2012. Out of 4915 HIV+ cases in 2012, 57% were diagnosed at PHC. In 2008, all ART care was provided in secondary facilities, and in 2012, 56% of ART patients were followed at PHC. ART coverage increased from an estimated 30% in 2008 to universal treatment coverage (>80%) in 2012, and 6-month retention in care improved from 82% to 88% during the same period. More than 74% of HIV patients were co-infected with TB in all reporting periods. Out of 2,819 patients with TB treated in 2009, 11% did not know their HIV status compared to 2% in 2012. TB treatment initiation at PHC increased from 4% (n=121) in 2009 to 54% (n=608) in 2012. Among HIV co-infected cases, treatment success for bacteriologically-confirmed TB increased from 64% in 2009 to 75% in 2012, and ART uptake from 41% to 82%.
Conclusions: HIV/TB service integration was feasible and achieved good programmatic outcomes in this rural setting with high HIV/TB prevalence. Integration was made possible through task-shifting and involvement of lay health cadre. These outcomes should encourage decision makers to integrate HIV services in other resource constrained settings.

TUPED817

Baseline assessment on FP service utilization among eligible HIV-positive women in Amhara, Tigray, Oromia, SNNPR and Addis Ababa

N. Barega
National Network of Positive Women Ethiopia, M and E, Adddis Ababa, Ethiopia
Presenting author email: nahomw@nnpwe.org

Background: NNPWE is a specialized Network of PLHIV association aimed to support positive women associations and regional networks across the country.
The aim of this baseline assessment is to address key gaps, including preventing vertical transmission of HIV and poor sexual reproductive service uptake among HIV-positive people, through peer support, community led social & behavioral change communications, male involvement and increasing community to facility referral linkage. The use and continued use of FP and PMTCT services for women living with HIV is extremely low in Ethiopia when compared globally; only 24% of women, who were in need of PMTCT services in 2012, were able to access services.
Methods: Baseline assessment was conducted in four regions (Oromia, Amhara, Tigray and SNNP) and one city administration (Addis Ababa) from August 4-22, 2014 using quantitative and qualitative data collection methods. A total of 402 HIV positive women were interviewed.
Results: The mean of age at first birth was 18.62 years. Despite the fact that 15.3% of mothers gave birth to HIV positive children which is indicative of need for strong work on PMTCT, 20.5 % of the study subjects want to give birth in the future. The number of ever-users of family planning (81%) was considerably higher than that of current users (56.6%), which is an indication of a significant dropout rate. Unmet need for family planning was found to be 14.6%, which is as high as 37.5% in some regions. Future intention to use family planning was found to be 71.6%, which is higher than current use and lower than ever use.
Conclusions: It is essential that access to family planning services is increased, to enable all HIV-positive women to "make informed reproductive choices". Such improvements can occur through integration of family planning and HIV services. Thus, integrated service will increase the proportion of HIV-positive women who are aware of their status and will educate them about the benefits of contraceptive use as a means of preventing mother-to-child transmission.

TUPED818

The favorable value of targeting an alcohol intervention to persons living with HIV/AIDS in Kenya

J. Kessler[1], K. Ruggles[1], A. Patel[2], K. Nucifora[1], L. Li[1], S. Braithwaite[1]
[1]NYU School of Medicine, Population Health, New York, United States, [2]University of British Columbia, Vancouver, Canada
Presenting author email: jason.kessler@nyumc.org

Background: Unhealthy alcohol consumption is both prevalent and is an important risk factor for HIV acquisition and progression in Kenya. Cognitive behavioral therapy (CBT) based interventions addressing unhealthy alcohol consumption in Kenya have shown promising results, increasing abstinence and decreasing risky sex. We sought to determine the value and impact of targeting this intervention to HIV-infected individuals enrolled in HIV care and treatment programs in Kenya.
Methods: We developed a computer simulation to inform HIV prevention decisions in East Africa across a wide range of possible interventions. Unhealthy alcohol use was modeled as increasing the risk of:
(a) condom nonuse (RR 1.29)
(b) ART non-adherence (RR 2.33) and
(c) sexually transmitted infection (STI) prevalence (RR 1.72).
CBT was assumed to decrease unhealthy alcohol consumption by 45% and cost $5 per person/yr. We compared 3 intervention targeting strategies -
(1) all HIV infected persons
(2) pre-ART patients or
(3) patients receiving ART.

We compared these targeting strategies to a hypothetical scenario where an alcohol intervention was delivered to all adults regardless of HIV status. Time horizon of simulation is 20 years.
Results: CBT aimed at HIV infected patients in Kenya could prevent 18,000 new infections over the 20yr time horizon. This would add 46,000 QALYs, yielding an incremental cost effectiveness ratio (ICER) of $600/QALY (see Table). Targeting to only the pre-ART HIV infected patients results in 15,000 infections averted, and the addition of 21,000 QALYs, but would be cost saving. As a comparison expanding ART access to all HIV infected individuals with a CD4 ≤ 500 cells/mm^3 results in the prevention of 100,000 new HIV infections, the addition of 250,000 QALYS, yielding an ICER of $1,600/QALY. The value of CBT and its prioritization was strongly influenced by its estimated cost.

	Target- All HIV	Target- pre-ART	Target-ART
QALYs gained	23,000	21,000	9,000
HIV infections averted	18,000	15,000	10,000
Incremental cost	$13M	cost saving	$3M

[Impact of CBT intervention among PLWH in Kenya]

Conclusions: We demonstrate the improved value (at the cost of the overall clinical impact) of targeting the CBT intervention amongst the HIV infected community and those within it who are already engaged in care and who may be hazardous alcohol users. Our results highlight the favorable value and cost-effectiveness of alcohol focused interventions in Kenya as a means to improve HIV related outcomes and population health.

TUPED819

Parents' views and acceptability of early infant male circumcision (EIMC) integrated into maternal child health (MCH) services in Iringa, Tanzania

M. Amuri[1], G. Msemo[2], J. Lija[3], M. Plotkin[4], A. Christensen[1], R. Lemwyi[1], D. Boyee[1], A. Hellar[5], E. Mlanga[6], E. Njeuhmeli[7], H. Mahler[1]
[1]Jhpiego - an affiliate of Johns Hopkins University, Dar es Salaam, Tanzania, United Republic of, [2]Ministry of Health and Social Welfare, Maternal and Child Health Unit, Dar es Salaam, Tanzania, United Republic of, [3]Ministry of Health and Social Welfare, National AIDS Control Programme, Dar es Salaam, Tanzania, United Republic of, [4]Jhpiego - an affiliate of Johns Hopkins University, Baltimore, United States, [5]Jhpiego - an affiliate of Johns Hopkins University, Tanzania Country Office, Dar es Salaam, Tanzania, United Republic of, [6]USAID Tanzania, Dar es Salaam, Tanzania, United Republic of, [7]USAID, Washington, DC, United States
Presenting author email: augustino.hellar@jhpiego.org

Background: Evidence suggests that EIMC is less expensive, safer, easier to perform, and heals more quickly than adult male circumcision. Current WHO guidelines recommend that EIMC be integrated into MCH services and performed 24 hours to 60 days after delivery, and therefore parents are the key gatekeepers. A study associated with the pilot implementation of EIMC services in Iringa, Tanzania, examined parental views, decision-making processes and experiences with EIMC services.
Methods: From May to August 2014, 24 group discussions (total of 154 participants, 26% and 74% were male and female respectively) were held with parents attending reproductive and child health services at four EIMC pilot sites. Parent FGDs were stratified by those who decided to circumcise their infant son after being provided with EIMC education (n=8 FGDs); those who declined to circumcise their infant son (n=8 FGDs); mothers who received EIMC education during ANC services (n=4 FGDs); and mothers who received EIMC education during their postnatal or well child services (n=4 FGDs). Data from routine EIMC service delivery records were also analyzed.
Results: 1,739 infants were circumcised in MCH services between April 2013 and September, 2014, including 106 HIV- exposed infants. 69% were circumcised at the same facility where they were delivered, 42% were circumcised within 14 days of delivery. Satisfaction was high among parents who had chosen to circumcise their infants within recommended time; fast healing of the penis was the key reason. Among those who declined, their main reason concerns about safety; fathers expressed more safety concerns than mothers. Generally female parents were more supportive than male parents, both parents are generally involved in the decision to circumcise or not, and extended family can have an influence.
Conclusions: EIMC, integrated into MCH services, is acceptable among most parents in Iringa, Tanzania. Increasing community awareness of the benefits of EIMC, with a focus on quick healing and safety is important; targeted awareness-raising, especially for male parents who expressed safety concerns and reluctance to circumcise their infant sons, is needed.

TUPED820

Can male partners play a role in cervical cancer screening? The knowledge and attitudes of HIV-positive men towards cervical cancer screening in Kenya

F. Lee[1], P. Masitsa[2], T.K.H. Constant[3], M.H. Stilwell[4], N. Yatich[2], S.R. Sakr[5], N.R. Mugo[6], M.H. Chung[2]
[1]University of Washington, Department of Medicine, Seattle, United States, [2]University of Washington, Department of Global Health, Seattle, United States, [3]University of Washington, Department of Anthropology, Seattle, United States, [4]University of Washington, Department of Public Affairs, Seattle, United States, [5]Coptic Hospital, Coptic Hope Center, Nairobi, Kenya, [6]Kenyatta National Hospital, Department of Obstetric and Gynecology, Nairobi, Kenya
Presenting author email: fanlee55@gmail.com

Background: Cervical cancer is a leading cause of cancer deaths among women in sub-Saharan Africa and an AIDS-defining disease. Despite efforts to integrate cervical cancer screening into HIV care, screening rates remain low. Studies focused on women have identified lack of spousal support as a barrier to screening, but little is known about men's perspectives.
This study explores HIV-positive men's knowledge and perception of cervical cancer and the potential for male partner support for cervical cancer screening in Kenya.
Methods: We conducted 18 in-depth-interviews and 3 focus-group-discussions with partners of HIV-positive women and HIV-positive men. Participants were recruited at Coptic Hope Center for Infectious Diseases, an HIV treatment clinic, in Nairobi, Kenya between November and December 2014. Interviews were audiotaped, transcribed and a baseline codebook was validated through a grounded theory approach. Extensive in-text memos assured reliability of coding, and a preliminary comparative analysis between transcriptions was performed to assure validity of the findings.
Results: While knowledge of cervical cancer was limited, participants understood general concepts of screening for early detection and disease prevention and felt that cervical cancer screening was important. Many participants used HIV-related terminology (e.g. knowing one's "status") to describe the need for screening. Participants regarded men as decision-makers in the family with significant influence over healthcare seeking behavior of their female partners. They reported that they were amenable to learning about women's health to make more informed decisions to support the health of their partners. Participants identified a lack of knowledge among men about cervical cancer and stigma associated with promiscuity and HIV/sexually transmitted infections as major barriers to male partner support.
Conclusions: HIV-positive men in Kenya appear to appreciate the importance of cervical cancer screening for disease-prevention in this preliminary analysis. This perspective is likely influenced by their exposure to health information from their HIV-related care. Cervical cancer awareness efforts in Kenya should target men as well as women, since men may act as gatekeepers to women's access to healthcare. HIV clinics and their messages of HIV prevention may help HIV-positive men better understand cervical disease, and could be leveraged to promote male partner support in cervical cancer screening.

TUPED821

Patient preference and willingness-to-pay for standalone, integrative and satellite models of dispensing methadone for the treatment of opioid dependence in Vietnam

B.X. Tran[1], V.M. Nong[2], H.T.T. Phan[3], C. Latkin[1]
[1]Johns Hopkins Bloomberg School of Public Health, Department of Health, Behavior and Society, Baltimore, United States, [2]Hanoi Medical University, Institute for Preventive Medicine and Public Health, Hanoi, Vietnam, [3]Ministry of Health, Authority of HIV/AIDS Control, Hanoi, Vietnam
Presenting author email: bach@jhu.edu

Background: The rapid expansion of Methadone Maintenance Treatment (MMT) in large drug using populations requires sustainable resources and highly efficient services delivery models.
We assessed the preference and willingness of patients to pay (WTP) for standalone, integrative and satelite MMT services in Vietnam.
Methods: A facility based survey was conducted among 1,016 MMT patients (98.7% male, 42% aged 35 or less, and 67% living with spouse) in five MMT clinics in Hanoi and Nam Dinh province in 2013. Socioeconomic and health status, HIV risk behaviors and experiences with drug rehabilitation were interviewed. WTP was assessed using contingent valuation method, including a set of double-bounded binary questions and a follow-up open-ended question. Point and interval data models were used to estimate maximum willingness to pay.
Results: 95.5% patients were willing to pay for MMT with the monthly mean cost of US$ 29 - 32, and it was higher in urban MMT sites co-located with general health care services. Residence in households with higher income, educational level, younger age and HIV negative status predicted willingness to pay more among respondents. Meanwhile, higher expenditure on drug costs was associated with lower WTP for MMT. 33% patients reported experiencing some difficulties in accessing and utilizing MMT services, including primarily long distance to

MMT sites (45%), long waiting time (7%), lack of information on health care services (2%), and others (47%). 64% clients supported the satellite model which integrates MMT into commune health stations that may improve the convenience of use.
Conclusions: It is feasible to implement co-payment MMT services in Vietnam. Integrating and co-locating MMT with other general health care facilities, decentralizing to commune level are highly preferred and could be considered to improve the efficiency of MMT services.

TUPED822

Impact of peer nutritional counseling on ART patients' food insecurity and nutritional outcomes: a pilot study in Honduras

K.P. Derose[1], M. Felician[2], B. Han[3], K. Palar[4], B. Ramirez[5], H. Farias[6], H. Martinez[1]
[1]RAND Corporation, Health Program, Santa Monica, United States, [2]Pardee RAND Graduate School, Santa Monica, United States, [3]RAND Corporation, Statistics Group, Santa Monica, United States, [4]University of California, San Francisco, United States, [5]World Food Program, Tegucigalpa, Honduras, [6]World Food Program, Panama City, Panama
Presenting author email: derose@rand.org

Background: Food insecurity and poor nutrition are key barriers to anti-retroviral (ART) adherence, particularly in resource-poor settings. Culturally and locally-appropriate and sustainable interventions that provide nutrition counseling for people on ART and of diverse nutritional statuses are needed, particularly given rising rates of overweight and obesity among people living with HIV (PLHIV).
Methods: As part of scale-up of a pilot intervention that used professional nutritionists, we recruited and trained 17 lay peer workers from 14 government-run HIV clinics in Honduras to deliver peer nutritional counseling using a highly interactive curriculum that was developed after extensive formative research on locally available foods and dietary patterns among PLHIV. At baseline and 2 month follow-up, assessments included: 1) in-person surveys to collect data on household food insecurity (15-item scale), nutritional knowledge (13-item scale), dietary intake and diversity (number of meals and type and number of food groups consumed in past 24 hours); and 2) anthropometric measures (body mass index or BMI, mid-upper arm and waist circumferences). We used multivariable linear regression analysis to examine the effects of the intervention on food insecurity score and the various nutritional outcomes while controlling for baseline characteristics (gender, education, and work status) and clinic-level clustering.
Results: Of 482 participants, we had complete data on 364 (76%), of which 62% was female, median age was 39, 34% reported having paid work, 52% had completed primary school, 34% was overweight or obese, and 73% reported moderate or severe food insecurity. Between baseline and follow-up, household food insecurity showed a significant decrease among all participants (n=356, β=-0.47, p< .05) and among those with children under 18 (n=303, β=-1.16, p< .01), while nutritional knowledge and dietary intake and diversity also significantly improved, (β=0.88, p< .001; β=0.30, p< .001; and β=0.15, p< .001, respectively). Nutritional status (BMI, mid-arm and waist circumferences) showed no significant changes, but the brief follow-up period may not have been sufficient to detect changes.
Conclusions: A peer-delivered nutritional counseling intervention for PLHIV can improve dietary quality and reduce food insecurity among a population of diverse nutritional statuses. Future research should examine if such an intervention can improve adherence among people on ART.

TUPED823

Integrating HIV and reproductive health services to increase consistent condom use for HIV prevention: a multicentre, non-randomized trial

R. Mutemwa[1], S. Mayhew[2], C. Warren[3], J. Kikuvi[2], D. Wang[4], Integra Initiative Group
[1]London School of Hygiene and Tropical Medicine, Department of Population Studies, Fareham, United Kingdom, [2]London School of Hygiene and Tropical Medicine, Department of Global Health, London, United Kingdom, [3]Population Council, New York, United States, [4]London School of Hygiene and Tropical Medicine, Department of Medical Statistics, London, United Kingdom
Presenting author email: richard.mutemwa@lshtm.ac.uk

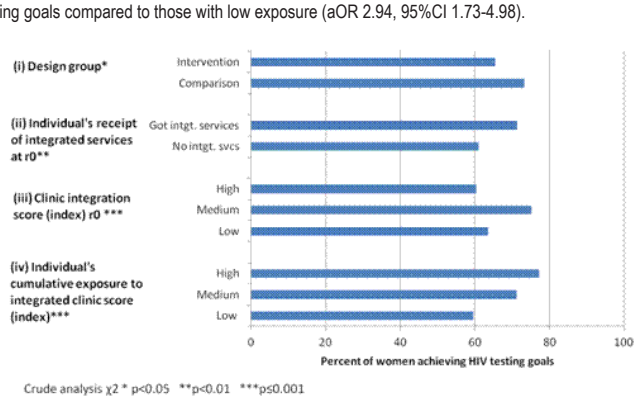
Background: Condom-use has generally been below optimum in HIV-affected countries and uptake for HIV prevention remains challenging. Published evidence suggests that integration of HIV and reproductive health services can address the structural/service challenges and improve condom uptake.
However, effective HIV prevention requires consistent condom-use, beyond just condom uptake. This study assessed the effectiveness of integrating HIV and reproductive health services on consistent condom-use in women of reproductive age in generalised HIV epidemic settings.
Methods: We assessed the effect of integrated HIV and reproductive health services on consistent condom-use in 3660 women (≥15 years old) in Kenya and Swaziland. Repeated condom-use measures were taken on each woman at enrolment and at 6, 18 and 24 months after enrolment. Both countries implemented integration in all health facilities nationwide; therefore we assessed consistent condom-use using both the original-design intervention/control contrast, as well as an individual-level exposure-to-integration index binarized into '*high integration*' and '*low integration*'. Assessment was performed in the combined study population and different sub-populations: PNC and FP clients, HIV-positive and HIV-negative clients, single and married clients. We fitted a series of 3-level random intercept mixed-effects logit models. Propensity score analysis was used to correct for potential selection bias due to non-randomized design of the study.
Results: In the combined population, the odds for consistent condom use in the high integration group were almost twice those in the low integration group (OR: 1.80; 95%CI: 1.31, 2.48), with propensity for consistent condom-use increasing with increase in exposure to integrated services. No difference in consistent condom-use was found between women in intervention and control groups (OR: 1.50; 95%CI: 0.32, 7.08). Consistent condom-use had higher odds among HIV-positive than HIV-negative women, especially among HIV-positive women exposed to high integration (OR: 2.42; 95%CI: 1.05, 5.56). Married women were less likely to report consistent condom-use than single women; however, married women exposed to high integration were more likely to practice consistent condom-use than those exposed to low integration (OR: 1.96; 95%CI: 1.33, 2.88).
Conclusions: Integration of HIV and reproductive health services can produce significant increases in consistent condom-use among women attending public health services in generalised HIV-epidemic settings.

TUPED824

The impact of integrated reproductive health and HIV services on HIV testing uptake: results from a cohort study among family planning clients in Kenya

K. Church[1], G. Ploubidis[2], I. Birdthistle[1], J. Mak[3], K. Tomlin[4], W. Zhou[5], C. Warren[6], S. Mayhew[5], Integra Initiative
[1]London School of Hygiene and Tropical Medicine, Population Health, London, United Kingdom, [2]Institute of Education, London, United Kingdom, [3]London School of Hygiene and Tropical Medicine, Faculty of Public Health and Policy, London, United Kingdom, [4]London School of Hygiene and Tropical Medicine, Disease Control, London, United Kingdom, [5]London School of Hygiene and Tropical Medicine, Global Health and Development, London, United Kingdom, [6]Population Council, Washington DC, United States
Presenting author email: joelle.mak@lshtm.ac.uk

Background: Integrating HIV testing and counselling (HTC) into reproductive health services is a policy priority in Kenya, where only one third of adults are aware of their HIV status. Developing effective models of care to deliver HTC is critical, and family planning (FP) clients are an important target group as they are sexually active and usually not current condom users.
Methods: We assessed the impact of integrated FP-HIV services on HIV testing rates among FP clients (N=882) using a non-randomized cohort design within 6 intervention and 6 'comparison' facilities in Central Province, Kenya. Participants were interviewed at four time points over two years. Due to intervention fidelity issues, we assessed clients' exposure to integration in four ways: (i) design group (clinics received training and resources for HTC); (ii) woman's reported receipt of both RH and HIV services at recruitment visit (r0); (iii) a functional measure of facility integration ('index'), at r0; (iv) a woman's cumulative exposure to functionally integrated care across different clinics over the two-year cohort. Those who achieved 'HIV testing goals' reported two HIV tests over the two year period; or one test among those who sero-converted. Measures of effect were assessed using conditional logistic regression models accounting for clustering at facility level.
Results: HIV testing generally increased over the cohort period, from 28% at r0 to 66% after 2 years. Figure 1 shows testing uptake according to exposure group. While crude analysis showed that receipt of integrated care at recruitment visit increased testing uptake, the only exposure that demonstrated long-term impact in multivariable analysis was a woman's cumulative exposure to integrated care over the two year study period. Those with a high level of exposure to integrated facilities, as measured by the 'index', were three times more likely to achieve testing goals compared to those with low exposure (aOR 2.94, 95%CI 1.73-4.98).



[Figure 1. Proportion of women achieving HIV testing goals over the 2 year cohort, by different exposure groups (n=882)]

Conclusions: Assessing the impact of organisational changes on service outcomes is complex, and sensitive to measurement and definition choices. Delivering an integrated intervention is not sufficient to ensure practice changes over time, and repeated contact with integrated care delivery is required.

TUPED825

What influences successful delivery of integrated HIV and FP/PNC services? Evidence from a non-randomised, longitudinal, evaluation trial in Kenya and Swaziland

S. Mayhew[1], R. Mutemwa[1], M. Colombini[1], J. Mak[1], M. Collumbien[1], I. Lut[1], I. Birdthistle[1], C. Ndwiga[2], Integra Initiative
[1]London School of Hygiene & Tropical Medicine, London, United Kingdom, [2]Population Council, Nairobi, Kenya
Presenting author email: joelle.mak@lshtm.ac.uk

Background: Integration of HIV testing and treatment services into FP and reproductive health services has long been seen as important for improving health outcomes for both HIV-clients and PLWHA. Human and physical resource integration is the usual outcome measure of "successful" service integration but this neglects the actions of individual providers and their managers in combination with systems and other factors. This paper analyses multiple datasets from the Integra Initiative to investigate the influences on successful "functional" service integration.
Methods: Integra is a non-randomised, longitudinal evaluation trial in 24 intervention and 18 comparison facilities in Kenya and Swaziland. This paper reports data from:
1) Time-series Client Flow data 2009-2011 tracking clients over a week, to measure integrated services received: base-line (9,242 clients) and end-line (10,604 clients) are reported.
2) Structured surveys with 128 providers conducted at four time-points between 2009-2011;
3) In-depth interviews with 56 providers conducted in 2010 and 2012.
Data were analysed by degree of facility integration to compare results from "high functioning" and "low functioning" clinics.
Results: Analysis of Client Flow data revealed a "capacity-delivery" gap across all clinics, even those highly functioning: there is a large gap between the % days on which integrated care was accessed (i.e. capacity to deliver integrated care) and the % visits/consultations actually receiving integrated care (i.e. functional delivery of integrated care).
Qualitative and quantitative provider data indicate that among staff at clinics achieving high-functioning integration, despite challenges of increased workloads, less quality time with clients and occupational stress they coped through better communication, team-working and load-sharing which facilitated better integration. Providers also valued skills enhancement, more variety and challenge in their work and better job satisfaction through increased client-satisfaction - these helped override frustrations about systems constraints. Qualitative data particularly highlight the importance of facility management, supervisory support and innovation for on the job training and mentorship of providers.
Conclusions: Achieving successful service integration requires attention not only to staffing numbers and training (the usual focus of "success" in health systems and services), but also developing mechanisms to enhance the motivation, team-working and communication of health workers to overcome inevitable systems constraints.

Integration of HIV services with other development programmes

TUPED826

An integrated treatment model for opioid addiction to enhance HIV prevention and treatment in Vietnam

C.M. Denis[1], D.S. Metzger[1], L. Huang[2], V. Trias[2], M. Auriacombe[3], G. Raguin[2], S. Mai Thi Hoai[4], G. Le Truong[4], J.-P. Daulouede[5], C.P. O'Brien[1]
[1]University of Pennsylvania, Center for Studies of Addiction, Philadelphia, United States, [2]ESTHER, Paris, France, [3]University of Bordeaux, Addiction Psychiatry, USR CNRS 3413 Sanpsy, Bordeaux, France, [4]HCMC AIDS Committee, Ho Chi Minh City, Vietnam, [5]BIZIA Addiction Clinic, Bayonne, France
Presenting author email: dsm@mail.med.upenn.edu

Background: In Vietnam, the main source of HIV infection is injection drug use. About 46% of opioid users are estimated to be HIV-positive. 13,000 opioid users are currently receiving methadone treatment, 26% of them are HIV-positive but only 70% received HIV treatment. Since November 2013, we have implemented an integrated treatment program within an HIV treatment setting in Ho Chi Minh City, Vietnam. The integrated treatment program consists of opiate maintenance medication (methadone or buprenorphine/naloxone), structured counseling sessions focused on substance use and risk-taking behavior, systematic screening for HIV and HCV, and linkage to HIV treatment if needed.
Methods: The aim of this study was to evaluate the implementation and impact of the integrated treatment program on HIV treatment adherence, HIV incidence and risk-taking behavior. At baseline and every 6 months, HIV and HCV screening were performed; HIV risk-taking behavior was assessed with the Risk Assessment Battery.
Results: Since December-01-2013, 145 daily heroin users were enrolled. They were mainly males (96.4%), 32.4 y.o. (SD= 5.2) and living with family (81%). Participants reported using heroin for an average of 7.8 years (SD= 3.6, min-max= 1-20). Program retention was very high, with only 3 participants having dropped out. Fifty-one (35.2%) were HIV-positive, with four not previously known to be positive. Eighty-nine (68.0%) were HCV-positive, 42 (46.7%) were newly diagnosed. All 51 HIV-positive participants were treated for their HIV, and 84.3% received ARV (mean CD4= 434 (SD=249), range: 4-1108). At 6-month follow-up, there was a significant decrease of any injection (100% vs. 63.4%), and a significant decrease of sharing needle/paraphernalia (47.2% vs. 31.7%) and injection-related risk taking behavior (F(1,15)=7.567, p= .015). At 6 months, there was no reduction in sex-related risk-taking behavior, which was reported by 61% of the subjects and no new HIV infections were found.
Conclusions: These preliminary findings support the efficacy of integrated HIV treatment and substance-use treatment. Long-term follow-up is needed to confirm the impact of this approach.

TUPED827

Decriminalization and public health on the ground: measuring policing and risk environment for people who inject drugs (PWID) in Tijuana, following the Mexican "Nacormenudeo" reform

J. Arredondo[1], A. Bañuelos[2], T. Rocha[1], G. Rangel[3], S.A. Strathdee[1], L. Beletsky[1]
[1]University of California San Diego, Global Public Health, School of Medicine, La Jolla, United States, [2]Tijuana Municipal Government, Ministry of Public Safety, Tijuana, Mexico, [3]United States-Mexico Border Commission, Tijuana, Mexico
Presenting author email: jarredon@ucsd.edu

Background: In 2009, Mexico enacted a drug policy reform known as the "Narcomenudeo" reform, decriminalizing possession of small amounts of illegal drugs, establishing a harm-reduction strategy regarding drug dependence, and mandating the local justice system to prosecute retail drug sale. The HIV risk environment for people who inject drugs (PWID) and other criminalized groups is substantially shaped by drug laws and their enforcement. We designed a study to assess whether the implementation of this law resulted in significant changes in drug law enforcement in Tijuana, a Mexican border city that is a major drug trafficking and consumption area with elevated HIV prevalence among PWID.
Methods: Using police department data, this study assessed changes in drug-related stops and arrests between 2009-2014 throughout the city of Tijuana. Generalized Linear Models were utilized to analyze trends in internal enforcement activity data, while controlling for environmental variables, such seasonal variations and changes in local administration.
Results: Although initial results indicated a precipitous drop in drug arrests directly following the enactment of the narcomenudeo reform, broader analysis suggests that the observed decline was part of a secular trend. Controlling for other factors, statistical modeling failed to identify significant impact of the law on drug-related stop or arrest trends.
Conclusions: Drug possession arrests in Tijuana are likely influenced by factors other than the implementation of the "Narcomenudeo" reform. The high level of police encounters with drug users in the city could produce negative consequences that translate to HIV and Hepatitis C risk, but those encounters may also serve as an opportunity to link high-risk individuals in prevention and other services. A targeted police education program in the city could help modify the officers' knowledge and attitudes toward drug use and harm reduction in order to better align the goals between public safety and health.
Funding: NIH/NIDA grant number R37 DA019829 (Strathdee, PI), Open Society Foundations Latin America Program grant OR2013-11352 (Strathdee, PI), and UCSD CFAR International Pilot Grant (NIAID 5 P30 AI036214) (Magis and Beletsky, PIs).

TUPED828

Community-led integrated service delivery 'war rooms' game changing the fight against HIV/AIDS and TB: case study of the *Operation Sukuma Sakhe* model in KwaZulu-Natal, South Africa

T. Zhuwau[1], V. Naidu[2], C. Hugo[3], F. Ndlovu[4], S. Mkhize[4], T. Ngwenya[4], N.I. Ndlovu[5]
[1]BroadReach Healthcare, Technical Services, Pretoria, South Africa, [2]BroadReach Healthcare, Technical Services, Durban, South Africa, [3]BroadReach Healthcare, Technical Services, Cape Town, South Africa, [4]KwaZulu-Natal Office of the Premier, Durban, South Africa, [5]Office of the Premier, Priority Programmes, Pietermaritzburg, South Africa

Background: KwaZulu-Natal is South Africa's second largest province - home to 10.2 million (20% of the population). It has an adult HIV prevalence of 27.9%, compared to 18.8% nationally. More than 67% live below the poverty line, 5.7% are illiterate, 2.9% have no access to safe water and 25.2% are unemployed. These socio-economic determinants negatively impact health outcomes, especially HIV/AIDS, TB and maternal and child mortality. In 2009, the KwaZulu-Natal government rolled out *Operation Sukuma Sakhe* (Lets Build Together), an integrated model of service delivery to fight poverty, HIV and TB infections in poor communities using community-led service delivery "war rooms". The model was implemented with technical support from BroadReach Healthcare and has been acknowledged by UNAIDS and government as a best practice model.
Methods: Communities, supported by dedicated teams of community health workers, plan and direct service delivery to where it is needed through the war rooms. This forms the foundation of integrated service delivery planning at ward, district, and provincial levels. Each household is seen for its integrated needs and a basket of services is provided in an integrated fashion. Services include supporting HCT, TB screening, defaulter tracing, condom distribution and promotion, child wellbeing, early pregnancy booking, medicines distribution, community-based care services and addressing social issues obtaining vital documents and accessing social grants.
Results: Data from OSS "war rooms" and linked health facilities show positive trends for certain indicators since the introduction of CCGs. Table 1 presents data for 2010-2014 from Ugu district (population 740,000) where OSS was implemented in the district in 2011 and supported by trained CCGs from 2012. In 2014 CCGs in Ugu served almost 370,000 households; performed around 358,000 household visits in 2013 increasing to 472,000 in 2014, with almost 90,000 visits resulting in referral to a facility over the two years.

Indicator/Year	2009/10	2010/11	2011/12	2012/13	2013/14
PHC Utilisation rate	2.62	2.68	2.89	3.11	3.07
% HIV tested	94%	95%	96%	99%	99%
% tested HIV positive* [95% CI]				13% [12.7-13.0%]	10% [9.9-10.1%]
% Antenatal visit before 20 weeks [95% CI]	34% [32.8-34.2%]	35% [34.0-35.5%]	35% [34.3-35.9%]	49% [47.9-49.5%]	59% [57.8-59.3%]
Condom distribution rate (no. condoms per male population 15-44yrs)	13.12	14.44	10.86	24.72	41.67
Condom distribution rate by CCGs* (no. condoms distributed by CCGs per male population)				6.61	9.23
*Data elements and indicator not available prior to 2012					

[Key indicators from Ugu district, KwaZulu-Natal]

Conclusions: The implementation of OSS suggests that poorly resourced communities can play a significant role in improving health outcomes including HIV/AIDS and TB. Community-led health interventions directly impact facility-based interventions and investing in community structures can be a cost-effective approach towards healthcare delivery in communities and improvement of overall health outcomes.

Translation, incorporation and use of key IR findings into programmes and practice

TUPED829

Strengthening EMTCT & EID program performance through mobile technologies in Uganda

W. Bikokye Kafeero
Baylor College of Medicine - Mulago Hospital, Monitoring and Evaluation, Kampala, Uganda
Presenting author email: wbikokafeero1@gmail.com

Background: In Uganda, health facility in-charges submit EMTCT data from health facilities to the Ministry of Health (MOH) operated District Health Information System monthly. The reports do not capture data on pregnant women receiving HIV counseling and testing at their first ANC visit, the proportion of pregnant women with known HIV positive results at the first ANC, the total of missed appointments within the ANC, or adequate ARV and test kit stock out data. In response, the MOH and CDC-funded META project rolled out a weekly mobile phone text message (SMS) reporting system in February 2013 supported by midwives working at health facility level. Baylor-Uganda is mandated by CDC to coordinate weekly PMTCT SMS reporting at 375 public health facilities in 23 districts and to update a weekly early infant diagnosis (EID) dashboard for real time reporting of infants' DNA PCR results.
Methods: The purposive sampling technique was used to select midwives with mobile phone contacts. A total of 1179 midwives from 275 health facilities were trained on how to submit data on 9 PMTCT indicators using their mobile phones. The midwives then submit their health facility PMTCT data for the previous week to a toll free SMS number and automatically receive SMS feedback.
Results: Through intensified monitoring and follow up through biweekly SMS and phone call reminders, inclusion of multiple users per facility, engagement of district health officers, and weekly and monthly feedback to stakeholders (to inform evidence-based decision making), the overall reporting rate increased by over 4%. The average weekly SMS reporting rate for January-March 2014 was 69% and increased to 100% from October-December 2014. The stock out of ARVs and test kits reduced from 47 facilities to 2 and of test kits from 68 to 5. 98% of EID results returned to the facility on time and were provided to caregivers, and all positive infants were stated on ART timely. There was also a significant reduction in mothers missing appointments from 187 in October 2013 to 27 in October 2014.
Conclusions: Mobile technologies that enhance the timeliness of data collection and reporting and inform decision making are essential to virtual EMTCT.

TUPED830

Community-owned electronic repository: improving data access and uptake to develop evidence-informed policies and programs

Y. Paul[1], M. de Bruin[1], S. Mcleish[2], M. Fitzgerald[2], K. Morrison[2]
[1]University of the West Indies, UWI HARP, Kingston, Jamaica, [2]Health Policy Project Futures Group, Kingston, Jamaica
Presenting author email: yolandapaul@gmail.com

Background: Country-specific HIV-related strategic data are often inaccessible to end-users such as programmers and policymakers. Jamaican stakeholders including program developers, advocates and policymakers report obstacles in accessing data on the political, social, economic and legal aspects of the HIV epidemic. This leads to overlap in local research initiatives and less-effective responses. Civil society organizations report challenges in understanding the technical jargon used in framing research findings and recommendations.
To address these concerns, the University of the West Indies' HIV and AIDS Response Programme developed a user-friendly online electronic repository aimed at improving stakeholders' access to and efficient use of local strategic data to inform program design and implementation, advocacy, and policy development in Jamaica.
Methods: Local ownership by potential users was achieved through a participatory approach, including stakeholder meetings with nongovernmental organizations, academia, and government representatives; inclusion of stakeholders in a steering committee; and beta testing, which provided preliminary feedback.
Content was identified by searching academic databases and local materials obtained from partners. Annotations of select publication types were also included. The general criteria used to include material in the repository were: publications from 2000 onward; a focus on Jamaica, not excluding the wider Caribbean; and information on all aspects of sexual health and HIV prevention, treatment, care, and support.
Development of a searchable website allowed for basic and advanced search features to increase access.
Results: This repository has become the primary Jamaican mechanism through which local and regional research is collated and accessed. The user-friendly summaries of research make it possible to better inform local HIV-related program design and implementation, advocacy, and policy development. Meaningful involvement of end-users throughout the process has increased their interest and capacity to use the data.

Conclusions: The response received from beta testing and launch has been very positive and supportive of this intervention. Users emphasized the benefit of gaining access to centralized information and learning about existing program data to avoid duplication. Phase 2 of this intervention focuses on the development of a mechanism through which all local stakeholders routinely feed their research material into the repository, ensuring sustainability.

TUPED831

Overcoming barriers to opening supervised injection services in the United States

L. Thomas
Drug Policy Alliance, San Francisco, United States
Presenting author email: lthomas@drugpolicy.org

Background: Supervised injection services (SIS) are an effective, evidence-based HIV prevention intervention not available in the United States because of the current legal and political approaches to people who use drugs. SIS are settings where people can inject or consume drugs under clinical supervision and can receive health care, counseling, and referrals to health and social services, including drug treatment. They have been extensively studied and evaluated and are effective at addressing a number of health and safety outcomes.SIS are the next step beyond syringe access to end HIV and HCV transmission among people who use drugs. Analyses of Insite in Vancouver have shown it to be cost-effective in reducing new HIV cases. It has reduced the overdose rate in its neighborhood by 35%.
Overall the evaluation found no community or health-related harms and a large number of benefits.
Methods: This analysis reviews the policy and legal barriers to the incorporation of research findings into practice in the United States. It describes the various legal concerns for people who inject drugs, the current political atmosphere, and the history of building support for harm reduction interventions in the US. Current efforts in a number of US cities to open SIS will be described, including strategies and successes.
Results: The legal and policy analysis reveals a number of untested legal barriers to opening an SIS. The larger barriers among key stakeholders and elected officials remain stigma, fear of controversy, and lack of understanding of the legal environment, exacerbated by a low level of concern about the key population of people who inject drugs. Communities across the U.S. are developing strategies to address those barriers, including additional research, building community pressure, and working directly with grassroots community organizations to open SIS out of view of legal authorities.
Conclusions: This is a global best practice that could bring public health benefits to the U. S, Policy makers and elected officials as well as public health leaders need to be educated about legal and health realities and the benefits of SIS. Political opinion needs to shift to allow the US to fully implement SIS as an effective HIV intervention.

Monitoring and evaluation of prevention

TUPED832

Process evaluation of behavioural change communication materials developed and utilized for HIV prevention by non-governmental organizations in Oyo State, Nigeria

B. Kazeem Kolawole
Oyo State Agency for the Control of AIDS, Project Management, Ibadan, Nigeria
Presenting author email: bolarinwa_kolawole@yahoo.com

Background: Public health education is a strategy for controlling the spread of HIV. An important component is the effective utilization of Behavioural Change Communication (BCC) materials. Forty Non-Governmental Organizations supported by the Oyo State World Bank-assisted HIV and AIDS programme produced BCC materials targeting audiences. However, the process evaluation of the development of the materials was not systematically conducted. This study was therefore designed to assess the level of adherence by these NGOs to basic WHO standards in the process of development of the materials.
Methods: The study was a descriptive cross-sectional survey. Balloting was used to select 20 out of the 40 supported NGOs. The NGOs were categorized into five equal groups based on target audience that is; Female Sex Workers, Mission Birth Attendants, In-school Youth, Women and People Living with HIV. Checklists were used to assess compliance with each of the following seven stages of educational materials development in line with the WHO model: Needs Assessment (NA); message conceptualization; design; pre-testing; production procedure; implementation and outcome evaluation. In-depth Interviews (IDIs) were conducted for the twenty NGO project coordinators while one Focus Group Discussion (FGD) was conducted among each of the five target groups. Descrptive statistics was used to analyze quantitative data while the FGD and IDI data were transcribed and analyzed using thematic approach.
Results: Only two out of twenty NGOs complied with all the seven stages of WHO model. 95.0% carried out implementation involving target audience and 85.0% conducted outcome evaluation of the materials. 80.0% pre-tested materials, 65.0% conceptualized communication messages while 25.0% of the NGOs involved target audience in the production procedure. Only 40.0% project coordinators had training on BCC. Weak technical capacity in BCC material development was a major challenge reported by the project coordinators.
Conclusions: Poor skills in Behaviour Change Communication material development observed. Training and supportive supervision are needed to enhance the skills of project coordinators in the development of behavioural change communication materials.

TUPED833

Preliminary reliability and validity results for measures of intergenerational disjuncture that may reflect pathways between social structural change and HIV outbreaks

E. Pouget, M. Sandoval, Y. Jones, G. Nikolopoulos, S. Friedman
National Development and Research Institutes, Inc., Institute for Infectious Disease Research, New York, United States
Presenting author email: pouget@ndri.org

Background: HIV/AIDS researchers have called for new measurements of pathways by which HIV outbreaks or epidemics may be affected by structural interventions or by "big events" like wars, civil unrest or transitions. One potential pathway is intergenerational disjuncture, in which youth become alienated or the degree to which their behavior is controlled by the norms of older generations is reduced; or conversely, in which older adults become alienated from youth.
We have recently developed preliminary pathways measures assessed at the individual level, including scales for intergenerational disjuncture for younger (IGD-Y) and older (IGD-O) adults through mixed methods research in New York City. Items for these scales tapped into aspects of disjuncture, e.g., "The older generation's ideas about prioritizing sacrifice over fun just don't work for me and my generation."
Methods: We collected data from people who inject drugs and heterosexuals living in high poverty areas by referral from a large study using respondent driven sampling, and by participant referrals during 2012-2014. We analyzed data from 92 younger (ages 18-24) and 443 older adults (ages 25-67) using Cronbach's alpha reliability analysis, and Pearson's correlations with criterion validator variables reflecting risk behaviors in the last month.
Results: The sample was 45% female, 38% Hispanic ethnicity, and 62% Black/African American race; 93% had annual incomes below $15,000. Alpha was 0.82 for the 10-item IGD-Y scale, and 0.88 for the 9-item IGD-O scale. IGD-Y was significantly ($p < 0.05$) *positively* correlated with having participated in sex work (r = 0.56), attended group sex events (r = 0.42), injected drugs (r = 0.49), and smoked crack
(r = 0.53). IGD-O was modestly *negatively* associated with validators, correlating significantly with having attended group sex events (r = -0.11), and used marijuana (r = -0.24).
Conclusions: Preliminary IGD-Y and IGD-O scales show evidence of good reliability and validity. The pattern of associations suggests disapproval of youth risk behaviors by older adults, and perception of this disapproval by youth. Research in international settings is needed to assess whether these measures are reliable and valid in other contexts, and to see whether structural interventions that reduce intergenerational disjuncture can reduce HIV transmission.

TUPED834

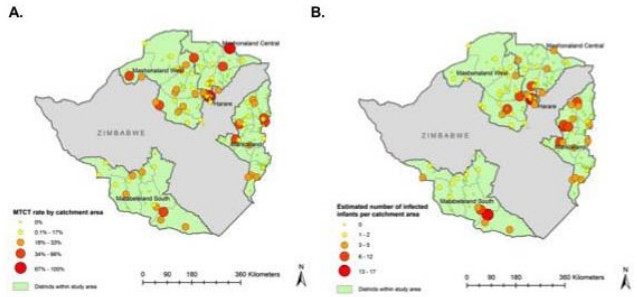
Targeting eMTCT efforts using geospatial analysis of mother to child HIV transmission in Zimbabwe

S.I. McCoy[1], C. Fahey[1], R. Buzdugan[1], A. Mushavi[2], A. Mahomva[3], N.S. Padian[1], F.M. Cowan[4,5]
[1]University of California, Division of Epidemiology, Berkeley, United States, [2]Ministry of Health and Child Welfare, Harare, Zimbabwe, [3]Elizabeth Glaser Pediatric AIDS Foundation, Harare, Zimbabwe, [4]Centre for Sexual Health, HIV & AIDS Research, Harare, Zimbabwe, [5]University College London, London, United Kingdom
Presenting author email: smccoy@berkeley.edu

Background: UNAIDS' goal for "virtual elimination" of mother-to-child transmission (eMTCT) is within reach for many low- and middle-income countries, including Zimbabwe. We evaluated the potential for geospatial analysis to support targeting and prioritization of enhanced PMTCT activities.
Methods: We analyzed 2012 cross-sectional serosurvey data from the evaluation of Zimbabwe's accelerated PMTCT program. Using multi-stage cluster sampling, women were randomly selected from catchment areas of 157 randomly selected health facilities offering PMTCT services in five provinces. Eligible women were ≥16 years old and biological mothers of infants (alive or deceased) born 9-18 months before the interview. We aggregated individual-level data within each catchment area to estimate: 1) the MTCT rate, and 2) the estimated number of HIV-infected infants. These data were linked to GPS coordinates of each facility and displayed on a map. We hypothesized that high MTCT rates indicate areas where the PMTCT cascade re-

quires strengthening, whereas catchment areas with large numbers of infected infants indicate locations at the highest priority for HIV prevention, enhancing infant ART training and delivery, and strengthening the ART supply chain.

Results: Overall, 1107 (12.9%) of 8,568 women surveyed were HIV-infected, and among these women, 8.8% of their HIV-exposed infants were HIV-infected. MTCT differed significantly by catchment area (median: 0%, mean: 11%, interquartile range (IQR): 0-50%), Figure, Panel A). Areas with higher MTCT rates were distributed across the five provinces with no discernible geographic clustering. The estimated number of HIV-infected infants 9-18 months of age also varied by catchment area (median: 0, mean: 1.7, IQR: 0-10.5, Figure, Panel B); areas with the highest burden of HIV-infected infants were clustered in Harare as well as Matebeleland South and Manicaland, provinces with the highest prevalence of HIV-infected antenatal care attendees.



[Figure. Two geospatial visualizations of mother-to-child HIV transmission (MTCT) in five regions of Zimbabwe in 2012 using data from a cross-sectional population-based serosurvey. Panel A displays the MTCT rate in 157 catchment areas of health facilities providing PMTCT services. Panel B displays the estimated number of HIV-infected infants 9-18 months of age per catchment area at the time of the survey]

Conclusions: Although MTCT is declining in Zimbabwe, geospatial visualization of local MTCT rates and the number of pediatric infections indicate variability distributed across several regions of Zimbabwe. The few catchment areas with both high MTCT rates and a high burden of HIV-infected infants (clustered in Harare, Matabeleland South, and Manicaland) should be the highest priority for intensifying HV prevention and PMTCT services to achieve and maintain eMTCT.

TUPED835

Improved HIV testing uptake, food security and reduced violence among orphans and vulnerable children in Zambia: the impact of using baseline data to define program scope

J. Chapman[1], M. Ngunga[2], Z. Chariyeva[3], J. Simbaya[4], J. Kamwanga[4], W. Kaira[5]
[1]Futures Group, Washington, United States, [2]Futures Group, Lusaka, Zambia, [3]Futures Group, Chapel Hill, United States, [4]University of Zambia, Institute of Economic and Social Research, Lusaka, Zambia, [5]World Vision, Lusaka, Zambia
Presenting author email: jchapman@futuresgroup.com

Background: The United States Agency of International Development awarded a high-value, 5-year agreement in Zambia to improve the wellbeing of people living with HIV/AIDS and orphans and vulnerable children called STEPS OVC (Sustainability through Economic Strengthening, Prevention and Support to OVC, Youth and Other Vulnerable Populations). To measure and maximize program impact, we evaluated beneficiary outcomes at the beginning and end of the project. In this paper we discuss the impact of programmatic shifts, resulting from the collection and use of baseline outcomes data, on orphans and vulnerable children.

Methods: We applied a quasi-experimental pre-test/post-test study design, randomly sampling 2,099 orphans and vulnerable children aged 11-17 years from program rosters to participate in a household survey in a maximum variation sample of nine districts in 2011 and again in 2014. Outcome measures included HIV testing uptake, sexual behavior, experience of violence, food security. Ethics approval was obtained in the US and Zambia.

Results: The response rate was 89% at baseline (N=1,869) and 86% at endline (N=1813). At baseline high food insecurity, abuse, and low HIV testing uptake was documented, as well as low condom use among sexually-active adolescents (aged 13-17). The program considered these data using MEASURE Evaluation's Framework for Linking Data to Action, and shifted its workplan to ensure fulfillment of these immediate and priority needs, particularly through economic strengthening programming. At endline, outcomes among children had improved significantly. Considering the last four weeks, children surveyed were less likely to report having gone a whole day and night without food (33% to 25%), having gone to bed hungry (58% to 51%), and having eaten a smaller meal than needed (67.5% to 62%). At endline children reported less reported physical violence in the last 6 months (49% to 21%), increased condom use (40% to 49%), and they were more likely to report having had an HIV test (21% to 28%). We found no differences in HIV/AIDS knowledge or age of sexual debut between baseline and endline.

Conclusions: Understanding the priority needs of a population is critical to ensuring impact. Interventions to improve the utility of data collection and data use will be discussed.

TUPED836

Households that choose to participate in community savings groups are better off than households that do not: findings from an evaluation in Zambia and implications for programming

J. Chapman[1], R. Mswia[2], Z. Chariyeva[2], M. Kanema[3], M. Ngunga[3], J. Chege[4], P. Funjika[5], J. Kamwanga[5]
[1]Futures Group, Washington, United States, [2]Futures Group, Chapel Hill, United States, [3]Futures Group, Lusaka, Zambia, [4]World Vision, Arusha, Tanzania, United Republic of, [5]University of Zambia, Institute of Economic and Social Research, Lusaka, Zambia
Presenting author email: jchapman@futuresgroup.com

Background: HIV-affected households suffer from more income/asset loss, and children living in HIV-affected households often receive less or less-nutritious food, drop out of school to work, and/or do not receive health services. Community savings group can mitigate these effects of HIV/AIDS on people living with HIV/AIDS and orphans and vulnerable children. This paper presents analyses of midline data from a larger evaluation of Savings and Internal Lending Communities (SILC), a user-owned, self-managed savings and credit group. Community members self-select into SILC group. We sought to determine the characteristics of self-selectors and how these compared to those of the general population.

Methods: Data are from a three-year, longitudinal, quasi-experimental study with intervention and comparison groups, aiming to determine the impact of SILC on child and household wellbeing. The study applies a multi-stage cluster sampling approach comparing 1,000 SILC households in 32 SILC wards with 1,000 households in 32 non-SILC wards. We collected data from five population groups in each household: head of household, primary caregiver, SILC participant (intervention wards), children aged 0-9 years, and children aged 10-17 years. Outcome measures include expenditures, assets, food security and dietary diversity, and self-efficacy. Midline data were collected during the hunger season (February 2014). Ethics approval was obtained in the US and Zambia.

Results: The response rate was 97.5% (N= 1,923 households). Overall, households, respondents, and children in the SILC household group were better off compared to those in the comparison group. SILC households reported higher expenditures, higher dietary diversity scores, and were less likely to report moderate to severe hunger than households in the comparison group. Caregivers in the SILC household group were more likely than those in the comparison group to report self-esteem and general, parental, and financial self-efficacy. Children in the SILC household group reported higher dietary diversity and less hunger. Differences between groups persisted even when controlling for level of exposure to SILC (length of time enrolled).

Conclusions: Community savings groups are an important HIV/AIDS mitigation strategy, but they target a particular sub-population. Programs need to profile their beneficiary populations appropriately and implement targeted strategies to mitigate the impact of HIV/AIDS equitably.

TUPED838

Utilization of Google Earth to georeference survey data among people who inject drugs: strategic application for HIV research

L. Beletsky[1,2], A. Vera[2], T. Gaines[2], J. Arredondo[2], D. Werb[2], A. Bañuelos[3], T. Rocha[2], M.L. Rolon[2], D. Abramovitz[2], J. Amon[4], K. Brouwer[2], S.A. Strathdee[2]
[1]Northeastern University, School of Law, Boston, United States, [2]University of California, San Diego, Global Public Health. School of Medicine, La Jolla, United States, [3]Tijuana Municipal Government, Ministry of Public Safety, Tijuana, Mexico, [4]Human Rights Watch, Health and Human Rights, New York, United States
Presenting author email: lbeletsky@ucsd.edu

Background: he integration of geospatial data in behavioral HIV and human rights research has become increasingly widespread in the last two decades. In survey-based research, these data have been typically gathered through initial identification of physical address or street intersection datapoints on paper maps, followed by a manual translation to geospatial coordinates for analysis. This methodology is limited by cartographic imprecisions, confusion over address nomenclature, and human error. Studies targeting migrants, refugees, and others who may lack particularized local geographical familiarity are especially impacted. We sought to overcome these challenges in the context of a large longitudinal study on HIV risk among people who inject drugs (PWID) in Tijuana, Mexico.

Methods: We integrated Google Earth and Google Street View into structured interview protocols. When asked for location information relevant to a specific interview item (e.g. most recent incident of physical abuse by police), respondents were able to pinpoint the exact position of the encounter by virtually navigating to this location with the assistance of the interviewer. Latitude and longitude coordinates were synched into the interview database for use in multivariate and spactio-temporal modeling of HIV risk.

Results: Between 2010-2013, we recruited 737 PWID in Tijuana at baseline. Only 37% of our sample was native to Tijuana, underscoring high levels of PWID migration. Areas frequented by our study population are poorly covered by formal maps and/or liminal locations where

a street address would have been difficult to determine (e.g. informal deportee encampments along the US-Mexico border). These geospatial data are now being used to enhance investigations of structural determinants of HIV and other infectious disease. This includes modeling of PWID experience of police assault and patterns of encounters and arrests in the immediate proximity to drug treatment facilities.
Conclusions: Integrating low- or no-cost real-time virtual navigation as part of data collection, especially among HIV risk groups vulnerable to spatial dispersion or migration is a powerful and low-threshold approach that can add important insights to investigations of the structural production of HIV risk. Implications for future applications are discussed.

TUPED839

Efficiency of facility-based HTC and its determinants: results from the ORPHEA study in Kenya, Rwanda, South Africa and Zambia

S.G. Sosa-Rubí[1], S. Bautista-Arredondo[1], M. Opuni[2], D. Contreras-Loya[1], I. Ochoa Moreno[1], ORPHEA Study Group
[1]Instituto Nacional de Salud Pública, Health Economics, Cuernavaca, Mexico, [2]UNAIDS, Geneve, Switzerland
Presenting author email: sbautista@insp.mx

Background: HIV testing and counseling (HTC) is a critical component of almost all HIV prevention, care, and treatment services. Understanding cost variation and the key determinants of efficiency of facility-based HTC within and across countries is critical to more effectively scaling up this intervention.
Methods: The data for this analysis come from the "Optimizing the Response in Prevention: HIV Efficiency in Africa" (ORPHEA) study - a facility-based study of the costs and technical efficiency of HIV interventions conducted in Kenya, Rwanda, South Africa, and Zambia between 2011 and 2013. The relationship between average unit cost and number of clients (scale of production) was assessed for two outputs in the HTC service cascade: clients tested and clients HIV positive. The log of cost per client tested and cost per client HIV positive were regressed on scale of production adjusting for service quality and management variables that measure governance, accountability, supervision, monitoring, and incentives.
Results: We found that a 10% increase in production scale correlates with a decrease of 5.8% in the average cost per client tested ($p< 0.001$). Hospitals that produce HTC show, on average, double the cost per client tested compared to smaller facilities such as health centers ($p< 0.001$). Regarding average cost per client tested and HIV-positive, scale of production and the facilities' positivity rate explain lower average costs variability, however the latter has a much stronger negative effect. Supervisions and funding linked to performance were strong predictors of average costs variability.
Conclusions: The relationship between unit cost and scale underscores the need to focus scaling up in sites with sufficient demand for services. Scale of HTC services production can increase overall efficiency, as well as targeting strategies to detect HIV-positive individuals. Hospitals tend to have a greater HTC average cost, explained by higher fixed costs and a low scale of production, making this setting of provision less efficient than the health center model. Monitoring and supervision are relevant factors that contribute to increase efficiency in contrast to incentives for performance. These results bring up the need to design an incentives scheme linked to increase the detection of HIV-positive clients.

TUPED840

Efficiency of VMMC and its determinants: results from the ORPHEA study in Kenya, Rwanda, South Africa, and Zambia

S. Bautista-Arredondo[1], S.G. Sosa-Rubí[1], M. Opuni[2], D. Contreras-Loya[1], I. Ochoa Moreno[1], ORPHEA Study Group
[1]Instituto Nacional de Salud Pública, Health Economics, Cuernavaca, Mexico, [2]UNAIDS, Geneve, Switzerland
Presenting author email: sbautista@insp.mx

Background: While VMMC programs have made significant progress since their inception, as the levels of coverage increase they face important challenges to reach their goals, including availability of resources. Scaling up VMMC coverage to achieve national targets will require that countries deliver the highest achievable quality of service at the lowest feasible cost.
Methods: The data for this analysis come from the "Optimizing the Response in Prevention: HIV Efficiency in Africa" (ORPHEA) study - a facility-based study of the costs and technical efficiency of HIV interventions conducted in Kenya, Rwanda, South Africa, and Zambia between 2011 and 2013. Quality was measured through patient exit interviews. The log of cost per VMMC client and a quality variable (bounded between 0 and 1) were analyzed as outcomes in a simultaneous regression model, including as covariates the scale of production, facility characteristics (type of facility and task-shifting) and management variables (governance, accountability, supervision, monitoring, and incentives).
Results: We found that average cost per VMMC decreased 4.1% with a 10% increase in the number of VMMC clients ($p< 0.001$), whilst this variable correlates positively with the quality score. The cost to provide VMMC at hospitals is 50% higher than health centers ($p=0.01$), and hospitals have on average the same quality score as health centers ($p=0.44$). The existence of a community council is significantly associated with both lower costs ($p< 0.001$) and quality ($p=0.02$). Facilities that shift tasks away from doctors produce VMMC at half the cost of facilities that employ doctors ($p=0.005$), however this characteristic does not have effect on quality ($p=0.629$). The degree of financial monitoring also shows an inverse association with average costs.
Conclusions: The large differences in unit cost found across facilities suggest high levels of inefficiency in the provision of VMMC. Implementation and management characteristics are important variables to explain the variability of the cost per VMMC, and are less relevant to explain quality. Health centers producing VMMC services with nurses determines better costs efficiency while maintaining the same levels of quality.
Beyond scale, there is considerable scope to increase efficiency in the production of VMMC services through reallocation of health inputs.

Wednesday 22 July

Oral Abstract Sessions

WEAA01 Immunity and Immunization

WEAA0101

Comparison of HIV-1 envelope specific IgA and IgG antiviral ability to prevent HIV-1 infection: additive, inhibitory and synergistic effects

S.G. Okala[1], D.F. King[1,2], R.J. Shattock[1]
[1]Imperial College London, Medicine, London, United Kingdom, [2]International AIDS Vaccine Initiative, London, United Kingdom
Presenting author email: s.okala12@imperial.ac.uk

Background: Despite the crucial role of IgA in mucosal immunity, very little is known about how IgG and IgA isotypes interact to prevent HIV-1 infection. This gap in the current knowledge was highlighted in the HIV-1 RV144 vaccine trial in which specific monomeric (m)IgA mitigated IgG effectors functions and correlated with increased risk of HIV-1 acquisition. Both IgG and dimeric (d)IgA are present in the female and male genital tracts, which are the main site of viral entry. However, the ratio of IgG to IgA varies between compartments. In this study, we compared the antiviral properties of IgG and IgA antibodies with the same epitope specificity at ratios found in genital secretions. Subsequently, we investigated whether the combination of antibody recognising discrete epitopes but from the same isotype resulted in improved antiviral activities.
Methods: CH31, b12, 2F5 and 7B2 mAbs binding to soluble HIV-1_{BaL} gp140 Env and kinetics parameters of these interactions were determined by competitive enzyme-linked immunosorbent assay and Bio-Layer Interferometry (BLI). HIV-1_{BaL} virus capture by the panel of mAbs was quantified by p24 ELISA, antibody mediated viral aggregation (AMVA) was determined using Nanoparticle Tracking Analysis (NTA) and neutralisation activity by TZM-bl neutralisation assay.
Results: We demonstrated that IgGs captured significantly more virions than IgAs and this was correlated with higher association rate constants whereas dIgA presented the ability to mediate viral aggregation. Strikingly, the combination of dIgA and IgG recognising the same epitope did not elicit any additive effects. In contrast, IgG prevented dIgA binding to HIV-1_{BaL} gp140 Env and its ability to capture and aggregate HIV-1_{BaL} virions. However, mixtures of IgGs or dIgAs recognising distinct epitopes but from the same isotype resulted in synergistic effects with higher proportions of captured viruses; antibody mediated viral aggregates and neutralisation activities.
Conclusions: This study compared the ability of IgG and dIgA to prevent HIV-1 infection with respect to the ratio IgG and dIgA found in genital secretions. Collectively, these results suggest that the combination of antibody targeting different epitopes provides enhanced general antiviral activities. Nonetheless, antibody binding to the same epitope but of different isotypes may lead to competition and inhibition of antiviral functions.

WEAA0102

Anti-V3/glycan and anti-MPER neutralizing antibodies, but not anti-V2/glycan-site antibodies are strongly associated with higher anti-HIV-1 neutralization breadth and potency

R.A. Jacob[1,2], T. Moyo[1,2], M. Schomaker[3], F. Abrahams[1], B. Grau Pujol[1], J. Dorfman[1,2]
[1]International Centre for Genetic Engineering and Biotechnology, Cape Town, South Africa, [2]University of Cape Town, Division of Immunology, Cape Town, South Africa, [3]University of Cape Town, Centre for Infectious Disease Epidemiology & Research, Cape Town, South Africa
Presenting author email: jeffrey.dorfman@icgeb.org

Background: Previous candidate HIV vaccines have failed to either induce wide-coverage neutralizing antibodies or substantially protecting vaccinees.
Therefore, current efforts focus on novel approaches never before successfully used in vaccine design, including modeling epitopes. Candidate immunogen models identified by broadly neutralizing antibodies include the membrane proximal eternal region (MPER, recognized by 4E10, 2F5 and 10E8 monoclonal antibodies (mAbs)), V3/glycans (typified by PGT121-128 mAbs) and the V2/glycan site (initially defined by PG9 and PG16 mAbs). Anti-MPER and anti-V3/glycan antibodies are often autoreactive or polyreactive, and this is thought to pose both direct and indirect barriers to achieving neutralization breadth.
Recent evidence shows that antibodies with moderate neutralization breadth are frequently attainable, with 50% of sera from chronically-infected individuals neutralizing ≥50% of a large, diverse set of viruses. Such moderately neutralizing antibodies may be more attainable in vaccinees. Despite these findings, there is little systematic information addressing which specificities are preferentially targeted among such commonly found, moderately broad neutralizing sera.
Methods: We explored associations between neutralization breadth and potency and presence of neutralizing antibodies targeting MPER, V2/glycan site and V3/glycans in sera from 177 antiretroviral therapy-naive HIV-1-infected (>1yr) individuals recruited in Cape Town, South Africa.
Results: Recognition of both MPER and V3/glycans was associated with increased breadth and potency. MPER-recognizing sera neutralized 4.62 more panel viruses than MPER-negative sera (95% prediction interval (PI) 4.41, 5.20), and V3/glycan-recognizing sera neutralized 3.24 more panel viruses than V3/glycan-negative sera (95%PI 3.15, 3.52). In contrast, V2/glycan site-recognizing sera neutralized only 0.38 more panel viruses (95%PI 0.20, 0.45) than V2/glycan site-negative sera and no association between V2/glycan site recognition and breadth or potency was observed.

Category	Less potent (Geo Mean ID50 < 220)	Potently neutralizing (Geo mean ID50 > 220)	Relative Risk (95% CI)	p value (X^2)	Less broad (neutralizes < 18/24 viruses)	Broadly neutralizing (Neutralizes >=18/24 viruses)	Relative Risk (95% CI)	p value (X^2)
Anti-MPER neg	124	20	1.00 (reference)		122	22	1.00 (reference)	
Anti-MPER pos	24	9	1.96 (0.99, 3.91)	0.061	23	10	1.98 (1.04, 3.78)	0.043
Anti-V2 glycan site neg	63	21	1.00 (reference)		62	22	1.00 (reference)	
Anti-V2 glycan site pos	29	5	0.59 (0.24, 1.43)	0.222	27	7	0.79 (0.37, 1.67)	0.522
Anti V3/ glycans neg	75	17	1.00 (reference)		73	19	1.00 (reference)	
Anti-V3/ glycans pos	12	9	2.32 (1.21, 4.46)	0.017	12	9	2.08 (1.10, 3.92)	0.033

[Broad/Potent neutralization and target recognized]

Conclusions: Despite autoreactivity of many neutralizing antibodies recognizing MPER and V3/glycans, antibodies to these sites are major contributors to neutralization breadth and potency in this cohort. This suggests that the autoreactivity effect is not critical and that the MPER and the V3/glycans should remain high priority vaccine candidates. The V2/glycan site result is surprising because broadly neutralizing antibodies to this site have been repeatedly observed. It may therefore be appropriate to focus on developing immunogens based upon the MPER and V3/glycans.

WEAA0103

Impact of HLA-B*35 alleles on HIV disease outcome in Mexico and Central America

H. Valenzuela-Ponce[1], S. Ávila-Ríos[1], D. Garrido-Rodríguez[1], T. García-Téllez[1], M. Soto-Nava[1], T. Escamilla-Gómez[1], C. García-Morales[1], J. Cortés-Álvarez[1], R. Hernández-Juan[1], A. Murakami-Ogasawara[1], C. Mejía-Villatoro[2], J. Pascale[3], G. Porras[4], C. Quant[4], I. Lorenzana[5], R. Meza[5], E. Palou[5], M. Manzanero[6], G. Reyes-Terán[1], Mesoamerican HIV Project Group
[1]National Institute of Respiratory Diseases, Center for Research on Infectious Diseases, Mexico City, Mexico, [2]Hospital Roosevelt, Guatemala City, Guatemala, [3]Instituto Conmemorativo Gorgas de la Salud, Panama City, Panama, [4]Hospital Metropolitano Vivian Pellas, Managua, Nicaragua, [5]HIV National Program, Tegucigalpa, Honduras, [6]Ministry of Health, Belize, Belize

Background: HLA-B*35 alleles have been classified into two groups, PY and Px, based on residues 114/116 in the HLA peptide binding groove, defining the amino acid preference at position 9 of the peptides they present. B*35:02/35:03, part of the Px group, have been associated with rapid HIV disease progression in the context of HIV-1 B clade infection. As B*35 is the most prevalent HLA-B allelic group in Mexico and Central America (expressed in 41.4% of individuals), including a number of relatively unstudied B*35 alleles, we investigated HIV disease outcome in this cohort.
Methods: HLA sequence-based typing was performed on 1971 chronically HIV-1 clade B infected, ART-naïve individuals from Mexico (n=1058), Guatemala (n=396), Nicaragua (n=218), Honduras (n=165), Panama (n=85) and Belize (n=49). Associations between HIV plasma viral load (pVL) and CD4 T cell count (CD4 count) with B*35 expression were evaluated using Mann-Whitney U tests and Storey q values. Only HLA-B heterozygous individuals were compared in order to exclude confounding effects resulting from HLA homozygosity.
Results: We observed 10 different B*35 alleles (n>5). Based on residues 114 and 116, B*35:01/08/14/16/17/20/43 were classified as PY, and B*35:02/03/12 as Px. Ranking HLA-

B*35 alleles according to median pVL or CD4 count showed a wide spectrum of associated HIV disease outcomes. B*35:01 (PY) and B*35:12 (Px), which are not considered disease-susceptible alleles, were associated with higher pVL and lower CD4 count ($p< 0.05$, $q< 0.05$). B*35:12 detrimental effect was stronger in Guatemala and Nicaragua than in Mexico, and the magnitude of B*35:01 effect in each country was frequency-dependent. B*35:08 (PY) had a modest protective effect on disease outcome (although not statistically significant). No significant impact on median pVL or CD4 count was observed between HLA-B*35 PY (n=359) and Px (n=134) groups.

Conclusions: These results challenge the B*35-PY/Px hypothesis, indicating that PY alleles can be disease-susceptible. Moreover, the previous observation that the negative effect of the B*35 group is due to all Px alleles is not supported by these data. Interestingly, differences in the detrimental effect of some B*35 alleles in different countries seemed to be frequency-associated, warranting further studies on HIV HLA-associated adaptation in previously uncharacterized populations.

WEAA0104

Type-1 programmed dendritic cells induce primary CTL capable of effectively targeting the HIV-1 reservoir

R.B. Mailliard[1], K.N. Smith[1], P. Piazza[1], J.I. Mullins[2], C.R. Rinaldo[1]
[1]*University of Pittsburgh, Infectious Diseases and Microbiology, Pittsburgh, United States,* [2]*University of Washington, Microbiology and Medicine, Seattle, United States*
Presenting author email: rbm19@pitt.edu

Background: The "kick and kill" strategy for the cure of chronic HIV-1 infection involves unmasking cells harboring the latent viral reservoir followed by their immune elimination. We hypothesize that a broad priming of de novo rather than memory HIV-1 specific CTL will be required to effectively target the autologous HIV-1 reservoir, and that this "kill" can be best achieved using specifically programmed type-1 dendritic cells (DC1).

Methods: Mature, IL-12p70 producing DC1 were generated using a combination of either TNFa, IL-1b, poly IC, IFNa and IFNg, or CD40L and IFNg. Mature, IL-12 deficient DC were generated using either a combination of TNFa, IL-1b, IL-6 and PGE2, or CD40L alone. $CD8^+$ T cells were purified from HIV-1 negative donors, and both naive (primary) and memory $CD8^+$ T cells were isolated from HIV-1 infected Multicenter AIDS Cohort Study participants who were on virus-suppressive cART for several years. These cells were stimulated with autologous DC loaded with HIV-1 Gag peptides or autologous AT2-inactivated HIV-1. Resulting CTL activity was assessed by IFNg ELISPOT and antiviral cytotoxicity assays targeting autologous HIV-1 infected $CD4^+$ T cells.

Results: DC1 proved far superior to the IL-12-deficient DC for inducing primary CTL responses in both infected and uninfected donors. Importantly, DC1 required CD40L "help" at the onset of priming cultures for successful CTL induction and expansion. Both primary and memory CTL each responded to distinct autologous HIV-1 Gag peptides with robust IFNγ production. However, a broader targeting of known MHC class I-restricted epitopes was achieved by the primary CTL responders than the memory cells. Importantly, despite substantial IFNγ production by both T cell subsets, the primary $CD8^+$ T cells were significantly superior to restimulated memory T cells in eradicated HIV-1 infected $CD4^+$ T cells in the CTL assays.

Conclusions: We demonstrate that naïve T cells from HIV-1 infected persons on cART have the repertoire and ability to be primed by high IL-12p70-producing DC1 to effectively target the HIV-1 reservoir, while memory CTL responses are suboptimal. These findings highlight the importance of directing HIV-1 curative strategies towards the induction of de novo rather than memory HIV-1-specific CTL responses.

WEAA0105

Molecular determinants of HIV-1 permissiveness and persistence in gut-homing CD4+ T cells expressing the Th17 marker CCR6

D. Planas[1,2], A. Gosselin[1], P. Monteiro[1], J.-P. Goulet[3], S. Da Fonseca[1,2], A. Cléret-Buhot[1,2], M.-A. Jenabian[4], J.-P. Routy[5,6], P. Ancuta[1,2]
[1]*CHUM-Research Center, Montreal, Canada,* [2]*University of Montreal, Microbiology Infectiology and Immunology, Montreal, Canada,* [3]*CATRaGENE, Montreal, Canada,* [4]*Université du Québec à Montréal (UQAM), Department of Biological Sciences and BioMed Research Centre, Montreal, Canada,* [5]*McGill University Health Center, Division of Hematology, Montreal, Canada,* [6]*McGill University Health Center, Immunodeficiency Service, Montreal, Canada*
Presenting author email: delphine.planas@gmail.com

Background: HIV-infected CD4+ T-cells are enriched in gut-associated lymphoid tissues (GALT). The integrin a4β7 and CCR9 mediate imprinting for gut-homing, and their expression is induced by retinoic acid (RA), a vitamin A metabolite produced by GALT dendritic cells. We previously demonstrated that CD4+ T-cells expressing the Th17 marker CCR6 are permissive to HIV *in vitro*, harbor replication-competent HIV reservoirs in ART-treated subjects, and that RA selectively increases HIV replication in these cells. To identify new molecular determinants of HIV permissiveness/persistence, we performed a genome-wide transcriptional analysis in RA-treated CCR6+ *versus* CCR6- T-cells.

Methods: CD4+ T-cells were sorted from PBMCs by negative selection using magnetic beads (Miltenyi). Memory (CD45RA-) CCR6+ and CCR6- T-cells were sorted by flow cytometry (BDAriaII). Cells were stimulated *via* CD3/CD28 and cultivated in the presence or absence of RA (10nM) for 4 days. Total RNA was extracted for microarrays analysis (HT 12v4 BeadChip, Illumina; >46,000 probe sets *per* chip). Validations of microarrays were performed by real-time PCR and/or flow cytometry. HIV-DNA integration was measured by nested real-time PCR. Functional validations were performed using RNA interference (Amaxa).

Results: Among 15,303 "present calls", 1,538 and 1,285 probe sets were modulated by RA in CCR6- and CCR6+ T-cells, respectively (*p-value* < 0.05; fold change cut-off 1.3). Gene Set Variation Analysis (GSVA), Ingenuity Pathway Analysis (IPA), and *Gene Ontology* tools were used to identify pathways/individual transcripts specifically induced by RA in CCR6+ *versus* CCR6- T-cells. This signature included an increased expression of gut homing markers (a4β7, CCR9), HIV-1 coreceptors (CCR5, CXCR6), and also pathways linked to the regulation of T-cell activation (CD38, Lck, PTPN13, MAP4K4), glucose metabolism (Glut1, Glut8), cell cycle (GADD45G), HIV replication *via* CCR5 expression (KLF2), and multidrug resistance (MDR1/ABCB1). In addition, the transcriptome of RA-treated CCR6+ T-cells showed decreased expression of known HIV-1 resistance factors
(PPAR-g, CCL3, CCL3L1).

Conclusions: Our studies demonstrate that RA-mediated imprinting for gut-homing is associated with HIV permissiveness in CCR6+ but not CCR6- T-cells and reveal molecular mechanisms underlying these differences. These findings will orient the discovery of new therapeutic strategies aimed at limiting HIV permissiveness, and subsequently the size of HIV reservoirs, specifically in gut-homing Th17 cells.

WEAA0106LB

The potential of attenuated *Mycobacterium tuberculosis* or BCG vaccines to enhance oral SIV acquisition in infant macaques

K. Jensen[1], M.G. dela Pena-Ponce[1], M. Piatak, Jr.[2], W. Jacobs, Jr.[3], G. Fennelly[4], K. Mollan[5], M. Hudgens[5], P. Kozlowski[6], A. Amedee[6], J. Estes[2], J. Lifson[2], K. Van Rompay[7], M. Larsen[3], K. De Paris[1]
[1]*University of North Carolina, Microbiology & Immunology, Chapel Hill, United States,* [2]*Leidos Biomedical, Inc., Frederick National Laboratory, Frederick, United States,* [3]*Albert Einstein Institute, New York, United States,* [4]*Rutgers New Jersey Medical School, Newark, United States,* [5]*University of North Carolina, CFAR, Chapel Hill, United States,* [6]*LSUHSC, Microbiology, Immunology, and Parasitology, New Orleans, United States,* [7]*UC Davis, CNPRC, Davis, United States*

Background: Infants bear a high burden of HIV-1 and tuberculosis (TB) infections, especially in sub-Saharan Africa. We previously demonstrated that the double auxotroph *Mycobacterium tuberculosis* (*Mtb)* strain $mc^2$6435, engineered to co-express SIV Gag, was safe and immunogenic in neonatal macaques. Here, we tested the efficacy of an oral $mc^2$6435 prime/intramuscular MVA-SIV boost regimen to protect against repeated low-dose oral SIVmac251 challenge in infant macaques.

Methods: The study included 75 infant rhesus macaques . Mock-vaccinated infants (n=15) received saline. Vaccinated animals (n=60) received attenuated auxotroph *Mtb*-vaccines with or without SIV gag/env inserts (n=53) orally, or BCG (n=7) intradermally at birth At 9 weeks, infants were exposed to a once-weekly low-dose oral SIVmac251 challenge regimen. Plasma viremia was determined by real-time PCR. Cellular immune activation was determined by flow cytometric analysis in blood and tissues, soluble plasma markers were measured with a Procarta 37plex. statistical analysis for risk-per-SIV exposure was determined by SAS and Kaplan-Meier plots; immune parameters were analyzed using Kruskal-Wallis with multiple Dunn´s comparison.

Results: A single administration of the $mc^2$6435 vaccine at birth induced persistent immune activation that was associated with oral SIV acquisition after fewer challenges compared to mock-vaccinated infants. The human BCG vaccine resulted in similar enhanced acquisition of SIV, and BCG-vaccinated infants showed higher peak viremia compared to mock- and *Mtb*-vaccinated infant macaques. The potential for enhanced oral SIV acquisition was independent of the mycobacterial vaccine strain, immunization route, and boost regimen. Analysis of blood and tissue samples revealed that both *Mtb* and BCG vaccines induced immune activation of myeloid cell populations and $CD4^+$ T cells, potential target cells of SIV. Immune activation was detected as early as three weeks post-vaccination and persisted for several months.

Conclusions: Our results in the infant macaque model are consistent with BCG-induced immune activation of $CD4^+$ T cells in human infants, reports of persistent monocyte activation in BCG-vaccinated human adults, and increased HIV-1 infection rates in human $CD4^+$ T cells exposed to *Mtb* complex *in vitro*. Thus, in areas of high HIV-1 prevalence, TB vaccines need to be tested for their risk of enhancing HIV-1 susceptibility in human infants.

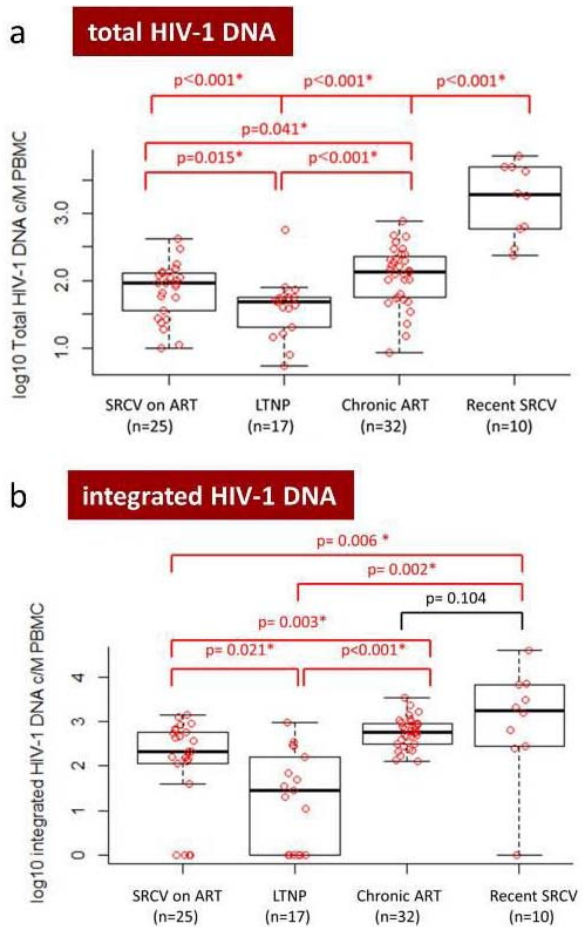
WEAB01 Primary HIV Infection: ART at the Start

WEAB0101

Long-term early antiretroviral therapy limits the HIV-1 reservoir size as compared to later treatment initiation but not to levels found in long-term non-progressors

E. Malatinkova[1], W. De Spiegelaere[1], P. Bonczkowski[1], M. Kiselinova[1], K. Vervisch[1], W. Trypsteen[1], M. Johnson[2], C. Verhofstede[3], D. de Looze[4], C. Murray[5], S. Kinloch-de Loes[2], L. Vandekerckhove[1]
[1]Ghent University and Ghent University Hospital, HIV Translational Research Unit, Department of Internal Medicine, Faculty of Medicine and Health Sciences, Ghent, Belgium, [2]Royal Free Hospital, Division of Infection and Immunity, London, United Kingdom, [3]Ghent University, AIDS Reference Laboratory, Department of Clinical Chemistry, Microbiology and Immunology, Ghent, Belgium, [4]Ghent University Hospital, Department of Gastroenterology, Ghent, Belgium, [5]Royal Free Hospital, Department of Gastroenterology, London, United Kingdom
Presenting author email: eva.malatinkova@ugent.be

Background: Early initiation of long-term antiretroviral therapy (ART) may lead to viral control after treatment discontinuation. Recent evidence indicates that ART initiated within seroconversion limits the HIV-1 reservoir size. Insight into the reservoir in patients with different timings of ART as well as those who can control HIV-1 without therapy should further inform new treatment strategies.
Methods: A cross-sectional study of HIV-1 reservoir size (total and integrated HIV-1 DNA) and dynamics (2-LTR circles and cell-associated HIV-1 unspliced RNA (usRNA)) was performed in peripheral blood mononuclear cells (PBMCs) in 84 HIV-1 infected patients from 4 cohorts in 2 clinical centers (London, UK and Ghent, BE): long-term treated patients with ART initiated during seroconversion (SRCV on ART; n=25) or chronic infection (Chronic ART; n=32), long-term non-progressors (LTNP; n=17) and ART-naïve recent seroconverters (Recent SRCV; n=10). Total HIV-1 DNA, 2-LTR and usRNA were measured by ddPCR and integrated HIV-1 DNA by *Alu*-HIV PCR. Clinical parameters including time on ART and aviremia, CD4 count and CD4/CD8 ratio were collected.



*[Figure 1. Total HIV-1 DNA (a) and integrated HIV-1 DNA (b) levels in four patient cohorts. Data is shown as log10 copies/million (c/M) PBMC and significant p-values are indicated by *. Differences between the cohorts were determined by Wilcoxon Signed Rank test]*

Results: Median total HIV-1 DNA copies were: 92, 48, 137 and 1901 c/10^6 PBMCs in SRCV on ART, LTNP, Chronic ART and Recent SRCV, respectively. Significantly lower levels of total (p=0.041) and integrated HIV-1 DNA (p=0.003) were detected in early as compared to chronically treated patients, however these were higher than those found in LTNP (Fig.1a, 1b). Interestingly, similar levels of integrated HIV-1 DNA were found in Recent SRCV compared to the Chronic ART cohort (p=0.104), confirming very fast seeding of the reservoir (Fig 1b). Levels of usRNA were significantly lower in early compared to chronically treated cohort (p=0.007), indicating a lower transcriptional activity in early treated patients and similar to LTNP (p=0.615). Furthermore, early treated patients exhibited a higher CD4/CD8 ratio compared to chronically treated patients (p=0.009), suggesting lower levels of residual immune activation.
Conclusions: Our data demonstrate that long-term early treated patients have smaller reservoir size as compared to patients treated during chronic infection, however not reaching levels found in LTNP.
Interestingly, the reservoir dynamics in terms of 2-LTR and usRNA as well as the CD4/CD8 ratio in early treated patients are comparable to LTNP.

WEAB0102

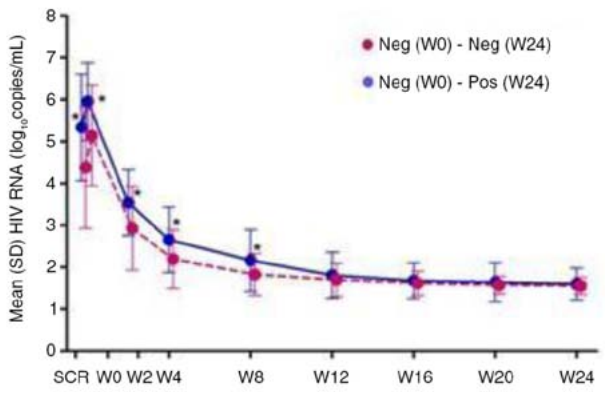
High rates of non-reactive HIV serology after antiretroviral treatment initiated in acute HIV infection

J.L.K. Fletcher[1], S. Pinyakorn[2], M. de Souza[1], S. Akapirat[3], R. Trichavaroj[3], T. Pankam[4], E. Kroon[1,3], D. Colby[1], P. Prueksakaew[1], D. Suttichom[1], J.H. Kim[2,3], P. Phanuphak[4,5], N. Phanuphak[1,4], J. Ananworanich[2,6], The SEARCH010/RV254 Study Group
[1]SEARCH, The Thai Red Cross AIDS Research Centre, Bangkok, Thailand, [2]U.S. Military HIV Research Program, Walter Reed Army Institute of Research, Silver Spring, United States, [3]Armed Forces Research Institute of Medical Sciences - United States Component, Department of Retrovirology, Bangkok, Thailand, [4]The Thai Red Cross Anonymous Clinic, Thai Red Cross AIDS Research Centre, Bangkok, Thailand, [5]Chulalongkorn University, Department of Medicine, Faculty of Medicine, Bangkok, Thailand, [6]Henry M. Jackson Foundation for the Advancement of Military Medicine, Bethesda, United States
Presenting author email: james.f@searchthailand.org

Background: Non-reactive HIV serology may be a marker of low HIV viral burden. We examined the evolution of HIV antibody in a cohort of individuals treated during acute HIV infection (AHI).
Methods: Between April 2009 and December 2014, adults attending voluntary HIV testing in Bangkok, Thailand, were screened for AHI, by either pooled nucleic acid testing (NAT) of 4th generation immunoassay (4G IA) non-reactive samples or by 3rd (3G) or 2nd generation (2G) enzyme immunoassay (EIA) of 4G IA reactive samples. Immediate antiretroviral therapy (ART) was offered. Western blot and p24 quantification were performed for Fiebig staging. HIV serology at baseline, weeks 12 and 24 were performed.
Results: 233 Thai adults were enrolled from 130,164 samples screened; 3 individuals did not initiate ART and were excluded from analysis. The median age of the volunteers was 27 years and 95% were male. Median time from history of HIV exposure to enrollment was 18 days and median time from enrollment to ART initiation was 1 day.

Non-reactivity to HIV enzyme immunoassay [N(%)]			
	Baseline (N=207)	Week 12 (N=150)	Week 24 (N=135)
2nd generation EIA	207 (100)	51 (34)*	53 (39)*
3rd generation EIA	99 (48)	5 (3)*	7 (5)*
4th generation IA	43 (21)	30 (20)	24 (18)
*McNemar's test, p<0.001, compared to baseline [Note: No significant difference between week 12 and week 24]			

[Table 1: Non-reactivity to enzyme immunoassay]



[Figure 1: Plasma viral load by 2G EIA reactivity]

Of 207 baseline 2G EIA non-reactive subjects, results were available for 150 at week 12 and 135 at week 24 (Table 1). At week 12, 34% were non-reactive by 2G, 3% by 3G and 20% by 4G IA; at week 24, 39% were non-reactive by 2G, 5% by 3G and 18% by 4G.
Baseline HIV RNA< 5 log_{10} copies/ml (p=0.02), CD4 count >350 cells/µL (p=0.01) and Fiebig stage 1 or 2 (p=0.03) were predictive of non-reactive 2G EIA at week 24. Lower $AUC_{0\text{-}24wk}$ for HIV RNA was also associated with non-reactive 2G EIA at week 24 (p=< 0.001, Figure 1).
Seroreversion was uncommon. 1 of 23 individuals with reactive 2G EIA at baseline was non-reactive at week 24; 11 of 207 demonstrated transient 2G EIA reactivity at week 12.
Conclusions: Approximately 40% of individuals who initiated treatment in AHI maintained non-reactivity to 2G EIA after 24 weeks of ART. Rapid ART initiation and HIV RNA decline as well as low HIV RNA and high CD4 at baseline predicted subsequent serological nonreactivity. HIV serologic non-reactivity is likely due to low viral burden, further supporting the benefits of early initiation of ART.

WEAB0103

Twenty-four weeks is too short to assess virological success in primary HIV infection treatment

A. Vandendriessche[1], T. Mourez[2,3], V. Lemée[2], Y. Debab[1], G. Peytavin[4,5], J. Ladner[6], F. Caron[1,3], J.-C. Plantier[2,3], J. Leporrier[1]
[1]Rouen University Hospital, Infectious Diseases, Rouen, France, [2]Rouen University Hospital, Virology, Rouen, France, [3]Université de Rouen, Institut de Recherche et d'Innovation Biomédicale (IRIB), Rouen, France, [4]APHP-Bichat Hospital, Pharmaco-Toxicology, Paris, France, [5]Université Paris 7, IAME Inserm 1137, Paris, France, [6]Rouen University Hospital, Epidemiology & Public Health, Rouen, France
Presenting author email: anne.vandendriessche@chu-rouen.fr

Background: The goal of HAART, in established HIV infection, is to obtain virological success (plasma HIV-RNA level (pVL) < 40 copies/mL) associated with CD4 increase at 24 weeks of treatment (W24).
Therefore, we analysed whether such W24 end-point is also pertinent for patients treated for primary HIV infection (PHI).
Methods: We conducted a 10-year retrospective analysis of the immuno-virological response in 55 adults receiving HAART within 3 months after diagnosis of PHI. Genotypic resistance tests were performed before HAART and at W24 for patients with virological failure (VF) as well as HAART plasma concentrations.
Results: Patients were mostly men (n=48, 87 %), White European (n=50, 91 %), MSM (n=29, 52 %) and mean age 35.9 years. At baseline, mean pVL was $2.6.10^6$ cp/mL (8.10^3 - $>10^7$) and mean CD4 count 479/mm^3 (77-1003). Patients were mostly infected with subtype B HIV-1 (n=30, 54 %). Due to the evolution of treatment recommendations over the 10-year study period, 9 different combinations of HAART were used, including mostly TDF/FTC (n=38, 69 %) and a protease inhibitor as third agent (n=49, 89 %).
At W24, 44/55 (80 %) patients had pVL< 40cp/ml, whereas 11/55 (20 %) had low residual pVL (45-391 cp/mL; mean: 155). In these latter patients, we observed neither mutation associated with resistance nor inefficient drug concentration. VF was correlated in univariate analysis with a significantly higher mean baseline pVL (p=0.03) and a significantly lower mean baseline CD4 count (p=0.04) than patients with undetectable pVL at W24. There was no relationship between age, sex, ethnicity, source of contamination, HAART combination or VF at W24.
Conclusions: Our results show that 24 weeks is too short to achieve virological success in patients with high pre-treatment pVL associated with low CD4 count. These data highlight that the usual W24 end-point to conclude virological success may not be appropriate in PHI.

WEAB0104

HIV transmitted drug resistance declined from 2009 to 2014 among acutely infected MSM in Bangkok, Thailand

D. Colby[1], N. Phanuphak[1], S. Sirivichayakul[2], P. Prueksakaew[1], P. Saengtawan[1], R. Trichavaroj[3], T. Crowell[4], J. Kim[4], J. Ananworanich[4], P. Phanuphak[5], RV254/SEARCH010 Study Group
[1]Thai Red Cross AIDS Research Center, SEARCH, Bangkok, Thailand, [2]Chulalongkorn University Hospital, Bangkok, Thailand, [3]Armed Forces Research Institute for Medical Sciences, Bangkok, Thailand, [4]U.S. Military HIV Research Program, Bethesada, United States, [5]Thai Red Cross AIDS Research Center, Bangkok, Thailand
Presenting author email: doctordonn@gmail.com

Background: Rates of transmitted drug resistance (TDR) have been reported to be 11-21% in the USA and Europe, where baseline genotype resistance testing prior to antiretroviral therapy (ART) is routine. In resource limited settings, baseline resistance testing is not the standard of care, but TDR data can ensure that first-line treatment regimens used in national HIV treatment programs remain effective.
Methods: The RV254/SEARCH010 cohort has enrolled patients with acute HIV infection from the largest HIV testing and counseling center in Thailand since 2009. Patients have baseline genotype testing prior to initiating ART: TRUGENE HIV-1 (Siemens Healthcare Diagnostics, Australia) was used for the first 66 patients and a validated in-house method for the remainder. Mutations were categorized following the World Health Organization surveillance drug resistance mutation (SDRM) list. Prevalence of resistance was calculated by dividing the number of subjects with mutations by the number enrolled during each time period. Change in prevalence over time was assessed by chi-square test for trend. Time periods were combined into 2-year blocks for analysis.
Results: Genotype resistance test results were available from 184 of the first 186 subjects enrolled in the study; virus from 2 patients could not be amplified. Median age was 28 years, 95% were male, and 92% were men who have sex with men (MSM). Median time (inter-quartile range, IQR) from HIV exposure to diagnosis was 18 (14-24) days. Median (IQR) HIV RNA was 5.7 (5.1-6.7) log_{10} copies/ml and was not significantly different between patients with and without resistance mutations. Median (IQR) CD4 was 352 (260-486) cells/mm^3. Prevalence rates for resistance mutations are shown in the table. Overall TDR was 7.1%, declining from 12.5% in 2009-2011 to 4% in 2013-2014, although the change was not statistically significance (p=0.07). The mutations most commonly found were the M46I (n=3), K103N (n=2), Y181C (n=2), and M41L (n=2).

	Total	2009-2010	2011-2012	2013-2014	p
	n (%)	n (%)	n (%)	n (%)	
N enrolled	184	32	52	100	
Any resistance	13 (7.1)	4 (12.5)	5 (9.6)	4 (4.0)	0.07
N with RT genotype	183	32	51	100	
NRTI mutations	6 (3.3)	2 (6.3)	2 (3.9)	2 (2.0)	0.23
NNRTI mutations	4 (2.2)	3 (9.4)	1 (2.0)	0 (0)	0.03
N with PR genotype	180	32	50	98	
PI mutations	6 (3.3)	1(3.1)	3 (6.0)	2 (2.0)	0.52

[Transmitted drug resistance among MSM in Bangkok]

Conclusions: TDR does not appear to be increasing among MSM in Thailand and may be declining. Routine genotype testing prior to initiating ART may not currently be necessary in this population, but surveillance for TDR should continue to monitor for any future changes.

WEAC01 Female Sex Workers: Insights for Intervention

WEAC0101

Social cohesion among sex workers has an independent effect on reduced client condom refusal in a Canadian setting

E. Argento[1], P. Duff[1,2], B. Bingham[1,3], P. Nguyen[1], S. Strathdee[4], K. Shannon[1,2]
[1]BC Centre for Excellence in HIV/AIDS, Gender & Sexual Health Initiative, Vancouver, Canada, [2]University of British Columbia, School of Population and Public Health, Vancouver, Canada, [3]Simon Fraser University, Faculty of Health Sciences, Burnaby, Canada, [4]University of California, Division of Global Health, Medicine, San Diego, United States
Presenting author email: eargento@cfenet.ubc.ca

Background: Despite substantial evidence in low and middle-income settings that community-led empowerment and collectivization can be a powerful determinant of successful HIV prevention, there is limited understanding of the impact of connectedness among sex workers on HIV risk in the global north. This study longitudinally modeled the impact of social cohesion on client condom refusal among street and off-street sex workers in Vancouver, Canada.
Methods: Longitudinal data were drawn from an open prospective cohort of female (trans*-inclusive) sex workers, AESHA (An Evaluation of Sex Workers Health Access), in Metro Vancouver (2010-2013). Participants were recruited through outreach to outdoor locations and hidden indoor and online venues and completed bi-annual interview questionnaires and HIV/STI testing by a project nurse. Lippman and colleagues' *Social Cohesion Scale* measured community connectedness (i.e., perception of mutual aid, trust, support) among sex workers. Bivariable and multivariable logistic regression using generalized estimating equations (GEE) were used to examine the independent effect of social cohesion on client condom refusal over three-years follow-up.
Results: Of 654 sex workers, one-third (n=221) reported client condom refusal over three-years follow-up. On average, a medium level of social cohesion was reported; median social cohesion scores were 24 (IQR 20-29, range=4-45). In the final multivariable confounder model, for every one point increase in the social cohesion score, the odds of client condom refusal decreased by 3%, (adjusted odds ratio=0.97; 95% CI: 0.95-0.99) after adjusting for age, injection drug use, and place of solicitation.

Conclusions: This is the first study to examine the independent effect of social cohesion on client condom refusal among sex workers in the global north. Findings suggest that community collectivization and sex worker-led empowerment efforts can have a direct protective effect on HIV risk reduction and shifting social norms among clients in the sex industry. Given public health and human rights concerns around new Canadian laws introduced this year to further criminalize sex workers' ability to work together (C-36), these findings highlight the urgent need for legal reforms and a structural framework that better promotes sex workers' ability to more formally collectivize, including sex worker-led efforts in the HIV response.

WEAC0102

Understanding the financial lives of female sex workers: implications for economic strengthening interventions for HIV prevention

E. Namey[1], B. Perry[1], J. Headley[1], K.A. Yao[2], M. Ouattara[2], C. Shighata[2], M. Ferguson[3]
[1]FHI 360, Social & Behavioral Health Sciences, Durham, United States, [2]Independent Consultant, Abidjan, Cote D'Ivoire, [3]FHI 360, Economic Development & Livelihoods, Washington, DC, United States
Presenting author email: enamey@fhi360.org

Background: Many women's decisions about whether and how to participate in sex work are driven by financial considerations. Despite the importance of economic factors in structural interventions for HIV prevention, data on the financial practices of female sex workers (FSWs) on which to base economic strengthening programs for HIV risk reduction are limited.
Methods: We collected qualitative data in Abidjan, Côte d'Ivoire, through structured participant observation activities conducted with 72 FSWs during non-working hours. Detailed notes were taken as FSWs discussed their expenditures, income-generation, and saving and borrowing strategies. We also collected quantitative financial diary data from a sub-sample (n=33) of FSWs. Women who kept financial diaries did so for six weeks, meeting weekly with researchers to systematically discuss and record all financial transactions. Participant observation notes were coded and analyzed using qualitative thematic analysis. Data from financial diaries were analyzed using descriptive statistics.
Results: All women in our sample reported sex work as their primary source of income; many supplemented their income with cash gifts and modest loans from clients, family, or peer FSWs. Food, clothing, and transportation accounted for the highest amounts of relatively-fixed spending. Around one-quarter of all expenses were related to costs of sex work (e.g., "work" clothing, beauty care, personal hygiene products, right to work payments, police pay-offs, etc.). Qualitatively, both income and expenditures were reported to fluctuate monthly (e.g., around pay day), seasonally (e.g., around holidays), and unexpectedly (e.g., illness or financial shocks). FSWs described saving money in their homes, through social tontines, or through formal systems (mobile money or banks), to help manage expenditures. They also reported increasing their sex work activities (e.g., traveling to other areas, offering sex for goods) to bridge financial shortfalls.
Conclusions: Economic strengthening interventions have, in theory, great potential to lower FSWs' risks of HIV by lessening the financial drivers of sex work. Our findings offer a rare glimpse into the earning, spending, saving, and borrowing practices of FSWs, providing evidence on which to base decisions about how best to design and implement economic strengthening elements of HIV prevention for FSWs.

WEAC0103

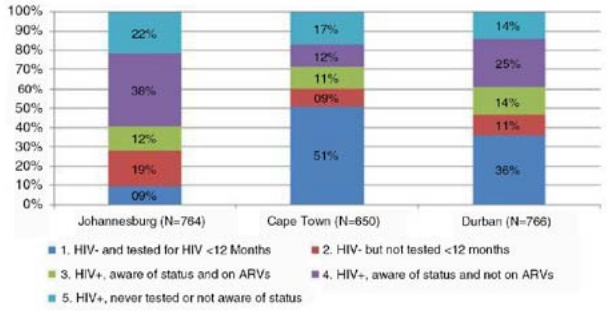
High utilization of health services and low ART uptake among female sex workers (FSW) in three South African cities: results from the South Africa health monitoring study (SAHMS-FSW)

T. Lane[1], M. Sibanyoni[2], A. Manyuchi[3], T. Osmand[4], A. Marr[4], M. Grasso[4], Z. Isdahl[4], N. Mutanha[2], P. Makhubela[2], M. Silima[3], N. Zuma[3], H. Struthers[3], J. McIntyre[3], H. Rees[2], F. Venter[2]
[1]University of California, San Francisco, Center for AIDS Prevention Studies, San Francisco, United States, [2]Wits Reproductive Health & HIV Institute, Johannesburg, South Africa, [3]Anova Health Institute, Johannesburg, South Africa, [4]University of California, Center for AIDS Prevention Studies, San Francisco, United States
Presenting author email: tim.lane@ucsf.edu

Background: The 2012-16 South Africa HIV National Strategic Plan calls for integrated behavioral and biological surveillance with female sex workers (FSW) to address critical HIV epidemiological and programmatic data gaps. In 2013-2014, we conducted the SAHMS-FSW in three metropolitan areas to estimate prevalence of HIV, syphilis, and associated risk factors, and assess current utilization of health and HIV services.
Methods: We recruited 764 FSW in Johannesburg, 650 in Cape Town and 766 in Durban using respondent-driven sampling (RDS) to take behavioral surveys, access voluntary counseling and testing and provide blood samples for HIV and syphilis surveillance. Serological testing followed national standards. We used RDSAT (version 7.1) to estimate population-adjusted prevalence for HIV, syphilis, selected behavioral and programmatic indicators; and SPSS (version 18.0) for multivariate logistic regressions with selected RDS-adjusted behavioral and programmatic indicators to identify site-specific significant associations with HIV-infection. We report adjusted odds ratios (aOR) and 95% Confidence Intervals (95%CI) in Table 1: Predictors of HIV - South African Health Monitoring Study, 2014, and current ART utilization in Figure 1.

		Johannesburg		Cape Town		Durban	
		aOR	95% CI	aOR	95% CI	aOR	95% CI
Venue of Sex Work (Street Based is Reference)							
	Brothel Based Only	0.59	0.35 - 0.99	2.13	1.46 - 3.12	2.31	1.37 - 3.89
	Street and Brothel Based Only	3.01	1.15 - 7.89	0.01	0.0 - 149.77	0.18	0.02 - 1.69
Health Care Utilization		1.35	1.16 - 1.56	---	---	1.26	1.13 - 1.41
ANC Utilization		0.28	0.17 - 0.47	1.63	1.10 - 2.43	1.8	1.07 - 3.03
Peer Education Exposure		3.1	1.88 - 5.12	0.31	0.19 - 0.51	---	---
UAI with Non-Paying Partner		---	---	---	---	28.55	10.52 - 77.56
Age		1.13	1.08 - 1.18	---	---	1.19	1.15-1.24

[Table 1]



[Figure 1. Previous HIV testing, knowledge of HIV-status, and utilization of ART among FSW in Johannesburg, Cape Town and Durban, 2013-14]

Results: HIV prevalence was 71.8% (95%CI 56.5%-81.2%), 39.7% (95%CI 30.1%-49.8%), and 53.5% (95%CI 37.5%-65.5%) in Johannesburg, Cape Town, and Durban respectively. After controlling for age, consistent condom use, and hazardous drinking, brothel-based FSW had significantly higher odds of HIV-infection in Cape Town (aOR 2.1, 95%CI 1.5-3.1) and Durban (aOR 2.3, 95%CI 1.4-3.9); those working both brothels and streets in Johannesburg were more likely to be HIV-positive (3.0, 95%CI 1.2-7.9). Those accessing healthcare in Johannesburg and Durban (aOR 1.4, 95%CI 1.2-1.6 and 1.3, 95%CI 1.1-1.4, respectively), and ANC services in Cape Town and Durban (aOR 1.6, 95%CI 1.1-2.4 and 1.8, 95%CI 1.1-3.0, respectively), were significantly more likely to be HIV-positive. However, uptake of ART remains low among FSW.
Conclusions: Although FSW accessing healthcare services are more likely to be HIV-positive, current ART utilization demonstrates a substantial gap to be addressed as South Africa begins implementing universal treatment. Identification and expansion of effective outreach models are needed to increase utilization of ART, as well as effectively target prevention services for HIV-negative FSW. Health outreach strategies must account for behavioral and structural factors in specific sex-work environments.

WEAC0104

Closing the gap: Integrating mobile HIV testing and point-of-care CD4 testing for timely identification of HIV-infected and ART-eligible venue-based female sex workers in Lilongwe, Malawi

K.E. Lancaster[1], T. Lungu[2], M.C. Hosseinipour[1,2], K. Chadwick[3], Z. Dibb[3], V.F. Go[1], B.W. Pence[1], K.A. Powers[1], I.F. Hoffman[1,2], W.C. Miller[1]
[1]University of North Carolina, Chapel Hill, United States, [2]UNC Project-Malawi, Lilongwe, Malawi, [3]Theatre for a Change, Lilongwe, Malawi
Presenting author email: klanc@unc.edu

Background: Female sex workers (FSW) are a hard-to-reach key population in sub-Saharan Africa with high HIV prevalence, infrequent access to HIV care services, and low uptake of antiretroviral therapy (ART). We describe HIV seroprevalence, HIV status awareness, and ART eligibility and use for venue-based FSW in Lilongwe, Malawi who received integrated mobile HIV and point-of-care (POC) CD4 testing.

Methods: From July through August 2014, FSW were recruited using venue-based sampling. 200 FSW, age ≥18 years, who reported exchanging money for sex in the past 12 months participated in a biological and behavioral survey to evaluate HIV testing, care, and treatment history. Seropositive FSW, identified using HIV rapid testing, received rapid Alere Pima CD4 counts. Eligibility for ART followed the Malawi national guidelines (CD4 ≤500 cells/mm^3, currently pregnant or breastfeeding, or any pregnancy after July 2011 following Option B+ policy). Proportions were estimated for HIV seroprevalence, self-reported previous HIV diagnosis, ART-eligibility based on national guidelines, and self-reported ART use.
Results: HIV seroprevalence was 69% (n=138); 20% (n=27) were newly diagnosed and 80% (n=111) were previously diagnosed. Among those newly diagnosed, 63% (n=17) were identified as ART-eligible (median CD4: 305; IQR: 237-427). Among those who were previously diagnosed, 65% (n=72) were currently on ART, 22% (n=24) were currently ART-eligible but not on ART (median CD4: 391; IQR: 261-474), and 13% (n=15) were ART-ineligible and not on ART. The most commonly reported reason among previously diagnosed and ART-eligible FSW for not being on ART was a prior high CD4 count (17%; n=4).
Conclusions: This study is one of the first to integrate mobile HIV and POC CD4 testing to identify HIV-infected and ART-eligible venue-based FSW in Malawi. The majority of newly diagnosed FSW were immediately identified as ART-eligible. A substantial proportion of previously diagnosed FSW were ART-eligible but not on ART, with many having a prior high CD4 count. Large-scale integration of frequent HIV and POC CD4 testing for timely identification of HIV-infected and ART-eligible FSW is urgently needed to improve health outcomes for FSW and decrease HIV transmission in sub-Saharan Africa.

WEAC0105

Injection drug use among female sex workers in Iran: findings of the first national bio-behavioural study

A. Sedaghat[1], M. Karamouzian[2], H. Sharifi[2], A. Mirzazadeh[2], M. Shokoohi[2], A. Haghdoost[2]
[1]Ministry of Health and Medical Education, Center for Diseases Control, HIV/STIs Office, Tehran, Iran, Islamic Republic of, [2]Regional Knowledge Hub and WHO Collaborating Center for HIV Surveillance, Institute for Future Studies in Health, Kerman University of Medical Sciences, Kerman, Iran, Islamic Republic of
Presenting author email: abased@gmail.com

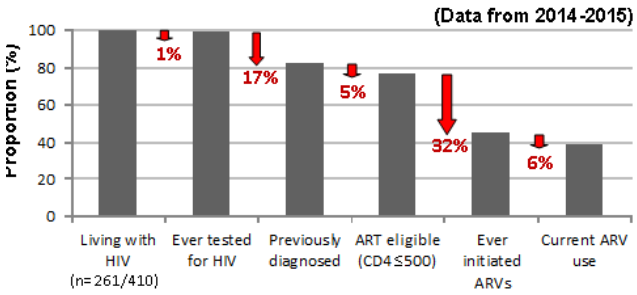
Background: While the prevalence of HIV among female sex workers (FSW) in Iran is approximately 4.5%, FSW who have ever injected drugs are believed to have a significantly higher HIV prevalence. This study tries to assess the determinants of injection drug use among FSW through Iran's first and only national bio-behavioural surveillance survey.
Methods: This survey was conducted in 2010, by recruiting 827 FSW through facility-based sampling from 21 sites in 14 cities in Iran. Data was collected through face-to-face interviews using a pilot-tested standardized risk assessment questionnaire. All analyses were weighted based on the response rate and adjusted for the clustering effect of the sampling sites. A predictive multivariable logistic regression model was constructed to investigate the determinants of injection drug use among FSW in Iran.
Results: Mean age of participants was 32, 50% had primary school educations, 36% were married, and most of them reported sex work as their primary source of income. Of all participants, 71.6% (95% CI: 68.5-74.6) had ever used drugs and 14.6% (95% CI: 12.2-16.9) had ever injected drugs. The most frequently injected drugs were methadone, crystal methamphetamine, and crack. Among those who had ever injected drugs, 36.6% reported that they had a drug injection during the previous month and the prevalence of HIV was 11.2% (95% CI: 5.4 to 21.5). In the multivariable model, history of HIV testing (AOR= 1.79, 95% CI: 1.19-2.69), duration of sex work (AOR=1.08, 95% CI: 1.04-1.12), drug use before sex in the past month (AOR=2.70, 95% CI: 1.79-4.10), and alcohol use before sex in the past month (AOR= 2.07, 95% CI: 1.35-3.17) were significant predictors of injection drug use.
Conclusions: The prevalence of injection drug use among FSWs in Iran is concerning which calls for special attention to be paid to FSWs who inject drugs. As selling sex to cover drug habit expenses is a likely practice among female drug users, a part of harm reduction programs for drug users should try to target this population in order to reduce their sex work practices.

WEAC0106LB

Engagement in the HIV care cascade and predictors of uptake of antiretroviral therapy among female sex workers in Port Elizabeth, South Africa

S. Schwartz[1], A. Lambert[2], N. Phaswana-Mafuya[3], C. Holland[4], Z. Kose[3], M. Mcingana[5], S. Sweitzer[4], S. Baral[4]
[1]Johns Hopkins University, Epidemiology, Center for Public Health and Human Rights, Baltimore, United States, [2]TB/HIV Care Association, Cape Town, South Africa, [3]Human Sciences Research Council, HIV/AIDS, STIs and TB (HAST), Port Elizabeth, South Africa, [4]Johns Hopkins School of Public Health, Epidemiology, Center for Public Health and Human Rights, Baltimore, United States, [5]TB/HIV Care Association, Port Elizabeth, South Africa

Background: Female sex workers (FSW) are 13-times more likely to be living with HIV than other reproductive-aged women. Data on FSW engagement in the HIV care cascade are limited, but suggest high rates of drop-off prior to viral suppression, with substantial drop-offs at HIV diagnosis.
Methods: FSW ≥18 years were recruited through respondent driven sampling into a cross-sectional study in Port Elizabeth, South Africa. Socio-demographics, reproductive, behavioral and healthcare history were assessed through interview-administered questionnaires. All FSW were tested for HIV and CD4 counts were assessed among women living with HIV. Engagement in the HIV care cascade is described, and predictors of self-reported antiretroviral therapy (ART) uptake among treatment-eligible, previously diagnosed FSW estimated using robust Poisson regression. As ART eligibility thresholds changed from ≤350 to ≤500 cells/mm^3 during the study period, eligibility was determined based on CD4 count and current guidelines at time of study participation.
Results: Between October 2014-April 2015, 410 FSW participated in study activities. Overall, 261/410 (63.7%) were living with HIV. Prior history of HIV testing and diagnosis were relatively high (>80%), however self-reported ART coverage among HIV-positive FSW was just 39% (Figure 1).



[Figure 1]

After adjusting for time since HIV diagnosis, women who had intimate partners and had not disclosed their HIV status to them were over 50% less likely to be on ART than FSW not in relationships (Table 1). Mothers and women with fewer clients per month were also statistically significantly less likely to be on treatment than non-mothers or FSW with more clients in the adjusted analyses.

		Prevalence Ratio [95% CI]	p-value	Adjusted Prevalence Ratio [95% CI]†	p-value
Age (REF ≥30 years)	18-29 years	0.78 [0.60-1.02]	0.069	0.87 [0.66-1.16]	0.346
Number of clients past 30 days	0-10	REF	0.074	REF	
	11 or more	1.24 [0.98-1.57]	0.074	1.29 [1.02-1.63]	0.032
Partnership & Disclosure	No non-paying intimate partner	REF	--	REF	--
	Disclosed to some or all intimate partners	0.87 [0.69-1.09]	0.219	0.86 [0.69-1.08]	0.188
	Has not disclosed to intimate partners	0.41 [0.19-0.87]	0.021	0.47 [0.23-0.95]	0.036
Mother	No	REF		REF	
	Yes	0.82 [0.62-1.08]	0.156	0.76 [0.58-0.99]	0.047

†Univariate analyses also assessed age, race, education, mobility, violence and depression. The adjusted model includes variables statistically significant at p<0.20 in univariate analyses, including variables listed, age, and time since HIV diagnosis.

[Predictors of ART use among ART-eligible FSW]

Among treatment eligible FSW not on ART, 16/61 (26.2%) had previously been initiated but were no longer taking ART.

Conclusions: HIV testing was common among FSW in this setting and awareness of HIV status was relatively high, however efforts are needed to improve ART uptake and retention in this population. Though viral suppression data were not available, this likely represents additional fall-out from the care cascade. Disclosure to partners and family appear to be key barriers to treatment uptake. Building HIV disclosure skills and efficacy may help to improve health outcomes for FSW living with HIV and prevent onward transmission.

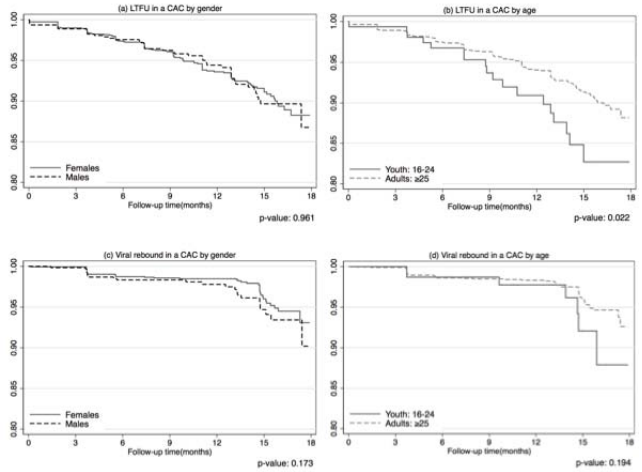
WEAD01 Implementation Strategies to Optimize HIV Care Continuum

WEAD0101

Community-based adherence clubs improve outcomes for stable antiretroviral therapy patients: findings from Gugulethu, South Africa

A. Grimsrud[1], M. Lesosky[1,2], C. Kalombo[3], L.-G. Bekker[2,4], L. Myer[1]
[1]Division of Epidemiology & Biostatistics, University of Cape Town, Cape Town, South Africa, [2]University of Cape Town, Department of Medicine, Cape Town, South Africa, [3]Gugulethu Community Health Centre, Provincial Government of the Western Cape, Cape Town, South Africa, [4]The Desmond Tutu HIV Centre, University of Cape Town, Cape Town, South Africa
Presenting author email: agrimsrud@gmail.com

Background: There are few data on patient outcomes from community-based models to deliver antiretroviral therapy (ART), with previous research focused on models for home-based delivery. We describe outcomes of ART patients decentralized to community-based Adherence Clubs (CACs) and compare outcomes with patients managed within a facility-based model.
Methods: This analysis included 8,150 adults initiating ART from 2002-2012 at a public sector clinic in Gugulethu, South Africa followed until the end of 2013. From June 2012, stable patients (ART >12 months, suppressed viral load) were referred to CACs. Kaplan-Meier methods estimated time to outcomes among CACs stratified by gender and age (youth: 15-24 years of age and older patients: >25 years of age). LTFU was compared between CACs and facility-based care using proportional hazards models with time-varying covariates and inverse probability weights of CAC participation.
Results: Of the 2,113 patients (68.8% female, 7.4% youth) decentralized to a CAC, 94% were retained on ART after 12-months. After the first CAC visit, LTFU among CAC patients was 5.6% and 6.4% at 12-months (Figure 1A) and viral rebound 2.2% and 1.5% (Figure 1C), for men and women respectively. LTFU was higher in CACs among youth compared to older patients (Figure 1B). Youth were twice as likely to be LTFU [(adjusted hazard ratio) aHR: 2.17, 95%CI 1.26-3.73] and experience viral rebound (aHR 2.24, 95%CI 1.00-5.04) in a CAC compared to older patients. Overall, CAC participation reduced LTFU by 67% (aHR: 0.33, 95%CI 0.27-0.40) compared to facility-based care, and this reduction persisted when stratified by patient demographic and clinic characteristics. Patients initiating ART most recently, in 2010 or 2011, had a 90% reduction in LTFU in a CAC compared to facility-based care (95%CI 0.05-0.21). Youth were the only sub-set of patients that did not have a significant decrease in risk of LTFU in CACs compared to the CHC
(aHR 0.68, 95%CI 0.37-1.22).



[Figure 1. Kaplan-Meier plots over the first 18-months in a Community-based Adherence Club: (a) LTFU by gender, (b) LTFU by age, (c) Viral rebound by gender, (d) Viral rebound by age]

Conclusions: Community-based Adherence Clubs appear to be associated with a decreased risk of LTFU compared to facility-based care. More research is needed on how to expand the role of community-based ART services and what components of these delivery models support long-term retention.

WEAD0102

Sustained viral suppression in persons living with HIV/AIDS receiving HAART in Peru

P. Caballero[1,2], C.M. Da Silva[3], M. Da Cruz[4]
[1]Universidad Nacional Mayor de San Marcos, Instituto de Medicina Tropical, Lima, Peru, [2]Instituto Nacional de Salud, Lima, Peru, [3]Fiocruz, Department of Epidemiology and Quantitative Methods, ENSP Sergio Arouca, Rio de Janeiro, Brazil, [4]Fiocruz, Department of Endemias Samuel Pessoa, ENSP Sergio Arouca, Rio de Janeiro, Brazil
Presenting author email: zcaballeron@unmsm.edu.pe

Background: Successful treatment for HIV infection requires sustained viral suppression (SVS). Patients with undetectable HIV-RNA levels have a significantly lower risk of clinical disease progression. And at community level viral suppression is important to reduce HIV transmission and the emergence of resistant strains. The study aimed to analyze the frequency and duration of viral suppression (VS) in the first cohort of people living with HIV/AIDS (PLWHA) under treatment.
Methods: We retrospectively evaluated data from all PLWHA uninsured adults who initiated HAART through the National Program during 2004-2006 and followed-up until 2012. Patients with complete records in the National Laboratory Reporting System Data Base were included. The duration of VS was analyzed using survival analysis (Kaplan-Meier) in PLWHA who achieved viral suppression. Survival time was measured between the first control with viral load < = 400 copies/ml until the presence of first interruption or failure of viral suppression (FSV) with viral load>400 copies/ml. Persons lost to follow up and those without FSV were censored. R Software 3.0.3.was used.
Results: During the study period a total of 6289 PLWHA had access to health care settings for initial evaluation and only 5142 received HAART. Of these, 4530(88%) achieved VS for variable time (responders) and 612 never presented VS (non-responders). Cumulative survival rate was analyzed in responders: 91.1% maintained VS up to 1 year, 84,6% up to 2 years, 80,2% to 3 years, 77,1% to 4 years, 74,1% to 5 years and 70,1% to 6 years. According to survival analysis, Kaplan-Meier curves presented lower duration of VS in young adult patients, females, persons in prisons and those who did not increase their CD4 above baseline. No differences were observed with baseline CD4 and viral load.(p< 0,05).
Conclusions: This findings suggest that SVS as a program indicator is feasible and useful for monitoring health care settings and ranking them like a control quality measure. SVS could also be included as another parameter in cascade of treatment measures.

WEAD0103

Entry into care following universal home-based HIV testing in rural KwaZulu-Natal, South Africa: the ANRS TasP 12249 cluster-randomised trial

M. Plazy[1,2], K. El Farouki[3,4], C. Iwuji[5,6], N. Okesola[5], J. Orne-Gliemann[1,2], J. Larmarange[5,7], M.-L. Newell[8], D. Pillay[5,9], F. Dabis[1,2], R. Dray-Spira[3,4], for the ANRS 12249 TasP Study Group
[1]INSERM U 897 - Centre Inserm Epidémiologie et Biostatistique, Bordeaux, France, [2]Université Bordeaux, Institut de Santé Publique, d'Epidémiologie et de Développement (ISPED), Bordeaux, France, [3]INSERM, UMR_S 1136, Pierre Louis Institute of Epidemiology and Public Health, Team of Research in Social Epidemiology, Paris, France, [4]Sorbonne Université, UPMC Univ Paris 06, UMR_S 1136, Pierre Louis Institute of Epidemiology and Public Health, Team of Research in Social Epidemiology, Paris, France, [5]Wellcome Trust Africa Centre for Health and Population Studies, Mtubatuba, South Africa, [6]University College London, Department of Infection and Population Health, London, United Kingdom, [7]Ceped (UMR 196 Paris Descartes IRD), IRD, Paris, France, [8]Faculty of Medicine, University of Southampton, Southampton, United Kingdom, [9]Division of Infection & Immunity, University College London, London, United Kingdom
Presenting author email: melanie.plazy@isped.u-bordeaux2.fr

Background: In a Universal Test and Treat (UTT) strategy, entry into care soon after HIV diagnosis is crucial to achieve optimal population-antiretroviral treatment (ART) coverage. We evaluated the rate of, and factors associated with, entry into care following home-based HIV testing in a cluster-randomised trial of the effect of immediate ART on HIV incidence in rural KwaZulu-Natal, South Africa.
Methods: From March 2012 to May 2014, individuals ≥16 years in ten (2 x 5) clusters were offered home-based HIV testing; those ascertained HIV-positive were referred to TasP trial clinics and were offered universal and immediate ART (intervention clusters) or according to national guidelines (control clusters). Entry into care was defined as attending a TasP clinic within three months of referral among adults not actively in HIV care (no visit to local HIV programme within past 13 months). Associated factors were identified separately by sex, using multivariable logistic regression.
Results: Overall, 1,205 adults (72.6% women) not actively in HIV care were referred to a TasP clinic. Of these, 405 (33.6%) attended a TasP clinic within three months (no difference between trial arms): 32.5% of women, 36.7% of men. Participants who ever visited the local HIV programme (n=360) were more likely to enter into care than those who didn't (women: adjusted Odd-Ratio (aOR) 1.76, 95% Confidence Interval [1.26-2.45]; men: 2.07 [1.18-3.64]). In women (n=875), those less likely to attend a TasP clinic within three months had completed some sec-

ondary school (0.51 [0.33-0.79]) or at least secondary school (0.47 [0.29-0.76]) versus below primary school; were living 1-2 km from a TasP clinic (0.43 [0.30-0.62]) or 2-5 km (0.40 [0.27-0.61]) versus < 1 km; didn't know anyone HIV+ within their family (0.60 [0.43-0.81]) and didn't agree that it is good to initiate ART as soon as possible if infected (0.47 [0.26-0.85]); among men (n=330), none of the factors examined was significantly associated with entry into care.
Conclusions: Only one-third of HIV-positive adults referred after home-based HIV testing entered into care within three months in this rural South African community with a 30% HIV prevalence. Innovative interventions should be considered to ensure the success of a UTT strategy.

WEAD0104

Assessing the HIV care continuum in The Caribbean, Central and South America network for HIV epidemiology (CCASAnet): progress in clinical retention, cART use, and viral suppression

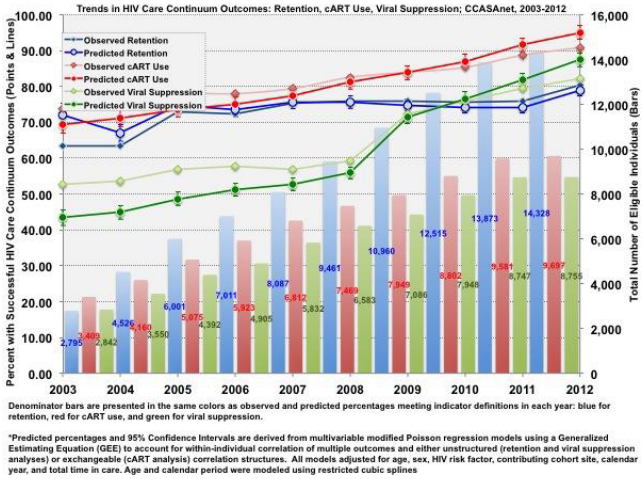
P.F. Rebeiro[1], C. Cesar[2], B.E. Shepherd[1], R.B. De Boni[3], C. Cortés[4], F. Rodriguez[4], P. Belaunzarán-Zamudio[5], J.W. Pape[6], D. Padgett[7], D. Hoces[8], C.C. McGowan[1], P. Cahn[2]
[1]Vanderbilt University School of Medicine, Nashville, United States, [2]Fundación Huésped, Buenos Aires, Argentina, [3]Instituto Nacional de Infectologia Evando Chagas, Fundação Oswaldo Cruz, Rio de Janeiro, Brazil, [4]Fundación Arriarán, Universidad de Chile, Santiago, Chile, [5]Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico, [6]Le Groupe Haïtien d'Etude du Sarcome de Kaposi et des Infections Opportunistes in Port-au-Prince (GHESKIO), Port-au-Prince, Haiti, [7]Instituto Hondureño de Seguridad Social and Hospital Escuela, Tegucigalpa, Honduras, [8]Instituto de Medicina Tropical Alexander von Humboldt, Universidad Peruana Cayetano Heredia, Lima, Peru
Presenting author email: p.rebeiro@vanderbilt.edu

Background: Retention, combination antiretroviral therapy (cART) use, and viral suppression are key stages in the HIV Care Continuum associated with delayed disease progression and reduced transmission. We assessed trends in these indicators within the large and diverse CCASAnet cohort over a decade.
Methods: Adults from CCASAnet clinical cohorts in Argentina, Brazil, Chile, Haiti, Honduras, Mexico, and Peru contributed data from first visit between 2003 and 2012 until final visit, death, or the end of 2012. Retention was ≥2 HIV care visits in a year, >90 days apart. cART use was prescription of a regimen of ≥3 active antiretroviral agents in a year. Viral suppression was HIV-1 RNA < 200 copies/mL at last measurement in the year. cART use and viral suppression denominators were subjects with ≥1 visit in the year. Multivariable modified Poisson regression models were used to assess temporal trends and predict percentages meeting each indicator in each year, adjusting for age, sex, HIV transmission mode, cohort, calendar year, and total time in care.
Results: Among 18,799 individuals contributing to retention analyses, 14,380 to cART use analyses, and 13,330 to viral suppression analyses, there were differences between those meeting indicator definitions vs. not by most characteristics (Table).

Characteristic	Not Retained[a]	Retained[a]	p-value*	Not on cART[b]	On cART[b]	p-value*	Not Virally Suppressed[c]	Virally Suppressed[c]	p-value*
Total	22,386	67,171	<0.01	11,565	57,312	<0.01	19,369	41,271	<0.01
Age (Years)	33.9 (28.2, 40.6)	36.4 (30.0, 43.9)	<0.01	32.5 (27.1, 39.3)	35.5 (29.6, 42.4)	<0.01	33.5 (27.7, 40.4)	36.0 (30.1, 42.9)	<0.01
Male Sex	14,238 (25.1)	42,487 (74.9)	0.35	8,119 (16.5)	40,982 (83.5)	<0.01	13,493 (31.0)	29,981 (69.0)	<0.01
Female Sex	8,148 (24.8)	24,684 (75.2)		3,446 (17.4)	16,330 (82.6)		5,876 (34.2)	11,290 (65.8)	
MSM HIV risk	7,050 (27.6)	18,503 (72.4)	<0.01	5,079 (18.6)	22,225 (81.4)	<0.01	7,537 (31.4)	16,489 (68.6)	<0.01
IDU HIV risk	820 (52.7)	735 (47.3)		203 (15.1)	1,141 (84.9)		349 (29.3)	842 (70.7)	
Hetero HIV risk	8,443 (29.2)	20,495 (70.8)		4,800 (16.1)	24,945 (83.9)		8,921 (34.4)	17,044 (65.6)	
Other/Unk. HIV risk	6,073 (18.1)	27,438 (81.9)		1,483 (14.2)	9,001 (85.9)		2,562 (27.1)	6,896 (72.9)	
Individual Years in Care	7 (4, 9)	7 (4, 9)	<0.01	6 (3, 8)	8 (5, 10)	<0.01	6 (4, 9)	8 (5, 10)	<0.01

[Person-years contributed and characteristics]

There were significant improvements in the indicators from 2003 to 2012: from 63% to 80% retained, 74% to 91% using cART, and 53% to 82% virally suppressed (p< 0.05, each). Predicted values from adjusted models revealed similar trends (Figure).



[Trends in HIV Care Continuum Outcomes in CCASAnet]

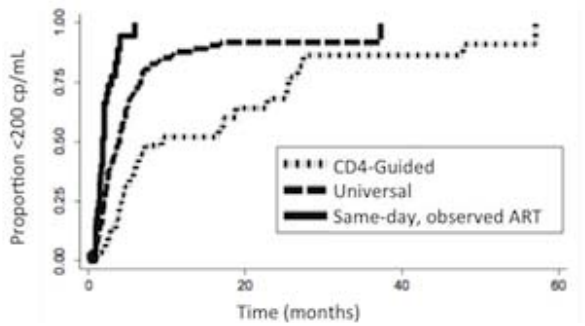
Female sex (Risk Ratio (RR)=0.96; 95% Confidence Interval [CI]: 0.93,0.99 vs. males) and injection drug use (IDU) as HIV transmission mode (RR=0.84; 95% CI: 0.74,0.94 vs. male sexual contact with males (MSM)) were associated with lower retention, but unrelated with cART use or viral suppression. MSM transmission (RR=0.96; 95% CI: 0.92,0.99) decreased probability of cART use vs. heterosexual transmission.
Conclusions: HIV Care Continuum outcomes have improved over time. However, efforts must be made to improve retention, particularly among females and IDUs, and cART use must be improved among MSM. Additional research is needed to sustain progress by identifying impediments to achieving positive Care Continuum outcomes, and their causes, in these settings.

WEAD0105 LB

Providing same day, observed ART to newly diagnosed HIV+ outpatients is associated with improved virologic suppression

C. Pilcher[1], H. Hatano[1], A. Dasgupta[2], D. Jones[1], S. Torres[1], F. Calderon[1], C. Ospina-Norvell[1], W. Hartogensis[1], E. Demicco[1], E. Geng[1], M. Gandhi[1], D. Havlir[1]
[1]UCSF, HIV/AIDS Division, Medicine, San Francisco, United States, [2]Tulane University Medical School, New Orleans, United States

Background: Despite known clinical and prevention benefits, ART is typically delayed by weeks-to-months after HIV diagnosis to allow linkage to care, HIV education, social stabilization and laboratory evaluation. The UCSF/San Francisco General Hospital (SFGH) RAPID program aimed to eliminate this delay by providing same-day/observed ART even as HIV care was being established. We investigated consequences of the RAPID treatment initiation strategy.
Methods: RAPID eligibility included new HIV diagnosis with acute/recent infection, active opportunistic infection or CD4< 200/mm^3. At referral, all RAPID-eligible or -ineligible patients with new diagnosis received a standard package of multidisciplinary services for social support, education, risk and stigma reduction; labs were drawn; and regular provider follow-up was arranged. The RAPID intervention consisted of 1) same-day access to an on-call provider; 2) a 5-day ART supply facilitated by 3) an accelerated process for insurance benefits. Focusing on a July 2013-Dec 2014 program period, survival analysis was used to compare time to achieving VL< 200 copies/mL between patients receiving or not receiving the RAPID intervention, and also between these patients and historical controls from two eras of ART provision at SFGH: pre-RAPID universal (2010-2013) and CD4-guided (2006-2009).
Results: We studied 227 newly diagnosed outpatients receiving RAPID (n=39), universal (n=149) or CD4-guided (n=39) ART. No patients had private insurance and 27% were homeless; mean(range) CD4 was 381(2-1031)/mm^3 and VL 4.6(1.6-7.0)$\log_{10}$cp/mL. Time to VL< 200 cp/mL was significantly faster in RAPID patients vs. both contemporaneous and historical controls (p< 0.001; see Figure).



[Viral suppression over time by ART initiation strategy]

Median(IQR) time to VL< 200 for RAPID ART was 56(40-87) days vs. 119(58-201) days for universal and 283(128-777) days for CD4-guided ART. After 3 months of ART, 75% RAPID vs. 38% non-RAPID patients achieved a VL< 200 cp/mL; after 6 months, 95% RAPID vs. 70% non-RAPID patients achieved VL< 200 cp/mL. Among the first 39 patients receiving RAPID ART and followed for 5-18 months, only 2 (5%) of had toxicity-related regimen changes, none discontinued ART and 35 (90%) remain engaged in care.

Conclusions: Combined with patient education and psychosocial support, same day-observed initiation of ART at the time of HIV diagnosis was feasible and associated with substantially faster sustained viral suppression.

WEAD02 Children and Adolescents Living with HIV: Discovery and Management

WEAD0201

Targeted HIV testing in home or clinic for older children of HIV-infected adults in care increases pediatric HIV testing rates and reveals high prevalence of previously undiagnosed HIV infection

A. Wagner[1], I. Njuguna[2], C. Mugo[2], I. Inwani[3], E. Maleche-Obimbo[2], K. Sherr[4], D. Wamalwa[2], G. John-Stewart[5], J. Slyker[4]
[1]University of Washington, Epidemiology, Seattle, United States, [2]University of Nairobi, Pediatrics & Child Health, Nairobi, Kenya, [3]Kenyatta National Hospital, Nairobi, Kenya, [4]University of Washington, Global Health, Seattle, United States, [5]University of Washington, Global Health, Pediatrics, Medicine, Epidemiology, Seattle, United States
Presenting author email: anjuliwagner@gmail.com

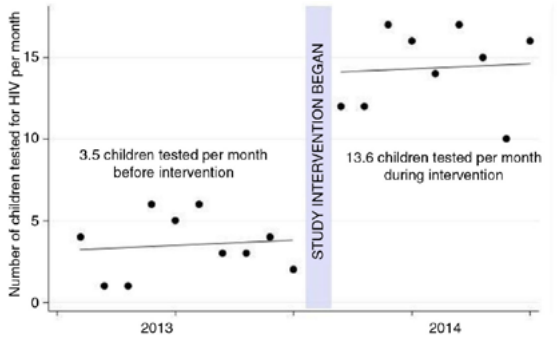
Background: Health systems offer infant HIV testing as part of prevention of mother-to-child HIV transmission (PMTCT) programs, but are not built to systematically diagnose HIV infection in older children before symptomatic illness. Offering HIV-infected adults attending HIV treatment programs targeted testing in home or clinic may increase early diagnosis of pediatric HIV.

Methods: HIV-infected parents attending HIV care clinic at Kenyatta National Hospital (KNH) in Nairobi, Kenya were asked about their children's HIV status. Adults with untested children ≤ 12 years old chose to test children either at home (HBT) or in a clinic (CBT). Multinomial relative risk regression was used to identify cofactors of testing acceptance.

Results: During the 9-month period when targeted testing was routinely offered, approximately 4 times as many children were tested per month as in the previous 10-month period (13.6 vs 3.5 per month, RR: 3.9, 95%CI: 2.8-5.5).

Among 116 enrolled adults, 23 (20%) chose HBT and had 46 children tested, 48 (41%) chose CBT and had 58 children tested, and 45 (39%) did not complete testing. More adults chose CBT than HBT (p=0.003), but more children were tested per adult by HBT (2.0 vs 1.2, p<0.001). HIV prevalence among 104 tested children was 8% overall; 6 infected children were identified by CBT and 2 by HBT (median age: 8 years (IQR: 2-11)).

Compared to adults who chose CBT, adults who chose HBT were more likely to have higher income, more education, be male, have a partner, have an unemployed partner, and have a partner known to be HIV negative (p<0.05), while adults who did not test their children were more likely to have higher income and have a partner who was known to be HIV negative or of unknown HIV status (p<0.05). In multivariate analyses, income and partner status remained significantly associated with testing choice.



[Active referral increases pediatric HIV testing]

Conclusions: Targeting HIV-infected parents in care increased the rate of pediatric testing and found high prevalence of pediatric HIV. CBT was preferred over HBT at this urban referral hospital. Efforts to increase pediatric HIV testing and to understand parental characteristics are important to provide timely diagnosis and linkage to care.

WEAD0202

Moving towards targeted HIV testing in older children at risk of vertically transmitted HIV

T. Bandason[1], G. Mchugh[1], R. Ferrand[1], S. Munyati[2], K. Kranzer[3], P. Chonzi[4]
[1]Biomedical Research and Training Institute, ZENITH, Harare, Zimbabwe, [2]Biomedical Research and Training Institute, Harare, Zimbabwe, [3]London School of Hygiene and Tropical Medicine, London, United Kingdom, [4]Harare City Health, Harare, Zimbabwe
Presenting author email: tbandason@brti.co.zw

Background: WHO recommends PITC to all in high-burden countries. Symptom screening algorithms have been used widely for other diseases like tuberculosis. Prompt identification of undiagnosed HIV infection remains a priority in Southern Africa. We previously proposed a simple algorithm where a child is asked to respond to any of the four questions, namely, whether child

a) has previously been admitted to hospital,
b) has had recurring skin problems,
c) is a single or double orphan
d) has experienced poor health in the past 3 months which can be asked by any cadre at primary care level for screening older children at risk of HIV infection and requiring an HIV test. The objective of this study was to validate the performance of this algorithm in a primary care setting.

Methods: All previously untested children, aged 6 to 15 years attending 7 selected Primary Health Care Clinics of Harare, Zimbabwe with parental/guardian consent were tested for HIV infection and asked to respond to four algorithm questions. Each positive response was scored as one.

Results: 6,102 (74%) children with median age 9(IQR:7 to 11)years, 3,138 (51%) male consented to an HIV test. HIV prevalence was 4.8% (95% CI:4.2-5.3) and positivity increased successively as the score increased with those who scored zero, 55/3,830 (1%): scored one, 110/1,609 (7%); scored two 80/489(16%); scored three 26/96 (27%); scored four 10/16(63%). A child with a score of one or more had 8 times odds (95% CI:6-11) of testing HIV positive with a sensitivity of 80% (95% CI: 75-85), specificity of 66% (95% CI: 64-67). Sensitivity was higher in those aged 10 years or more (86% vs 70%, p=0.001). Overall, we needed to test 11 children to identify one HIV positive.

Conclusions: The algorithm maintained its integrity and demonstrated that it is a sensitive tool screening older children at risk of HIV infection. The algorithm can be used by lower cadre healthcare workers and can help prioritize limited resources.

WEAD0203

Impact of implementing "Test and Treat" policy on paediatric ART enrolments and coverage in Uganda

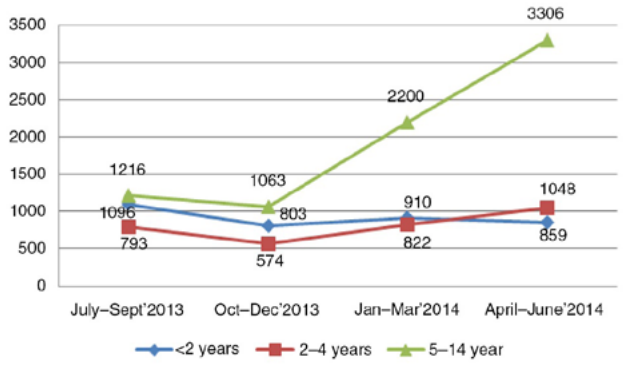
P. Elyanu[1,2], E. Magongo[1], B. Asire[1], I. Lukabwe[1], H. Bitimwine[3], C. Katureebe[1], P. Achii[4], V. Mulema[1,5], E. Dziuban[6], N. Sugandhi[7], V. Musiime[8], N. Namuwenge[1], J. Musinguzi[1]
[1]Ministry of Health, STD/AIDS Control Program, Kampala, Uganda, [2]University of Texas, School of Public Health, Houston, United States, [3]Baylor College of Medicine Children's Foundation-Uganda, Kampala, Uganda, [4]Ministry of Health/Management Sciences for Health, Pharmacy Division, Kampala, Uganda, [5]Clinton Health Access Initiative (CHAI), Kampala, Uganda, [6]CDC, Atlanta, Uganda, [7]Clinton Health Access Initiative (CHAI), Boston, United States, [8]Makerere University College of Health Sciences, Pediatrics and Child Health, Kampala, Uganda
Presenting author email: eleanormagongo@gmail.com

Background: In 2013, it was estimated that 193,500 of children under 15 years were living with HIV in Uganda and 83% would be eligible for treatment according to WHO guidelines; recommending lifelong treatment for all children under 5 years and all older patient based on clinical or immunologic staging. However despite efforts to scale up pediatric treatment, coverage remained low at 22% in 2013. Programmatic barriers to ART initiation in children include the perception that pediatric ART is complicated, unavailability of CD4 testing and difficulty in accurate clinical staging. In September 2013, Uganda adopted a "test and treat" antiretroviral therapy (ART) policy for all HIV infected children under 15 years of age to simplify recommendations and remove programmatic barriers to ART initiation in children.

Methods: The MOH launched and disseminated these guidelines to all stakeholders though 3 day health facility based trainings and mentoring during the period January to December 2014. To evaluate the impact of this new policy a comparison was made between the number of children initiated between June-December 2013 and those initiated between January-June 2014.

Results: By December 2014, 1340 (84%) of 1600 ART providing health facilities and 17,238 health workers were trained on the new guidelines. There was 1.4 fold increase in the number of HIV infected children newly initiated on ART from 5540 in June-Dec 2013 to 9145 in Jan-June 2014. The increase was greater among children aged 5-14 years and 2-4 years (2.4 and 1.4 fold respectively), however there was no change among the under 2 year old's(see figure 1). Pregnant adolescents constituted 2.5% (229/9145) of children less than 15 years of age enrolled on ART in Jan-June 2014. Paediatric ART coverage has increased from 22% (43,481/193,500) in December 2013 to 27% (51,305/193,500) in June 2014.

Conclusions: Expanding eligibility criteria increases initiation of older children on ART but to enroll those who are at higher risk of disease progression/mortality, more work needs to be done to improve EID and early case detection.



[Fig 1: Children 0-14 years newly initiated on Antiretroviral therapy (July 2013 to June 2014)]

WEAD0204

Immunization practice and vaccine safety perception in centres caring for children with perinatally acquired HIV: results from the Pediatric European Network for Treatment of AIDS survey

E.C. Manno[1], A. Bamford[2], P. Rojo Conejo[3], L. Marquez[4], M.J. Mellado[5], M.Á. Muñoz-Fernández[6], V. Spoulou[7], N. Klein[8], J. Ananworanich[9,10], M. Della Negra[11], J.B. Ziegler[12], E. Meanson[13], H. Lyall[14], D. Shingadia[15], A. Di Biagio[16], V. Giacomet[17], R. Vibeke[18], H.H. de Sousa Marques[19], E. Salo[20], A. Volokha[21], H.J. Scherpbier[22], T. Niehues[23], J. Levy[24], M. Marczynska[25], M. Mardarescu[26], V. Reliquet[27], C. Giaquinto[28], S. Bernardi[1], P. Palma[1]

[1]Children's Hospital "Bambino Gesu", University Department of Pediatrics, DPUO, Unit of Immune and Infectious Diseases, Rome, Italy, [2]Evelina London Children's Hospital, Guy's and St Thomas' NHS Foundation Trust, Department of Paediatric Infectious Diseases and Immunology, London, United Kingdom, [3]Hospital Universitario Doce de Octubre, Unidad de Inmunodeficiencias pediátricas, Servicio de Pediatría, Madrid, Spain, [4]Centro Hospitalar do Porto, Pediatric Infectious Diseases and Immunodeficiencies Unit, Porto, Portugal, [5]Hospital Universitario Infantil La Paz. Madrid, Servicio de Pediatría y Enfermedades Infecciosas y Tropicales, Madrid, Spain, [6]Hospital General Universitario Gregorio Marañón, Laboratorio InmunoBiología Molecular, Madrid, Spain, [7]Aghia Sophia' Children's Hospital, Department of Infectious Diseases, Athens, Greece, [8]Institute of Child Health, University College London, Infectious Diseases and Microbiology Unit, London, United Kingdom, [9]U.S. Military HIV Research Program, Walter Reed Army Institute of Research, Silver Spring, United States, [10]Henry M. Jackson Foundation for the Advancement of Military Medicine, Bethesda, United States, [11]Instituto de Infectologia Emílio Ribas, São Paulo, Brazil, [12]Sydney Children's Hospital, Department of Immunology & Infectious Diseases, Sydney, Australia, [13]Evelina London Children's Hospital, Guy's and St Thomas' NHS Foundation Trust, Department of Paediatric Infectious Disease and Immunology, London, United Kingdom, [14]Imperial College Healthcare NHS Trust, London, United Kingdom, [15]Great Ormond Street Hospital for Children NHS Foundation Trust, London, United Kingdom, [16]IRCCS San Martino University Hospital-IST, University of Genoa, Infectious Diseases Unit, Genoa, Italy, [17]L Sacco University Hospital, Department of Paediatrics, Milan, Italy, [18]Hvidovre University Hospital, Department of Paediatrics, Copenhagen, Denmark, [19]Instituto da Criança, Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo, São Paulo, Brazil, [20]Children's Hospital, Helsinki University Central Hospital and University of Helsinki, Helsinki, Finland, [21]Children Center of Clinical Immunology, Kiev, Ukraine, [22]Emma Children's Hospital, Academic Medical Center, Department of Pediatric Haematology, Immunology and Infectious Diseases, Amsterdam, Netherlands, [23]Helios Clinic Krefeld, Department of Pediatrics, Krefeld, Germany, [24]Saint-Pierre University Hospital, Brussels, Belgium, [25]Medical University of Warsaw, Pediatric Department of Infectious Diseases, Warszawa, Poland, [26]Prof. Dr. Matei Bal, National Institute for Infectious Diseases, Paediatric Immunodepression Department, Bucharest, Romania, [27]CHU Nantes, Infectious Diseases, Nantes, France, [28]University of Padova, Department of Paediatrics, Padova, Italy
Presenting author email: emma_m@hotmail.it

Background: Perinatally HIV-infected children are more susceptible to vaccine preventable infections and vaccine induced immunity is less robust than in healthy children because of precocious waning of protective immunity.
For this high risk population it is important to design specific vaccine schedules to define correct dosing and to set accurate correlates of protection. This survey was performed to give an overview of current vaccinations practice among pediatricians looking after vertically HIV-infected children.

Methods: An online questionnaire regarding vaccination practices in HIV-infected children was completed by investigators from the PENTA network. Data were collected between November 2013 and March 2014.

Results: 88 experts in the management of pediatric HIV-infection from 46 different units looking after 2465 patients completed the questionnaire. The majority of units (72%) did not perform routine childhood immunizations in HIV centres. Vaccination histories were incomplete for 40% of the studied population. Influenza, pneumococcal conjugate vaccine and human papilloma vaccine immunizations are widely administered (93%, 89% and 83% of units respectively). Varicella and Rotavirus vaccinations are less recommended (61% and 24% of the units respectively). Monitoring of vaccine responses is employed in 72% of centers. Serology appears to be the most feasible assay among the different centers (90%), mostly performed with immune-enzymatic assays.

Conclusions: Vaccination practices for perinatally HIV-infected children still vary widely between countries. A crucial issue is the incomplete adherence to varicella vaccine. Indeed only in few countries varicella vaccination is universally recommended for children at national. More efforts should be made to standardize mandatory and recommended vaccinations, as well as to guide timing of serological assays. The majority of units carry out immuno-enzymatic tests to evaluate specific antibody levels. However, methods vary with different cut-offs of protection and units of measurement employed. Moreover, especially in high risk groups (eg. children who started late HAART or performed vaccinations before treatment), researches on the development of novel methods to assess protective immunity and accurate correlates of protection are needed. The ultimate goal will be to design individualized vaccine schedules, developed on therapeutic and immunological features of individual patients, optimizing the chances of them gaining robust long-term vaccine induced protection.

WEAD0205

Lower ANC attendance and PMTCT uptake in adolescent versus adult pregnant women in Kenya

K. Ronen[1,2], C. Mcgrath[3], A. Langat[4], J. Kinuthia[5], D. Omolo[6], B. Singa[6], A. Katana[4], L. Nganga[4], G. John-Stewart[2]

[1]Fred Hutchinson Cancer Research Center, Seattle, United States, [2]University of Washington, Seattle, United States, [3]University of Texas Medical Branch, Galveston, United States, [4]Centers for Disease Control and Prevention, Nairobi, Kenya, [5]Kenyatta National Hospital, Nairobi, United States, [6]Kenya Medical Research Institute, Nairobi, Kenya
Presenting author email: kronen@fhcrc.org

Background: Although rates of pregnancy and HIV infection are high among Kenyan adolescent women, their engagement in PMTCT services is poorly characterized. We hypothesized that adolescent women show lower engagement in the PMTCT cascade than adult women, from antenatal care (ANC) attendance to HIV testing and antiretroviral (ARV) uptake.

Methods: We conducted a nationally representative cross-sectional survey of mothers attending 120 maternal child health clinics selected by probability-proportionate-to-size-sampling in Kenya in July-December 2013, with a secondary survey oversampling HIV-positive mothers in 30 clinics. Self-report questionnaires verified by clinic booklets recorded ANC attendance, HIV testing, ARV use and maternal characteristics. Data were compared between adolescent (age < 20) and adult mothers. Differences in maternal characteristics were assessed by Chi-square test. Logistic regression was used to analyze ANC attendance and HIV testing among all women and ARV uptake among HIV-positive women.

Results: Among 2521 mothers surveyed, 278 (12.8%) were adolescents. Adolescents were less likely than adults to have above primary education (25.0% vs. 42.9%, p< 0.001), intended pregnancy (40.5% vs. 58.6%, p< 0.001), and a current partner (73.1% vs. 90.9%, p< 0.001). Overall, 2471 (97.8%) reported attending ≥1 ANC visit. Among 1859 women with verified ANC visits, 898 (44.7%) attended ≥4 visits. Adolescents were less likely than adults to attend ≥4 ANC visits (35.2% vs. 45.6%, OR[95%CI]=0.65[0.49-0.86]). This effect remained significant when adjusting for education, primigravida, pregnancy intention and HIV status (aOR[95%CI]=0.59[0.36-0.97]). Among 2359 women who attended ≥1 ANC visit and were not known to be HIV-positive prior to pregnancy, 2298 (96.1%) received HIV testing during pregnancy. Testing rates were not significantly different between adolescents and adults. Among 288 HIV-positive women who attended ≥1 ANC visit and were not on HAART prior to pregnancy, 20 (6.9%) were adolescents, and 243 (84.4%) used any ARVs for PMTCT. Adolescents were less likely to use ARVs than adults (65.0% vs. 85.8%, OR[95%CI]=0.31[0.12-0.81]).

Conclusions: Adolescent mothers showed poorer ANC attendance and lower uptake of ARVs for PMTCT. This calls for further study on barriers to ANC and PMTCT services among adolescent women and development of targeted interventions to improve uptake and retention of this vulnerable population through the PMTCT cascade.

WEAD03 The Implementation and Measurement to Improve Health System

WEAD0301

Health resource use pattern analysis to inform targeted interventions alongside the HIV cascade of care and optimize the effect of treatment as prevention

E. Krebs[1], J.E. Min[1], R. Barrios[1], J. Montaner[1,2], B. Nosyk[1,3], STOP HIV/AIDS Study Group
[1]*BC Centre for Excellence in HIV/AIDS, Vancouver, Canada,* [2]*University of British Columbia, Division of Aids, Faculty of Medicine, Vancouver, Canada,* [3]*Simon Fraser University, Faculty of Health Sciences, Burnaby, Canada*
Presenting author email: ekrebs@cfenet.ubc.ca

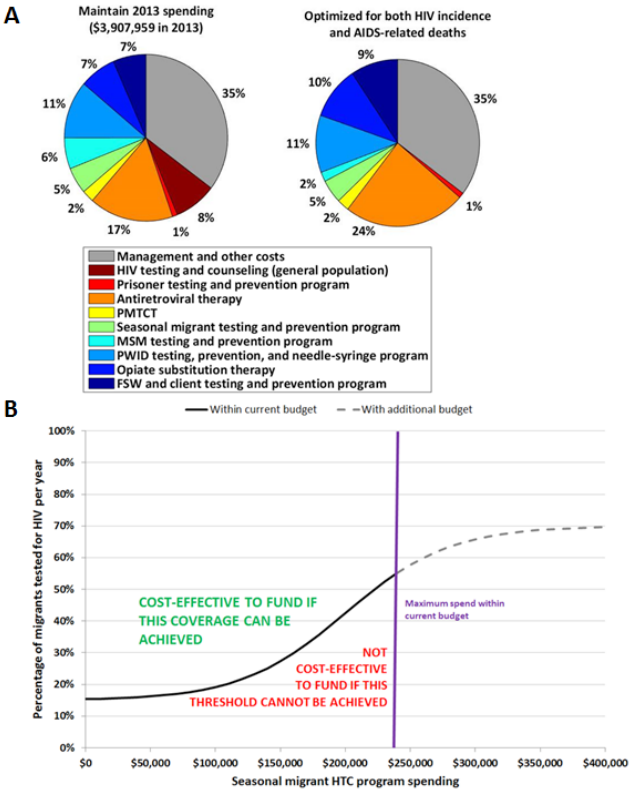
Background: Identifying patterns of health resource utilization (HRU) of people living with HIV/AIDS (PLHIV) can allow for comparison of their effects on longer-term health outcomes and costs. Further, identification of patterns associated with greater risk of attrition between stages of the cascade of care can help in the development of targeted interventions to effectively increase patient retention.
Methods: We conducted a population-level analysis of HRU for individuals having received a CD4 test after HIV diagnosis. All individuals 18 years or older in British-Columbia in the modern HAART-era (post-September 2006) were included. Using linked comprehensive administrative health databases in a probabilistic model-based clustering analysis with 14 HRU measures, we estimated parameters by maximum likelihood using the expectation maximization (EM) algorithm. Individuals with estimated parameters maximizing the probability of belonging to a similar HRU cluster were classified with each other, and the optimal number of clusters was estimated by the Bayesian Information Criterion. The analysis was conducted across CD4 count stratification (>200cells/mm^3; < 200cells/mm^3).
Results: Our study included 941 individuals with at least 1 year follow-up (median age 40, 21% female) and with a CD4 count obtained between September 1st, 2006 and March 31st, 2011. Individuals with CD4< 200 clustered in 2 HRU patterns. The high cost cluster (N=68; mean $18,169[SD$21,432]), driven by lengthy HIV-related emergency hospitalization stays (76.5% with>7days), had costs more than double the low cost cluster (N=147; $6,811[$13,592]). Individuals with CD4>200 were best classified in 4 clusters. The high cost cluster (N=74; $15,831[$19,180]) was characterized by non-HIV ER hospitalizations (100%≥1day, 55.4%>7days) and high prevalence of mental health issues. The second highest cost cluster (N=60;$5,058[$5,152]) was characterized by short-term non-HIV elective hospitalizations (48.3%=1day). The two lower cost clusters both had no hospitalizations; the higher (N=425;$3,378[$6,454]) with much more frequent physician visits and medication use than the lowest cost cluster (N=167;$1,291[$7,969]).
Conclusions: Even within relatively homogeneous cohorts in terms of disease progress at time of linkage to HIV care, individuals were found to have heterogeneous HRU patterns. Identifying classes of individuals according to HRU can help inform clinical response, as well as the design of public health interventions to optimize HIV care.

WEAD0302

Optimizing HIV/AIDS resources in Armenia: increasing ART investment and examining seasonal labour migrant programs

S. Kelly[1], A. Shattock[1], C. Kerr[1,2], R. Stuart[1,3], A. Papoyan[4], T. Grigoryan[4], R. Hovhannisyan[4], S. Grigoryan[4], D. Wilson[1]
[1]*Kirby Institute, UNSW Australia, Surveillance and Evaluation Program for Public Health, Sydney, Australia,* [2]*School of Physics, University of Sydney, Sydney, Australia,* [3]*University of Copenhagen, Department of Mathematical Sciences, Copenhagen, Denmark,* [4]*National Center for AIDS Prevention, Yerevan, Armenia*
Presenting author email: skelly@gmail.com

Background: HIV prevalence is declining in all key affected populations in Armenia (people who inject drugs, men who have sex with men, prisoners, and female sex workers); however, there are increases among labour groups who seasonally migrate to countries of higher HIV prevalence. We conducted a modeling study to assess the impact of optimizing the national strategic plan to minimize HIV incidence and AIDS-related deaths by 2020. We determined optimal funding levels for all programs to best achieve the strategic plan, and in particular, examined the outcomes required for migrant programs to warrant increased funding.
Methods: We used the Optima model to perform epidemiological and economic analyses. Demographic, epidemiological, behavioral, and HIV program cost data were obtained for Armenia from 2000 to 2014 and used to inform the model. Through internal and external consultations, assumptions were generated on what coverage levels among targeted populations could be attained for different investments, as well as their expected outcomes. A sensitivity analysis on migrant HIV testing and counselling programs was conducted around assumptions based on observed data.
Results: According to Optima's optimization algorithm, shifts in funding allocations are required to minimize incidence and deaths by 2020. The largest emphasis should be on antiretroviral therapy (ART), as optimal allocations nearly doubled the investment in treatment from 17% to 24% of the total budget. This is projected to avert almost 25% of new infections and 50% of AIDS-related deaths by 2020 compared to levels if 2013 spending were maintained. We show that funding for seasonal migrant programs should be maintained through to 2020 at 5% of the total budget. Sensitivity analysis demonstrated that these programs are cost-effective to fund if the coverage threshold for HIV testing and counselling for seasonal migrants, as illustrated in Figure 1B, can be achieved.
Conclusions: Optimization of HIV/AIDS investment in Armenia could significantly reduce HIV incidence and AIDS-related deaths by 2020, particularly by focusing more on antiretroviral therapy. We have also identified thresholds for program performance, prior to their scale-up, which can be used to evaluate whether they should be scaled-up or down in the future.



(A) Optimized spending to minimize HIV incidence and AIDS-related deaths by 2020 in Armenia. (B) Sensitivity analysis of cost-coverage for seasonal migrant HIV testing and counselling program in Armenia.

[Figure 1]

WEAD0303

Has performance-based financing (PBF) accelerated progress towards controlling the HIV epidemic? An impact evaluation of Mozambique's HIV-focused PBF program

Y. Rajkotia, O. Zang, P. Nguimkeu, I. Djurovic
ThinkWell, Maputo, Mozambique
Presenting author email: yrajkotia@collaborativedev.com

Background: As performance-based financing (PBF) gains global traction, evidence around its effectiveness to accelerate the elimination of HIV is needed. We evaluated the impact of a PBF program implemented by Elizabeth Glaser Pediatric AIDS Foundation (EGPAF), on the provision of HIV, PMTCT and MCH services. We also examined the temporal effects of PBF to better understand its lifecycle both in terms of onset and duration of effect. Finally, we evaluated the impact of PBF on non-incentivized services.
Methods: The impacts of PBF in Gaza (South) and Nampula (North) provinces were analyzed using a retrospective observational study design in which PBF provinces were matched with control provinces Eighteen indicators related to HIV, PMTCT, and MCH services were reviewed. Due to regional heterogeneity, we evaluated the North and South as separate experiments. Beginning January 2011, up to eleven quarters of data from 134 PBF facilities after matching (84 North and 50 South) were used. Data sources include PBF program data and health management information system data. Our econometric framework employed a multi-period, multi-group difference-in-difference model on data that was matched using propensity

scoring. The regression design employed a generalized linear mixed model with both fixed and random effects, fitted using the seemingly-unrelated regression (SUR) technique.

Results: PBF resulted in positive impacts on MCH, PMTCT, and pediatric HIV program outcomes. The majority of the 18 indicators responded to PBF (77% North and 66% South), with at least half of the indicators demonstrating a statistically significant increase in average output of more than 50% relative to baseline. Most adult HIV (excluding pregnant women) initiation and retention indicators did not respond to PBF. On average, it took 6 quarters of implementation for PBF to take effect, and impact was generally sustained thereafter. Indicators were not sensitive to price, but rather inversely correlated to the level of effort associated with marginal output. No negative impacts on incentivized indicators nor spill-over effects on non-incentivized indicators were observed.

Conclusions: The PBF program in Mozambique has shown to produce large, sustained increases in the provision of PMTCT, pediatric HIV, and MCH and should be considered as a powerful alternative to traditional input-based financing.

WEAD0304

The estimated need of second-line antiretroviral therapy in sub-Saharan Africa 2015-2030: mathematical modelling study

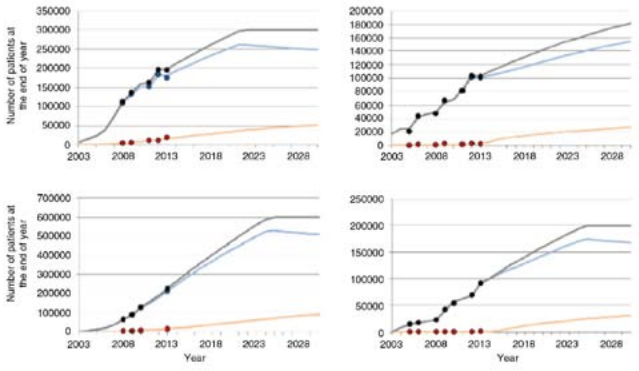
J. Estill[1], N. Ford[2], L. Salazar-Vizcaya[1], A. Haas[1], N. Blaser[1], M. Egger[1], V. Habiyambere[2], O. Keiser[1], IeDEA Southern Africa
[1]*University of Bern, Bern, Switzerland,* [2]*World Health Organisation, Geneva, Switzerland*
Presenting author email: olivia.keiser@ispm.unibe.ch

Background: At the end of 2013, about 300,000 patients were on second-line antiretroviral therapy (ART) in sub-Saharan Africa. The need for second-line ART may increase substantially with increasing duration of patients on ART and roll-out of viral load monitoring. We aimed to estimate the need of second-line ART in sub-Saharan Africa between 2015 and 2030 under various scenarios.

Methods: We developed a mathematical simulation model of HIV progression on ART to project second-line needs up to 2030 for individual countries. The model allows the user to vary key input parameters, including annual numbers of patients starting ART, delay in switching after detection of treatment failure, possibility of treatment interruptions, background mortality, and monitoring strategies. We applied the model to all countries in sub-Saharan Africa assuming twelve scenarios that combine different future ART scale-up scenarios (accelerated until universal coverage; stable; no future scale-up), monitoring (routine viral load monitoring in all or only selected countries), and retention and switching (including or excluding possibility of treatment drop-out and delayed switching). The input parameters were chosen to fit the numbers of patients on first- and second-line ART in 2005-2013 to observed estimates.

Future scale-up of ART initiation	Treatment interruptions and switching	2020				2030			
		Universal routine viral load monitoring		Targeted or routine viral load monitoring depending on country		Universal routine viral load monitoring		Targeted or routine viral load monitoring depending on country	
		1st-line	2nd-line	1st-line	2nd-line	1st-line	2nd-line	1st-line	2nd-line
Accelerated scale-up until universal coverage reached	No interruptions, immediate switching	18,272,800	2,480,100	19,143,300	1,672,400	19,561,700	4,144,300	20,730,300	2,992,200
	Interruptions included, delayed switching	18,334,300	1,771,300	18,869,600	1,221,200	20,161,000	3,561,500	21,143,100	2,539,400
Stable scale-up	No interruptions, immediate switching	13,306,000	1,899,200	13,807,300	1,387,100	15,717,400	3,239,100	16,397,400	2,555,600
	Interruptions included, delayed switching	12,598,600	1,445,300	12,970,000	1,056,600	15,892,600	2,758,100	16,462,900	2,166,900
No future scale-up	No interruptions, immediate switching	7,655,600	1,397,200	7,447,200	987,100	7,305,900	1,757,000	7,082,000	1,352,300
	Interruptions included, delayed switching	7,697,300	1,186,700	8,009,900	872,700	7,314,800	1,569,200	7,619,000	1,262,700

[Table 1]



[Figure 1]

Results: If the scale-up of ART is accelerated across the region, patients are retained in care, switching is immediate, and all countries implement routine viral load monitoring, the number of patients on second-line ART will increase to 4.1 million by 2030 (17% of all patients on ART). In a scenario with a stable scale-up and realistic drop-out and switching delay, the corresponding numbers were 2.8 million (15%) with universal routine viral load monitoring, and 2.2 million (12%) with routine viral load monitoring only in selected countries.

Conclusions: We expect that by 2030, 2-3 million people will receive second-line ART in sub-Saharan Africa, but the number of patients in need may be over 4 million. Routine viral load monitoring, timely switching and minimizing treatment interruptions will further increase the number of patients on second-line ART.

WEAD0305

Kenya private health sector HIV care services costing using the management accounting system for hospitals (MASH) framework

B. Chuma[1], S. Koseki[2], S. Musau[2], B. Johns[2], A. Gatome-Munyua[2]
[1]*Abt Associates, International Health, Nairobi, Kenya,* [2]*Abt Associates, Washington, United States*
Presenting author email: bensonchuma@gmail.com

Background: The private sector is a key HIV service provider in Kenya, but few data on the cost of private service provision are available. The lack of cost data has inhibited the design of reimbursement mechanisms and health insurance packages, as well as policy decisions on private sector financing. This study estimated unit costs for private sector HIV services disaggregated by facility type and level, as a contribution to ongoing efforts to implement health insurance products covering HIV services.

Methods: Cost and service volume data were collected from 149 private sector facilities in 2013 as part of a nationwide systematic sampling of public and private healthcare costing study supported by GIZ, the USAID-funded Strengthening Health Outcomes Through the Private Sector (SHOPS) Project Kenya, and the Ministry of Health. The MASH (Management Accounting System for Hospitals) tool was used to analyze data. Multiple facilities were eliminated due to lack of complete data with only 60 used.

Results: Average unit costs per inpatient day and per outpatient visit were generated by sector and facility levels 2-4 (as defined by Kenya Norms and Standards 2006). HIV specific unit costs estimated included for HIV counseling and testing (HCT) services and provision of ART. The authors estimated operational costs, but were unable to estimate capital costs following lack of data. Average outpatient visits ranged from Ksh. 689 to 1,036 in level 2 and level 4 respectively. ART visit costs ranged from Ksh. 1,575 to 3,660 across the facilities sampled. HCT visit services ranged from Ksh. 537 to 1,151 across level 2 and 4 facilities respectively.

Conclusions: The study contributed to health financing policy discussions in the provision and financing of HIV services in Kenya. Data generated was presented to insurers and providers who expressed intentions of using it for decision making. Possible applications include design of HIV care inclusive insurance products and advising reimbursement decisions regarding the same. Providers offering HIV services can also use it to benchmark their efficiency. Due to poor record keeping in most facilities only 60 of the 149 facilities had enough data for analysis-hence the need to support facilities improve on data keeping.

WEAD0306LB

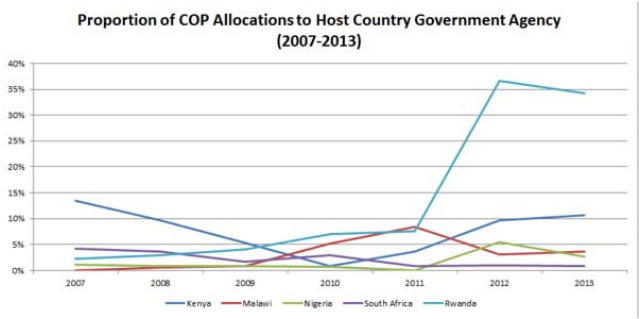
The PEPFAR COPs allocation database: a comprehensive database to monitor PEPFAR spending, increase data transparency, and improve civil society engagement in country operational plans

B. Honermann, G. Millett, K. Lindsey, S. Wijayaratne, J. Sherwood, J. MacAllister
amfAR, Public Policy Office, Washington, United States

Background: $29.5 billion has been allocated by PEPFAR from 2007 to 2014 through the annual country operational plan (COP) process. COPs serve as a planning tool for activities of US government and in-country partners funded by PEPFAR. Historically, utilizing data from COPs has been difficult due to their inflexible PDF/RTF format hindering the ability to query and manipulate data, create graphical representations of the financial data, or identify trends in PEPFAR allocations over time. As PEPFAR moves toward greater civil society engagement during COPs' development, it is increasingly important that COPs' data are readily accessible, categorizable, and interpretable for civil society organizations (CSOs).

Methods: Utilizing standard open source tools, amfAR - funded by MAC AIDS - created a navigable database and website of all allocation data contained in published COPs from 2007 through 2014. Data are categorized and can be graphically represented and disaggregated by year, primary partner, host country, strategic area, budget code, and organizational type of recipient. Text narratives of individual budgetary mechanisms captured directly from the COPs are also included in the database and provide users with detailed information for specific allocations. In addition, epidemiological profiles and PEPFAR targets are available by country to provide context for the public health impact of investments.

Results: From 2007 through 2014, $29.5 billion was allocated through the COPs process. By organizational type, the primary recipients of PEPFAR funds were NGOs ($8.3 billion), private contractors ($5.4 billion), and universities ($3.5 billion). Another $5.5 billion was not allocated to an identifiable partner or program. Trends varied substantially by country. In Rwanda, resources shifted dramatically to Rwandan government agencies (from 7.6% of PEPFAR resources in 2011 to 34.2% of PEPFAR resources in 2013). Comparatively, PEPFAR 2013 host government funding was lower for Kenya (10.72%), Malawi (3.66%), Nigeria (2.64%), and South Africa (0.8%).



[Host Country Government Agency Allocations]

Conclusions: amfAR´s COPs database provides corresponding financial and graphical information about progress toward country ownership, and gives the most granular view to date of PEPFAR budgets. The database will be an invaluable tool to help CSOs and others digest and utilize PEPFAR budgetary information.
The database is available at http://copsdata.amfar.org

Wednesday 21 July

Oral Poster Discussions

WEPDA01 Immunology and Virology of the Global Epidemic

WEPDA0101

Evolution of neutralizing antibodies in HIV-1 subtype C infection

B. Ndlovu[1], T. Hermanus[2], N. Tumba[2], P. Moore[2], M. Jaggernath[1], B.D. Walker[3], L. Morris[2], T. Ndung'u[2]
[1]University of KwaZulu-Natal, HIV Pathogenesis Programme, Durban, South Africa, [2]National Institute for Communicable Diseases, AIDS Virus Research Unit, Johannesburg, South Africa, [3]University of Cambridge, Ragon Institute of MGH, MIT & Harvard, Boston, United States
Presenting author email: bongiwendlovu4@ukzn.ac.za

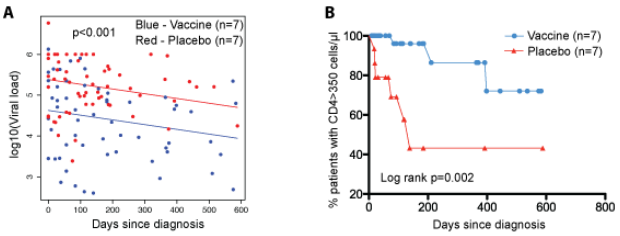
Background: The development of a preventative HIV-1 vaccine will most likely require induction of broadly neutralizing antibodies (BCN). Neutralizing antibodies develop in almost all HIV-1 infected individuals, however they develop months following HIV-1 infection and they are strain-specific. The development of BCN antibodies occurs only in 20-30% of HIV-1 infected individuals. However, the mechanism that leads to the development of BCN is unknown and not all epitopes have been identified. The aim of the study was to evaluate pathways and mechanisms that lead to the development of broadly neutralizing antibodies.
Methods: Twenty individuals with acute HIV-1 infection were identified and followed longitudinally for three years in Durban, KwaZulu-Natal. A panel of 18 viruses (6 subtype A, 6B and 6C) was used to screen the patients for neutralizing antibodies at 2-3 years post-infection using the TZM-bl neutralization assay. The patients that developed broadly neutralizing antibodies were followed up longitudinally at 8, 10, 14, 16, 18, 71, 88, 100, 124, 150, 200 weeks to determine the timing of emergence of the BCNs. Specificity of BCNs was determined using single point mutagenesis at 3 years post-infection.
Results: Three out of 20 individuals (AS3-268, AS2-1037, AS2-358) developed broadly neutralizing antibodies. AS3-268 developed potent BCN activity peaking at 3 years post-infection and it targets N276A glycan on the CD4 binding site of gp120. AS2-1037 developed potent broadly neutralizing activity peaking at 2 years post-infection and it targets N332A glycan on the V3 loop of gp120. AS2-358 developed BCNs peaking at 2 years post-infection and it did not map to any known specific epitope.
Conclusions: Broadly neutralizing antibodies could be detected at approximately 1 year post-infection and they targeted different epitopes on the viral envelope. Work is currently in progress to assess the maturation of breadth and to assess antibody-virus co-evolution.

WEPDA0102

HLA-B*58:02-specific benefit of MRKAd5 Gag/Pol/Nef vaccine in an African population

E.M. Leitman[1], J. Hurst[2], M. Mori[1], P.C. Matthews[2], N. Frahm[3], J. Kublin[3], G.E. Gray[4], P.J.R. Goulder[1,5]
[1]University of Oxford, Department of Paediatrics, Oxford, United Kingdom, [2]University of Oxford, Nuffield Department of Medicine, Oxford, United Kingdom, [3]Fred Hutchinson Cancer Research Center, HIV Vaccine Trials Network, Vaccine and Infectious Disease Division, Seattle, United States, [4]South African Medical Research Council, Cape Town, South Africa, [5]Doris Duke Medical Research Institute, University of KwaZulu-Natal, HIV Pathogenesis Programme, Durban, South Africa
Presenting author email: ellen.leitman@st-hughs.ox.ac.uk

Background: The MRKAd5 Gag/Pol/Nef vaccine increased the risk of HIV acquisition. However, the Step study suggested an HLA-specific benefit in viral setpoint to vaccinees who subsequently became infected. The Phambili trial, using the same MRKAd5 vaccine, presented an opportunity to investigate the existence of an HLA-specific effect in a genetically distinct South African population. Gag-specific CD8 T-cell responses restricted by protective South African HLA alleles such as HLA-B*57 are associated with successful control of infection, while disease-susceptible alleles such as HLA-B*58:02 present non-Gag epitopes and are associated with rapid progression. We hypothesized that the MRKAd5 Gag/Pol/Nef vaccine might redirect responses towards Gag in HLA-B*58:02+ Phambili subjects who would not target it naturally.
Methods: Viral loads (VL), CD4 T-cell counts, HLA types and ELISpot anti-HIV CD8 T-cell responses were analyzed in subjects blinded to vaccine/placebo assignment. All data analyzed were from ART-naïve subjects.
Results: HLA-B*58:02 was the most prevalent allele (population frequency 23%). HLA-B*58:02+ vaccinees (n=7) had lower viral setpoints than placebo-recipients (n=7) (25,670 vs 215,500, p=0.03), a 0.8log lower VL calculated using all longitudinal pre-ART data via a mixed effects model (p< 0.001, Fig1A), reached CD4< 350 cells/µl slower (p=0.002, Fig1B) and showed an increase in Gag breadth in ELISpot assays (p=0.04) compared to HLA-B*58:02+ placebo-recipients.



(A) Graphical presentation of patient longitudinal pre-ART data and regression lines obtained from a variable intercept linear mixed effects model showing longitudinal VL differences in infected B*58:02+ vaccinees (blue, n=7) and placebo-recipients (red, n=7); ANOVA. **(B)** Kaplan-Meier curves showing time to CD4<350 cells/µl in infected HLA-B*58:02+ vaccinees (blue, n=7) and placebo-recipients (red, n=7); log rank test.

[Figure 1]

Conclusions: In addition to the known increased risk of HIV acquisition resulting from the MRKAd5 Gag/Pol/Nef vaccine, these current data suggest a therapeutic effect of the same vaccine in subjects expressing HLA-B*58:02, an African HLA allele strongly associated with rapid progression in natural HIV infection. HLA-B*58:02+ vaccinees showed a lower viral setpoint and slower time to CD4< 350 cells/µl, associated with increased Gag-specific ELISpot responses. Caveats to the study include limitation of ELISpot assays to only 60 of 100 study subjects, selected based on cell availability; and of HLA typing to 79 subjects, based on material availability. These factors potentially introduced unintended selection bias effects. Nonetheless, these data on ART-naïve subjects are consistent with Step studies, indicating a beneficial therapeutic MRKAd5 HLA-specific effect that in South Africa includes the most prevalent HLA-B allele, HLA-B*58:02.

WEPDA0103

HIV-1 subtype C is significantly more infectious than other subtypes

T. Demarco[1], W. Rountree[1], B. Hora[1], Y. Chen[1], S. Keinonen[1], L. Racz[1], L. Daniell[1], R. Louzao[1], A. Sanchez[1], M. Busch[2], T. Denny[1], F. Gao[1]
[1]Duke Human Vaccine Institute and Departments of Medicine, Duke University Medical Center, Durham, United States, [2]Blood Systems Research Institute, San Francisco, United States
Presenting author email: todd.demarco@dm.duke.edu

Background: HIV-1 subtype C accounts for about 50% of the global HIV-1 infections. It is the predominant subtype in India, Ethiopia and countries in southern Africa. However, virological attributes to this unique epidemiological pattern have not yet been fully defined.
Methods: A total of 207 HIV-1 positive plasma or established strains were cultured and expanded to higher titer stocks by culturing in PBMCs from HIV-1 negative donors. Near full-length genome (NFLG) sequences were obtained by amplifying two overlapping half genomes. The newly obtained sequences were aligned to the HIV-1 whole genome reference sequences for subtyping. Viral genome copy numbers, tissue culture infection doses (TCID) and p24 concentrations were determined for virus stocks and compared via linear regression among major subtypes. Mann-Whitney U tests were used for the infectivity comparisons at the alpha 0.05 level.
Results: Analysis of NFLG sequences showed that these viruses belonged to subtype A1 (16), subtype B (48), subtype C (53), subtype D (10), CRF01_AE (12), other subtypes and CRFs (F1, F2 G, CRF02, and CRF022; each with ≤8 sequences) and URFs (45). Only subtypes with ≥10 NFLG sequences were subjected to further analysis. No biologically relevant differences (a 0.5 log10 difference) among all compared subtypes were observed for three measurements: viral genome copy numbers, TCID, and p24 concentrations. The only exception was that the TCID of subtype C was 0.51 log higher than that of CRF01 (p=0.04). The infectivity per viral genome (TCID/RNA copy) was the highest for subtype C (0.00452 TCID/RNA copy) and was significantly higher than those of all four compared subtypes (A1, B, D and CRF01_AE; p= 0.0286, p=0.0004, p< 0.001 and p=0.0205, respectively). The p24/RNA copy ratios of subtypes C and B (0.13 and 0.12 pg/RNA copy, respectively) were the highest and were significantly higher than those of subtypes A1 and D (p< 0.05), but similar to that of CRF01_AE.
Conclusions: The high infectivity of HIV-1 subtype C may give it more replication advantages and allow it to disseminate faster in HIV-1 infected populations in some geographic areas compared to other subtypes. High infectivity may play a critical role in the global epidemic of subtype C.

WEPDA0104

Functional differences in the viral accessory protein Nef between major HIV-1 subtypes

A. Johnson, R. Jacob, M. Haeryfar, J. Dikeakos
University of Western Ontario, Microbiology and Immunology, London, Canada
Presenting author email: aaronjohnson13@gmail.com

Background: The HIV-1 accessory protein Nef is essential for HIV-1 pathogenesis and progression to AIDS. By hijacking the cellular trafficking machinery Nef is able to alter T cell activation, increase viral replication and permit viral immune evasion via downregulation of the cell-surface receptors CD28, CD4 and MHC I respectively. However, only recently have these functions been studied outside of laboratory-adapted strains of HIV-1. This proposal aims to investigate how the high degree of HIV-1 genetic diversity impacts Nef function.
Methods: An HIV-1 based lentiviral expression system was used to express Nef proteins from 10 group M subtypes (A1, A2, B, C, F1, F2, G, H, J and K) in the context of an HIV-1 infection. T cell lines were infected with pseudoviruses encoding Nef proteins and analyzed for surface levels of CD28 and MHC-I using fluorescent antibody staining and flow cytometry. Alternatively, CD4 cell surface levels were measured by transfecting $CD4^+$ HeLa cells with expression plasmids encoding Nef-GFP fusion proteins followed by fluorescent antibody staining and flow cytometry. Nef expression was determined by a combination of western blot analysis and flow cytometry to measure fluorophore fused Nef proteins.
Results: Our results demonstrate that MHC I, CD28 and CD4 are differentially downregulated between HIV-1 subtypes. Notably, subtype C Nef, the most common subtype globally, was significantly less efficient at downregulating MHC I and CD28 when compared to the laboratory strain NL4.3. Subtype G Nef, found predominantly in Central and West Africa, was significantly less efficient at downregulating all three cell surface receptors. Differences in downregulation efficiency for all three receptors were attributed to variations in Nef protein expression.
Conclusions: This study represents a comprehensive analysis of Nef function among 10 HIV-1 subtypes and adds to the growing evidence that HIV-1 genetic diversity impacts viral protein function. Due to the pathogenic role Nef plays in an HIV-1 infection, these results may help explain recent studies that show differences in disease progression in individuals infected with different HIV-1 subtypes. Finally, these findings support further study of all major HIV-1 subtypes and emphasize the need to consider subtype differences when developing alternative treatment options.

WEPDA0105

Characterization of HIV-1C gp120 in recently and chronically infected individuals in Botswana

T. Mohammed[1], S. Gaseitsiwe[1], K. Matlhagela[2], M. Matsheka[3], S. Moyo[1], R. Musonda[1]
[1]Botswana Harvard AIDS Institute Partnership, Research Laboratory, Gaborone, Botswana, [2]University of Botswana, School of Medicine, Gaborone, Botswana, [3]University of Botswana, Biological Sciences, Gaborone, Botswana
Presenting author email: tmohammed@bhp.org.bw

Background: Viral diversity provides a major challenge in the development of a vaccine against HIV-1. A potential target for HIV-1 vaccines is gp120 envelope protein, which is involved in viral entry and is a target of the host immune system. It has been shown that Envelope characteristics have a role to play in disease progression. However some studies have demonstrated conflicting results. In this study, we aim to analyze HIV-1gp120 characteristics, specifically: potential N- glycosylation sites, amino acid sequence length and net electric charge in cell associated and cell free RNA derived from recently and chronically infected individuals in Botswana.
Methods: This was a retrospective study using stored samples collected from treatment naïve HIV-1C infected cohorts at Botswana Harvard AIDS Institute Partnership, representing recently infected and long term infection as determined by serological assays for recency and longitudinal follow up. A 1200 base pairs fragment of V1 to V5 region of gp120 was amplified by nested PCR and sequenced on both strands using Big Dye Technology in proviral DNA and cell free RNA. Potential N-glycosylation sites were determined using Los Alamos HIV sequence database while subtype was assigned using REGA HIV subtyping tool.
Results: There was a significant increase in amino acid sequence length of V2 ($p= 0.027$) and V4 ($p=0.0099$) in proviral DNA in the chronic stage as compared to the recent stage of infection. Similar changes were also observed in cell free RNA in V4 ($p=0.0074$). In addition, the number of potential N-linked glycosylation sites in proviral DNA was significantly increased in chronic infection in V4 ($p=0.0253$). No significant changes in net electric charges were observed. There was an association between viral load and V4 region ($p< 0.001$). All samples were classified as subtype C.
Conclusions: The increase in amino acid sequence length and potential N-Glycosylation sites in the V2 and V4 region may be essential in disease progression. The changes observed in V2 and V4 warrant further investigation. A clear understanding of envelope characteristics is important for development and design of new vaccine and therapeutics.

WEPDA0106LB

Early loss of splenic Tfh cells in SIV-infected rhesus macaques

F. Moukambi[1], H. Rabezanahary[1], V. Rodrigues[2], G. Racine[1], L. Robitaille[1], C. Soundaramourty[2], M. Laforge[2], J. Estaquier[1,2]
[1]Centre de Recherche en Infectiologie, Université Laval, Quebec, Canada, [2]CNRS FRE 3235, Université Paris Descartes, Paris, France

Background: Follicular T helper cells (Tfh), a subset of CD4 T lymphocytes, are essential for B cell activation and provide help to B cells in the production of antigen-specific antibodies. Although several studies have analyzed the dynamics of Tfh cells in the context of AIDS by analyzing peripheral blood and LNs of HIV-infected patients, paradoxically, none of these studies in HIV/SIV infection have addressed the role of Tfh cells in the primary organ of B cell activation, the spleen.
Methods: To address these questions we have infected rhesus macaques with SIVmac251 (20 AID50). Animals were sacrificed at different time points post infection and lymphoid organs were recovered. Tfh cells ($PD\text{-}1^{high}CXCR5^+$) and CD4+ T cell subsets were monitored by flow cytometry. Concomitantly B cell subsets were also analyzed. CD4 T cell subsets were sorted and SIV DNA was quantified by RT-PCR.
Results: Herein, we demonstrated for the first time that the percentages and numbers of splenic Tfh cells decrease early during the acute phase in macaques infected with SIV. This profound loss and abnormal differentiation of Tfh is also associated with the loss of memory B cell subsets. Moreover, SIV DNA is detected in splenic Tfh cells early after infection. Finally, our results showed at the chronic phase that the frequency of splenic Tfh and memory B cells are higher in slow-progressor compared to rapid progressor RMs.
Conclusions: Altogether, our results demonstrate the drastic depletion of splenic memory B cells which might be related to the loss of fully maturated Tfh cells.

WEPDB01 HIV Testing and Monitoring in the Field

WEPDB0101

Reliability of rapid HIV-1/HIV-2 INSTI® on plasma and capillary blood for diagnosis of non B subtypes and circulating recombinant forms of HIV-1 circulating in Gabon

A. Ndjoyi-Mbiguino[1], G.F. Nzengui Nzengui[2], H. M'Boyis Kamdem[2], L. Bélec[3]
[1]Université des Sciences de la Santé, Microbiologie, Libreville, Gabon, [2]Université des Sciences de la Santé, Libreville, Gabon, [3]Université Paris Descartes, Paris, France
Presenting author email: nzenguig@yahoo.fr

Background: *Point-of-care* or "rapid" serologic assays for HIV are widely used in resources-limited setting. Their evaluation in the field carried out independently of the fabricant is crucial to assess their capability to accurately detect non B subtypes or circulating recombinant form (CRF) of HIV-1.
Our objective was to evaluate the HIV-1/HIV-2 INSTI® test (distributed by Nephrotec, Rungis, France) for the diagnosis of non B subtypes and CRF of HIV-1 circulating in Gabon, a country of wide genetic diversity.
Methods: A panel of 250 HIV-positive and 250 HIV-negative plasmas was prospectively collected after informed consent in adult patients attending the Laboratoire National de Référence des MST et du SIDA, Libreville, as recommended by the WHO (Service delivery approaches to HIV testing and counselling: A strategic policy framework; 2012).The reference HIV serology consisted of ImmunoComb II HIV1&2 BiSpot (Inverness Medical Innovations, Yavne, Israel) as screening test followed by confirmatory Western blot (New Lav Blot I, Bio-Rad, Marnes-la-Coquette, France).
All HIV-positive plasma were furthermore subjected to HIV genotyping by *pol* nested PCR, amplicons sequencing, and analysis of resulting FASTA sequences by Genotyping software from NCBI. A subgroup of 1 out of 10 patients were also tested in parallel with finger-stick whole blood INSTI® test.
Results: All HIV-1 belong to HIV-1 group M with broad HIV-1 genetic diversity as assessed using *pol* sequences [CRF02_AG (53%), CRF14 (18%), CRF15 (12%), CRF01_AE (8%), A1 (4%), G (2%), K (2%), B (1%)]. Among 250 HIV-infected and 250 HIV-negative plasmas, 250 and 249, respectively, were positive or negative by INSTI®. Thus, INSTI® test sensitivity and specificity were 100% and 99.6%, respectively; positive and negative predictive values in Gabon were 91.5% and 100%, respectively. For the major subtype CRF_02AG, sensitivity and specificity were 100%. Finally, all 50 patients tested in parallel using plasma and capillary blood and were identified similarly.
Conclusions: HIV-1/HIV-2 INSTI® test is highly reliable for the detection of various non B HIV-1 antibodies, both in plasma and capillary blood; and it fulfills the WHO criteria for HIV test prequalification. The rapid INSTI® test could be useful for HIV screening in Gabon, as well as in other sub-Saharan African countries.

WEPDB0102

Evaluation of the Roche COBAS Ampliprep/COBAS TaqMan HIV-1 Qualitative version 2 assay on whole blood using specimens with unknown ARV exposure

R. Viana[1], T. Xaba[1], T. Stojiljkovic[1], N. Gunther[2], C. Wallis[1]
[1]Lancet Laboratories and BARC-SA, Department of Molecular Pathology, Johannesburg, South Africa, [2]Roche Products (PTY) LTD, Diagnostics Division, Johannesburg, South Africa
Presenting author email: carole.wallis@lancet.co.za

Background: Roche COBAS Ampliprep/COBAS TaqMan HIV-1 Qualitative version 2 (TaqMan v2 qual) has recently been released for testing of dried blood spot (DBS) for infants and plasma for adults that are antiretroviral (ARV) naïve; however, ARV status of patients is often unknown. This study evaluated the use of whole blood (WB) for HIV-1 detection using TaqMan v2 qual.
Methods: 133 samples (125 EDTA, 8 Virology Quality Assurance [VQA] WB) were used with known HIV-1 status (positive n=75; negative n=58) as per Roche Amplicor HIV-1 DNA PCR assay v1.5 (Roche v1.5). EDTA samples were split: 1ml plasma, 100ul WB and 70ul DBS. Samples were processed using TaqMan v2 qual according to manufacturer's instructions and results compared to Roche v1.5.
Sensitivity and specificity were determined for each sample type and compared to EDTA plasma viral load. Seven WB samples (HIV-1 positive n=4, HIV-1 negative n=3) were evaluated for reproducibility and precision using the TaqMan v2 qual.
Results: Of the 69 Roche v1.5 HIV-1 positive samples, 68 were detected using TaqMan v2 qual DBS or WB; whereas only 60 were detected using TaqMan v2 qual plasma. HIV-1 positive samples missed had either a viral load of not detected or <20 RNA copies/ml. The TaqMan v2 qual plasma samples missed 13% of HIV-1 positive samples.
No false positives were observed across the three different matrixes evaluated. Of the 8 VQA WB samples tested on TaqMan v2 qual and Roche v1.5, 100% concordance was observed (n=6 HIV-1 positive; n=2 HIV-1 negative). Diagnostic sensitivity and specificity are detailed in the table below. Reproducibility and precision was 100% for all samples tested.

Roche COBAS Ampliprep/COBAS TaqMan HIV-1 Qualitative version 2 Sample Type	Sensitivity	Specificity
Whole Blood	98.5%	100%
Plasma	87.0%	100%
Dried Blood Spot	98.5%	100%

[Table]

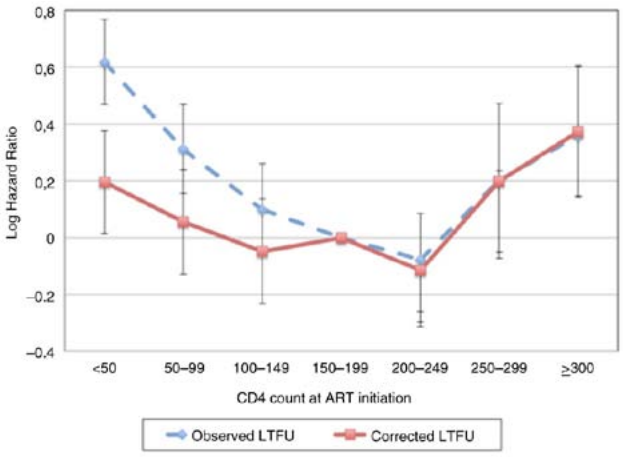
Conclusions: TaqMan v2 qual using DBS or WB had the highest sensitivity when compared to Roche v1.5 (98.5%). Plasma samples on TaqMan v2 qual missed 13% of HIV-1 positive samples. With the increase of microbicide use, pre-exposure prophylaxis and reported poor disclosure of prior ARV use, this study indicates that plasma samples are not the ideal sample matrix for testing adults when ARV exposure is unknown. The high percentage of adult samples that were missed would have serious implications for decreasing HIV-1 transmission rates.

WEPDB0103

CD4 count at antiretroviral therapy initiation and the risk of loss to follow-up: results from a multicentre cohort study

A. Grimsrud[1], M. Cornell[1,2], M. Schomaker[2], M.P. Fox[3,4,5], C. Orrell[6], H. Prozesky[7,8], K. Stinson[2,9], F. Tanser[10], M. Egger[11], L. Myer[2,12], International Epidemiologic Databases to Evaluate AIDS Southern Africa Collaboration (IeDEA-SA)
[1]Division of Epidemiology & Biostatistics, University of Cape Town, Cape Town, South Africa, [2]Centre for Infectious Disease Epidemiology & Research, University of Cape Town, Cape Town, South Africa, [3]Center for Global Health & Development, Boston University, Boston, United States, [4]Health Economics and Epidemiology Research Office, University of the Witwatersrand, Johannesburg, South Africa, [5]Boston University, Department of Epidemiology, Boston, United States, [6]Desmond Tutu HIV Centre, University of Cape Town, Cape Town, South Africa, [7]Division of Infectious Diseases, Department of Medicine, University of Stellenbosch, Stellenbosch, South Africa, [8]Tygerberg Academic Hospital, Cape Town, South Africa, [9]Médecins Sans Frontières, Cape Town, South Africa, [10]Africa Centre for Health and Population Studies, University of KwaZulu-Natal, Mtubatuba, South Africa, [11]Division of International and Environmental Health, Institute of Social and Preventive Medicine, University of Bern, Bern, Switzerland, [12]Division of Epidemiology and Biostatistics, University of Cape Town, Cape Town, South Africa
Presenting author email: agrimsrud@gmail.com

Background: Over the past decade of antiretroviral therapy (ART) scale-up, median CD4 counts at ART initiation have increased and ART initiation is recommended at progressively higher CD4 thresholds. However data on the relationship between CD4 count at ART initiation and loss to follow-up (LTFU) are limited and conflicting.
We investigated the association between higher CD4 counts at ART initiation and LTFU in South Africa (SA).
Methods: All adults initiating ART between 2008-2012 at 3 public sector sites in SA were included. LTFU was defined as no clinic visit in the 6 months before database closure. The Kaplan-Meier estimator and Cox's models examined the relationship between CD4 count at ART initiation and 24-month LTFU. Estimates of corrected LTFU were generated adjusting observed LTFU for unascertained deaths through linkage via identification numbers (IDs) with the SA National Population Register. Final models were adjusted for patient demographics, year of ART initiation, and programme expansion.
Results: Among 17,038 patients, the median CD4 at initiation increased from 119 [interquartile range (IQR): 54-180] in 2008 to 257 (IQR: 175-318) in 2012. In unadjusted models, observed LTFU was associated with both CD4 counts <100 cells/ml and CD4 counts ≥300 cells/ml compared to those with a CD4 count 150-199 cells/ml. After adjustment, patients with CD4 counts ≥300 cells/ml were 1.35 (95%CI: 1.12-1.63) times as likely to be LTFU after 24 months compared to those with a CD4 count 150-199 cells/ml. Correction for unascertained deaths attenuated the association between CD4 counts <100 cells/ml and LTFU while the association between CD4 counts ≥300 cells/ml and LTFU persisted (Figure 1). Increases in LTFU observed in patients with CD4 counts ≥300 cells/ml was greatest in the first 3 months on treatment. In sensitivity analyses imputing missing CD4 values at ART initiation and using inverse probability weighting to account for missing IDs, the association between higher CD4 counts and increased LTFU persisted.
Conclusions: Patients initiating ART at higher CD4 counts may be at increased risk for LTFU, particularly early after ART initiation. With programmes initiating patients at progressively higher CD4 counts models of ART delivery need to be reoriented to support long-term retention.



[Figure 1. Adjusted 12-month long log hazard ratios of observed and corrected LTFU from Cox's proportional hazards models by CD4 count at ART initiation]*
*Adjusted for year of ART initiation, gender, age, programme size and rate of expansion with CD4 150-199 cells/ml as the reference category

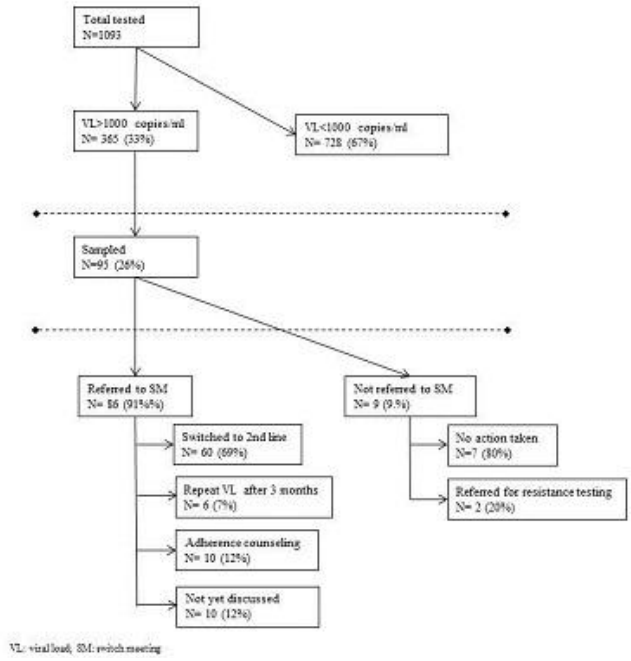
WEPDB0104

Clinical decision and outcomes of patients suspected of treatment failure and tested for HIV-viral load at the Infectious Diseases Institute (IDI), Kampala, Uganda

M.S. Nsumba[1,2], C. Barbara[1], R.Z. Musomba[3], A. Kaimal[4], K. Ivan[5], L. Isaac[6], J. Laurence[7], P.-R. Rosalind[7], K. Andrew[5]
[1]Infectious Disease Institute, Research Department, Kampala, Uganda, [2]Makerere University, Kampala, Uganda, [3]Infectious Disease Institute, Kampala, Uganda, [4]Infectious Disease Institute, PCT, Kampala, Uganda, [5]IDI, Research Department, Kampala, Uganda, [6]IDI, PCT, Kampala, Uganda, [7]IDI, Kampala, Uganda
Presenting author email: mnsumba@idi.co.ug

Background: WHO now recommends routine viral load (VL) monitoring, and the scale up of this has started in sub-Saharan Africa. Recent publications from the region suggest that often patients with detectable viral load delay switching to second line ART or are not switched.
Objective: To evaluate the outcome of patients with a VL>1,000 copies/ml accessing care at a large urban HIV Centre in Kampala, Uganda.
Methods: At IDI VL tests have been available since 2005. Until December 2014 these were reserved for patients with documented immunological or clinical failure. Those patients with detectable viral load are managed through a treatment failure path-way consisting of:
1) review of the results by the clinician,
2) case discussion in the weekly multidisciplinary "switch-meeting"
3) follow up by a clinician and counselor based on the decision reached during the "switch-meeting". We performed a retrospective audit of a sample of patients on first line ART with viral load >1,000 in 2014; data was extracted from 95 randomly sampled clinic files and the clinic database.

Results: 1093 patients on first line ART were tested for VL in 2014, of which 365 (33.4%) had a detectable VL; of these 95 (26%) clinical files were sampled. Median log10 VL was 4.9 (IQR: 4.7-5.3).
The diagram summarizes the action taken for the 95 sampled patients stratified by referral to the treatment failure path-way. 60/95 (63.1%) were switched to 2nd-line after a median time of 49 days (IQR: 14-84). Of note an action was taken for all patients referred to the treatment failure path-way.
Conclusions: The majority (65%) of patients with a detectable viral load were switched to 2nd-line, and an additional 28% had an action taken. This is a favorable outcome compared to outcomes in other treatment centers around SSA, and we believe that the "switch meeting" model has helped to ensure that action is taken. We advocate that this additional step be considered in WHO and national guidelines to ensure adherence strengthening and prompt switch to second line in patients failing ART.



[Summary]

WEPDB0105

Classification of HIV virological failure using whole blood versus plasma viral load

A. Khan[1], L. Hans[2], L. Gonzales[3], S. Carmona[2], N.-Y. Hsiao[1]
[1]Division of Medical Virology, University of Cape Town and National Health Laboratory Service, Cape Town, South Africa, [2]University of the Witwatersrand and National Health Laboratory Service, Department of Haematology and Molecular Medicine, Johannesburg, South Africa, [3]Alere Health Care, Johannesburg, South Africa
Presenting author email: aabida.khan@nhls.ac.za

Background: In resource limited settings, timely plasma separation and transportation to centralised laboratories is a major challenge to the scale-up of viral load (VL) testing. Whole blood (WB) collection and testing through either dried blood spots (DBS) or point-of-care VL assays are potential solutions. However, there is limited evidence on the performance of WB-based VL assays.
Methods: We evaluated three WB VL testing platforms, Alere q HIV-1/2, DBS Abbott RealTime HIV-1 and Roche CAP/CTM HIV-1 (DBS, free virus elution protocol) using routine clinical samples across a wide viral load spectrum chosen from South African public sector patients on combination antiretroviral therapy. Abbott RealTime HIV-1 was used as gold standard and virological failure (VF) was defined for plasma at 1000 copies/ml.
Results: Of the 299 samples selected, 153 (51%) had plasma VL>1000 copies/ml. Abbott DBS VL had the best overall VL correlation with its plasma counterpart (r^2=0.76), followed by the Roche DBS VL (r^2=0.62) and Alere q HIV-1/2 (r^2=0.46). Among samples with VF, Alere q HIV-1/2 and Abbott DBS assays were highly sensitive, correctly classified 100% and 98% of the samples respectively. Roche DBS assay was only able to identify 53% of the VF samples correctly. For samples with plasma VL< 1000 copies/ml there were upward misclassification due to further VL>1000 copies/ml identified by WB VL on both Alere q HIV-1/2 (81%) and Abbott DBS VL (21%) when compared to the plasma reference, while Roche DBS VL showed 99% agreement in this category. Receiver operating characteristic analysis revealed that the threshold of $\log_{10}$ 4.12, 3.43 and 2.60 copies/ml provided the best overall VF classification for Alere q HIV-1/2 (85%), Abbott DBS VL (94%) and Roche DBS VL (82%) respectively.

Abbott RealTime HIV-1 Plasma VL	LDL (lower than detectable limit)	Not LDL <1000 copies/ml	1000-10,000 copies/ml	>10,000 copies/ml
N =	94	52	52	101
Alere q HIV-1/2 WB % correct classification	22%	14%	100%	100%
DBS Abbott RealTime HIV-1 % correct classification	87%	63%	94%	100%
DBS Roche CAP/ CTM HIV-1 % correct classification	100%	98%	0%	80%

[% Correct Classification of VF by WB HIV VL]
Conclusions: Variability was noted between the different WB VL assays with difficulties assigning a uniform threshold across all platforms, reflecting the differences in sample treatment/processing (DBS versus fresh blood samples) and sample input volume. The performance at 1000 copies/ml of DBS protocols and point-of-care devices remains significantly varied and further development is required to ensure minimal VF misclassification.

WEPDC01 The Moving Epidemic: Demographics and Migration

WEPDC0101

Geographic origin trends among HIV+ mothers and children in Canada and impact on vertical HIV transmission rates

J. Brophy[1,2], T. Lee[3], L. Sauve[4,5], A. Bitnun[6,7], J. Singer[3], F. Kakkar[8,9], N. Lapointe[8,9], A. Alimenti[4,5], D. Money[4,10,11], W. Vaudry[12,13], L. Samson[1,2], for the Canadian Pediatric and Perinatal AIDS Research Group
[1]Children's Hospital of Eastern Ontario, Ottawa, Canada, [2]University of Ottawa, Department of Pediatrics, Ottawa, Canada, [3]CIHR - Canadian HIV Trials Network, Vancouver, Canada, [4]BC Women's Hospital and Health Centre, Vancouver, Canada, [5]University of British Columbia, Department of Pediatrics, Vancouver, Canada, [6]The Hospital for Sick Children, Toronto, Canada, [7]University of Toronto, Department of Pediatrics, Toronto, Canada, [8]CHU Ste-Justine, Montréal, Canada, [9]Université de Montréal, Department of Pediatrics, Montréal, Canada, [10]University of British Columbia, Department of Obstetrics, Vancouver, Canada, [11]Women's Health Research Institute, Vancouver, Canada, [12]Stollery Children's Hospital, Edmonton, Canada, [13]University of Alberta, Department of Pediatrics, Edmonton, Canada
Presenting author email: jbrophy@cheo.on.ca

Background: Migration contributes significantly to new HIV cases in Canada. This study describes geographic origin trends among HIV+ mothers and perinatally infected children and the impact of geographic origin on vertical HIV transmission (VT) rates among HIV+ mother-infant pairs (MIP) in Canada from 1990-2013.
Methods: The Canadian Perinatal HIV Surveillance Program collects data at 22 centres. The primary focus is on MIP with an infant born in Canada and identified prior to/within 3 months of birth; MIP with Canadian-born infants identified after 3 months and HIV+ children born abroad are also tracked. Data reviewed for this study included: maternal country of origin, clinical characteristics, antiretroviral usage and infant outcome. Logistic regression determined VT rate differences for foreign-born (FBM) versus Canadian-born mothers (CBM).
Results: Among 3877 MIP, 2089 (53.9%) mothers were FBM. Of 1481 (70.9%) African mothers, 30.7%, 20.1%, 17.7%, and 16.7% came from East, Central, Horn, and West Africa, respectively. CBM accounted for 66.7% (971/1456) in Western/Central Canada, whereas FBM predominated in Ontario (945/1357, 69.6%; greatest proportion East African, 25.0%) and Quebec (713/1020, 69.9%; greatest proportion Caribbean, 36.2%). The largest numbers of FBM originated from Haiti (12.5%), Ethiopia (8.7%), Congo (7.0%), Zimbabwe (5.4%), and Nigeria (4.6%). In the pre-cART era (1990-1996), Haiti contributed 29.9% (90/301) of FBM, decreasing to 13.0% (119/918) in 1997-2007, and 6.6% (52/782) in 2008-2013. Since 2008, Ethiopia (80/782, 10.2%), Congo (64/782, 8.2%), and Nigeria (62/782, 7.9%) predominated.
VT rate among Canadian-born children from 1990-2013 was 3.8% (3.0% among FBM) and 1.2% from 2008-2013 (0.7% among FBM). African mothers had lower risk of VT (1990-2013: OR = 0.45, 95%CI 0.29-0.71; 2008-2013: OR 0.35, 95%CI 0.12-1.08) compared to CBM; no differences were seen for other regions.
Of 353 HIV+ children (born in Canada or abroad) with FBM, the greatest numbers came from Haiti (48, 13.6%), Ethiopia (33, 9.3%), Burundi (30, 8.5%), and Congo (15, 4.2%).
Conclusions: Geographic origins of HIV+ FBM in Canada have changed over time, shifting from predominantly Haitian in the pre-cART era to predominantly African more recently. African mothers have lower VT rates than CBM. Understanding country-specific cultural and obstetrical/pediatric health issues is imperative to providing optimal care.

WEPDC0102

The Canadian perinatal HIV surveillance program (CPHSP): program description and trends in demographics, treatment and transmission

J. Singer[1,2], A. Bitnun[3], T. Lee[4], L. Samson[5], J. Brophy[5], D. Money[6], A. Alimenti[6], W. Vaudry[7], F. Kakkar[8], N. Lapointe[8], L. Sauve[6], Canadian Pediatric & Perinatal AIDS Research Group
[1]University of British Columbia, School of Population and Public Health, Vancouver, Canada, [2]CIHR Canadian HIV Trials Network, Vancouver, Canada, [3]Hospital for Sick Children, University of Toronto, Toronto, Canada, [4]CIHR Canadian HIV Clinical Trials Network, Vancouver, Canada, [5]Children's Hospital of Eastern Ontario, University of Ottawa, Ottawa, Canada, [6]BC Women's Hospital and Health Centre, University of British Columbia, Vancouver, Canada, [7]Stollery Children's Hospital, University of Alberta, Edmonton, Canada, [8]Hopital Ste-Justine, University of Montreal, Montreal, Canada
Presenting author email: singerjoel@hotmail.com

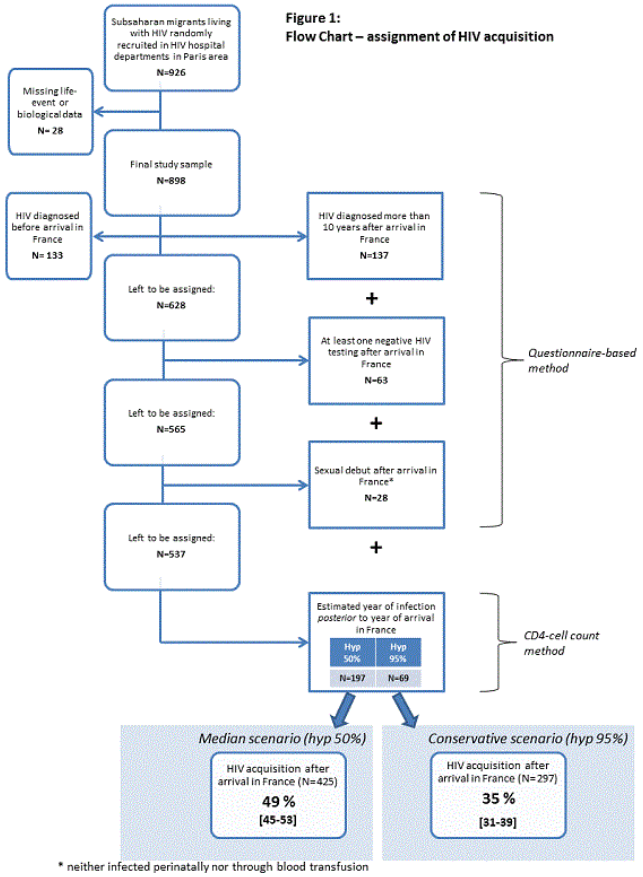
Background: The Canadian Perinatal HIV Surveillance Program (CPHSP) is an active surveillance program generating national data HIV+ women and their infants in Canada since 1990. We describe the CPHSP's evolving methodology and analyze mother-infant pair (MIP) demographics, antiretroviral treatment and vertical transmission (VT) rates in Canada from 1990-2013.
Methods: MIPs are identified at 22 centers following obstetric or pediatric referral for care. Data is entered via a secure web-based Oracle database, which is managed and analysed by the CIHR-Canadian HIV Trials Network. A nationally representative steering committee provides direction and oversight. Data collected include maternal characteristics, antiretroviral therapy (ART) and infant outcome. VT rates are based on data of MIP delivered in Canada and identified within 3 months after birth; infants identified beyond 3 months of birth are tracked separately.
Results: Among 2914 MIP from the combination ART (cART) era (1997-2013), the overall VT rate was 2.1% but only .7% in MIP receiving cART and 0.1% in women receiving >4 week of cART. Of 200 identified HIV+ women giving birth in Canada in 2013, 76% acquired HIV heterosexually, 17% through injection drug use (IDU) and 2% perinatally; 53% of mothers were Black and 23% Aboriginal. The proportion untreated steadily decreased from 20.3% in 1997 to 3.0% in 2013. Aboriginal women (7%) continued to represent the largest proportion of untreated women (7%) in 2013, though this decreased from a peak of over 20% during the period 2005-2009. . A similar improvement was seen among IDU, with only 3% untreated in 2013. In 2013, seven (3.5%) women had no antenatal cART or suboptimal treatment, the lowest annual number and percentage in the cART era, resulting in two children becoming infected.
Conclusions: The CPHSP allows for comprehensive identification of perinatal HIV exposure and outcome trends in Canada. Ongoing challenges include ensuring all MIPS are captured given Canada's geographically and demographically diverse population and low HIV prevalence. Despite continued improvement in treatment access for pregnant HIV+ women, VT continues to occur with Aboriginal women being at greater risk of inadequate treatment and VT.

WEPDC0103

HIV acquisition after arrival in France among sub-Saharan African migrants living with HIV in Paris area. Estimations from the ANRS PARCOURS study

A. Desgrees du Lou[1], J. Pannetier[1], A. Ravalihasy[1], A. Gosselin[1], V. Supervie[2], N. Bajos[3], F. Lert[4], N. Lydie[5], R. Dray-Spira[2]
[1]IRD, CEPED, Paris, France, [2]INSERM, IPLESP, Paris, France, [3]INSERM, CESP, Le Kremin Bicêtre, France, [4]INSERM, CESP, Villejuif, France, [5]INPES, Saint Denis, France
Presenting author email: julie.pannetier@ceped.org

Background: HIV acquisition among sub-Saharan migrants living in Europe has long been considered to predominantly occur before migration because of generalized HIV epidemics in sub-Saharan African countries. Recent evidence suggests that a substantial proportion have acquired HIV while they were living in Europe. In the UK, this proportion was recently estimated at 31% using a CD4-based modelling approach. Such an estimate is not currently available for France.
Methods: We estimated the proportion of sub-Saharan migrants who acquired HIV infection after their arrival in France using life-event and clinical information on a random sample of HIV-infected hospital outpatients born in sub-Saharan Africa in Paris region. We assumed that HIV infection had probably been acquired in France if at least one of the following life-event criterion was fulfilled:
i) HIV diagnosis >10 years after arrival in France,
ii) ≥1 negative HIV test in France,
iii) sexual debut after arrival in France.
If none of these criteria was fulfilled, we estimated the duration from HIV infection based on first CD4 count measurement using statistical modelling. Infection was assigned in France if, out of 500 durations estimated for each individual, >50% (median scenario) or >95% (conservative scenario) fell within the period while individuals were living in France.



[Flow chart - assignment of HIV acquisition]

Results: Of the 898 HIV-infected adults born in sub-Saharan Africa included in the analysis, we estimated that 49% [95% confidence interval: 45-53] in the median scenario and 35% [31-39] in the conservative scenario acquired HIV while living in France. This proportion was lower for women than men (30% [25-35] versus 44% [37-51] in the conservative scenario) and increased with duration in France.

	Men					Women			
		N	Weighted %	95%CI	p value	N	Weighted %	95% CI	p value
Overall		348	43.9	37.4-50.6		550	30.0	25.1-35.4	
Age at arrival in France	<25 y	84	78.1	65.5-87.1	<0.001	171	54.1	46.5-61.5	<0.001
	25-34 y	139	44.3	35.9-53.2		251	24.5	17.7-32.8	
	35 y and more	125	19.8	13.0-28.8		128	8.4	4.4-15.5	
Number of years in France prior to diagnosis	0 to 2	137	10.3	4.9-20.6	<0.001	254	5.4	3.2-8.9	<0.001
	3 to 5	45	19.3	7.0-43.0		93	23.4	18.6-29.0	
	6 to 9	39	54.0	36.2-70.9		67	52.5	36.3-68.3	
	10 or more	106	93.5	85.4-97.3		95	86.0	77.0-91.9	

[France HIV acquisition - conservative scenario]

Conclusions: The proportion of sub-Saharan African migrants having acquired HIV infection while living in France is high, highlighting the need for improved focused HIV prevention. This requires a better understanding of the determinants of HIV infection in France in this population.

WEPDC0104

Evidence of local HIV transmission in the African community of King County, Washington

R. Kerani[1,2], J. Herbeck[3], S. Buskin[2], J. Dombrowski[1,2], A. Bennett[2], E. Barash[4], L. Barbee[1,2], M. Golden[1,2]
[1]University of Washington, Medicine, Seattle, United States, [2]Public Health - Seattle and King County, HIV/STD Program, Seattle, United States, [3]University of Washington, Global Health, Seattle, United States, [4]Public Health - Seattle and King County, Communicable Disease Epidemiology, Seattle, United States
Presenting author email: rkerani@uw.edu

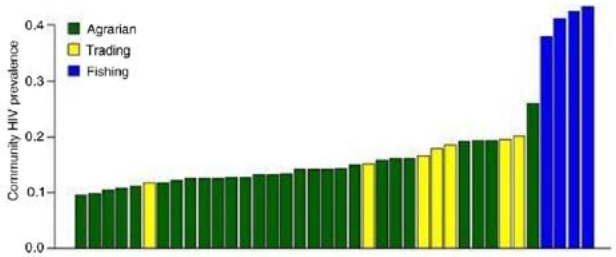
Background: In many parts of the U.S., immigrants from sub-Saharan Africa comprise a large proportion of heterosexual HIV cases. However, little is known about the frequency of ongoing HIV transmission within these communities.
Methods: Public Health-Seattle and King County staff routinely interview patients newly reported with HIV infection, and attempt to contact sex partners to ensure notification and HIV testing. We describe the characteristics, testing history, and partner outcomes for African-born persons newly reported with HIV infection in King County (KC), WA from 1/1/2010-12/31/2013. Additionally, we reconstructed an HIV-1 pol phylogeny for 1430 cases diagnosed in KC 2008-2014, with 100 sequences each from Kenya and Ethiopia added for African references.
Results: During the study period, 1,148 adults were reported with HIV in KC, including 101 (8.8%) born in Africa. Of 63 cases in African-born individuals with new HIV diagnoses, 49 (77.8%) were interviewed for partner services.
Seven reported being diagnosed with HIV-infection before U.S. arrival and were excluded from further analysis, leaving 42 individuals. Median time from U.S. arrival to HIV diagnosis was 7.0 years (range: 8 days-26.7 years). Most were born in East African countries (N=34, 81.0%).
Twenty-seven (64.3%) were women; mean age was 42.6 years (range: 24.9-62.2).
Sixteen (38.1%) cases reported at least one negative test prior to HIV diagnosis, and 11 (31.4%) reported ≥1 negative HIV test after U.S. arrival. Pol genotypes were available for 7 of these 11 cases; for 6 of these 7, a local case was the nearest phylogenetic neighbor, and 2 were infected with subtype B virus.
This suggests local transmission sources for these 6 cases. The 42 newly diagnosed individuals identified 47 partners; 6 (12.8%) partners had been diagnosed with HIV infection prior to the investigation. Thirteen partners were newly HIV tested as a result of index patients' HIV diagnoses; 5 (38.5%) were HIV-infected. Of the 11 partners who were previously positive (6) or newly diagnosed (5), 7 were interviewed and 6 were African-born.
Conclusions: We found substantial evidence of ongoing HIV transmission in the African community of KC. Additional efforts are needed to increase HIV testing and prevention among African immigrants in the U.S.

WEPDC0105

Heterogeneity of the HIV epidemic in rural Africa: findings from a geospatially informed study of HIV epidemiology in fishing, trading, and agrarian communities in Rakai, Uganda

L. Chang[1,2], M.K. Grabowski[2], R. Ssekubugu[3], F. Nalugoda[3], S. Reynolds[1,4], J. Lessler[2], S. Moore[2], T. Quinn[1,4], R. Gray[2], D. Serwadda[3], M. Wawer[2]
[1]Johns Hopkins School of Medicine, Division of Infectious Diseases, Baltimore, United States, [2]Johns Hopkins Bloomberg School of Public Health, Baltimore, United States, [3]Rakai Health Sciences Program, Kalisizo, Uganda, [4]National Institutes of Health, Laboratory of Immunoregulation, Division of Intramural Research, National Institute for Allergy and Infectious Diseases, Bethesda, United States
Presenting author email: mgrabows@jhsph.edu

Background: National and district level HIV prevalence rates may obscure substantial variation of HIV disease burden at the community level. Understanding the extent to which HIV differs across communities and the drivers of disparities and similarities within individual districts may offer opportunities for a more effective, targeted HIV response.
Methods: HIV prevalence and risk behaviors were assessed among 17,109 individuals (53.8% female vs. 46.2% male) in 40 communities in Rakai District, Uganda between August 2011 and October 2013 through the population-based Rakai Community Cohort Study. Communities were classified as lakeside fish landing sites (n=4), agrarian (n=27), or trading communities (n=9) based upon occupation analysis. HIV prevalence was geospatially mapped using Bayesian methods and variability across and within community classifications was characterized. Differences in risk behaviors between communities were assessed using modified Poisson regression models.
Results: There was large variation in HIV prevalence, ranging from 9% to 43%, across communities (see Figure below). Fish landing sites had a mean HIV prevalence of 41% (range: 37-43%). Mean HIV prevalence in trading communities was 17% with substantial variability (range: 11-22%) and 14% in agrarian communities, also with substantial variability (range: 9-26%). Agrarian and trading communities in close proximity (<18 km) to fishing landing sites had HIV prevalence ranging from 11% to 26%. Overall, HIV prevalence was higher among women than men (p=0.01), and the disparity was greatest in the fish landing sites (49% vs. 34%). The proportion of males and females reporting >=four sex partners in the last year was 6.4 (95%CI: 4.1-11.0) and 3.2 (95%CI: 2.7-3.8) times higher in fishing communities than in the agrarian/trading population, respectively. Levels of consistent condom use with non-marital partners were significantly lower in the fish landing sites (RR=0.80, 95%CI: 0.69-0.94).



[HIV prevalence in each of the 40 RCCS communities]

Conclusions: Large variations in HIV prevalence and risk factors across communities in rural Rakai underscores the need for a granular approach to HIV prevention and response based on local assessment of HIV burden and risks and locally tailored interventions that may include targeting of high risk groups such as those in fish landing sites.

WEPDD01 Novel Programmatic Approaches for Diagnostics

WEPDD0101

Cost-effectiveness of implementing CRAG-LFA screening for cryptococcal meningitis among people living with HIV in Uganda

A. Ramachandran[1], Y. Manabe[2], R. Rajasingham[3], M. Shah[2]
[1]Johns Hopkins University School of Medicine, Baltimore, United States, [2]Johns Hopkins University School of Medicine, Infectious Disease, Baltimore, United States, [3]University of Minnesota, Minneapolis, United States
Presenting author email: aramach7@jhmi.edu

Background: Cryptococcal meningitis (CM) constitutes a significant source of morbidity and mortality in resource-limited regions. One million cases occur annually, representing 10-30% of HIV-related death in prevalent regions. Optimal interventions for CM prevention remain unclear. The recently developed serum cryptococcal antigen lateral-flow assay (CRAG-LFA) is highly sensitive and specific, and may allow early detection of subclinical cryptococcemia in those at risk of developing CM. We sought to determine the cost-effectiveness of implementing CRAG-LFA screening for people living with HIV in Uganda compared to other interventions for CM prevention.
Methods: A decision-tree model was constructed to compare three strategies for cryptococcal prevention among people living with HIV (PLWH) with CD4< 100: Standard of care (SOC, i.e. no cryptococcal screening), CRAG-LFA screening followed by evaluation and treatment of cryptococcemia, or universal primary prophylaxis (UPP) with fluconazole for all patients and no CRAG-LFA screening. Primary outcomes were expected costs, DALY's, and incremental cost-effectiveness ratios (ICERs). In sensitivity analysis we analyzed the impact of costs, prevalence, and alternative clinical algorithms on the cost-effectiveness of CRAG-LFA screening.
Results: CRAG-LFA screening was associated with an ICER of $5.88 per DALY averted compared to SOC, and was highly cost-effective at current willingness to pay thresholds for Uganda. CRAG-LFA screening dominated the UPP intervention (i.e. both cheaper and more effective). Overall, implementation of CRAG-LFA screening was projected to cost $1.46 more per person than SOC, and could reduce the relative risk of cryptococcal-associated mortality by over 40%. When including the cost of lifetime ART, the ICER for CRAG-LFA screening was $557 compared to SOC and still considered cost-effective. In sensitivity analysis, prevalence of baseline CM and cost of the CRAG-LFA influenced cost-effectiveness. In probabilistic sensitivity analysis, the CRAG-LFA screening intervention was cost-effective in 100% of simulations, and cost-saving in 30% of simulations.
Conclusions: CRAG-LFA screening is extremely cost-effective with the potential to prevent significant morbidity and mortality from CM in vulnerable populations, and represents excellent value for money as a screening intervention for HIV programs in Uganda.

Intervention	Total Cost	Incremental Cost	Incremental Cost (including lifetime ART)	DALYs Accumulated	Incremental Effectiveness (DALYs averted)	Incremental Cost-Effectiveness Ratio (ICER)	Incremental Cost-Effectiveness Ratio (ICER) including lifetime ART
Standard of Care (SOC)	9.12	REFERENCE	REFERENCE	8.55	REFERENCE	REFERENCE	REFERENCE
CRAG-LFA Screening	10.58	1.46	139.48	8.30	0.25	5.88	557.60
Universal Primary Prophylaxis (UPP)	236.23	227.10	332.19	8.35	0.20	1141.96	1660.95

[Cost-Effectiveness Projection Results]

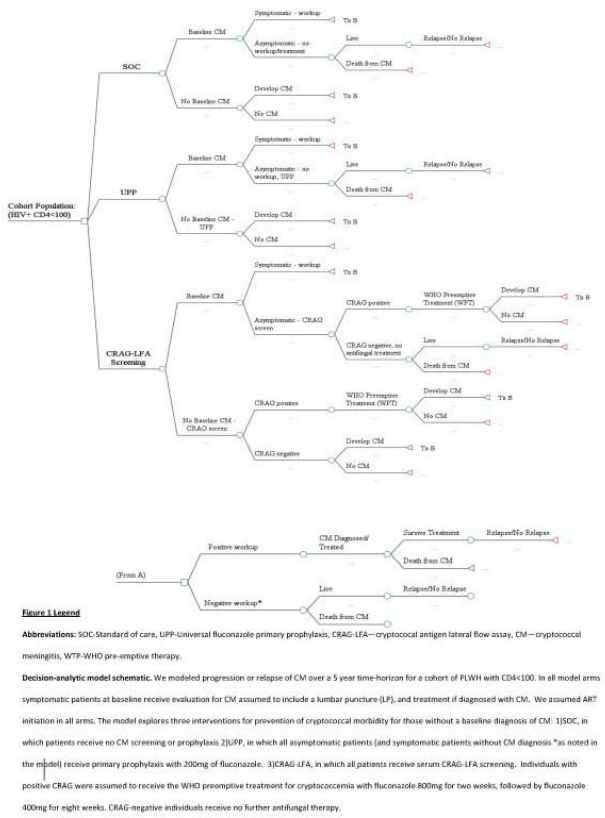


Figure 1 Legend

Abbreviations: SOC-Standard of care, UPP-Universal fluconazole primary prophylaxis, CRAG-LFA—cryptococcal antigen lateral flow assay, CM—cryptococcal meningitis, WTP-WHO pre-emptive therapy.

Decision-analytic model schematic. We modeled progression or relapse of CM over a 5 year time-horizon for a cohort of PLWH with CD4<100. In all model arms symptomatic patients at baseline receive evaluation for CM assumed to include a lumbar puncture (LP), and treatment if diagnosed with CM. We assumed ART initiation in all arms. The model explores three interventions for prevention of cryptococcal morbidity for those without a baseline diagnosis of CM: 1)SOC, in which patients receive no CM screening or prophylaxis 2)UPP, in which all asymptomatic patients (and symptomatic patients without CM diagnosis *as noted in the model) receive primary prophylaxis with 200mg of fluconazole. 3)CRAG-LFA, in which all patients receive serum CRAG-LFA screening. Individuals with positive CRAG were assumed to receive the WHO preemptive treatment for cryptococcemia with fluconazole 800mg for two weeks, followed by fluconazole 400mg for eight weeks. CRAG-negative individuals receive no further antifungal therapy.

[Figure 1. Decision-Analysis Model Schematic]

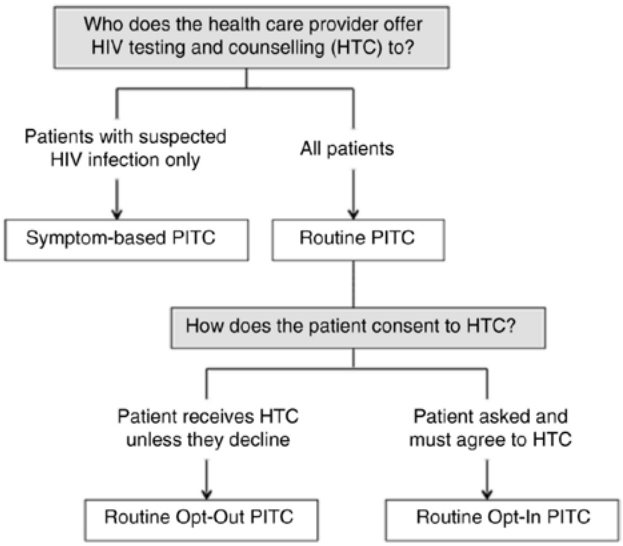
WEPDD0102

Lost opportunities to identify and treat HIV-infected patients: results from a comprehensive study of provider-initiated HIV testing and counseling (PITC) in Malawi

M. Schwarz[1], R. Flick[2,3], M. Harawa[2], K. Simon[2,4], M. Kim[2,4], J. Robison[5], S. Ahmed[2,4]
[1]University of Utah School of Medicine, Salt Lake City, United States, [2]Baylor College of Medicine - Abbott Fund Children's Clinical Center of Excellence, Lilongwe, Malawi, [3]University of Colorado School of Medicine, Denver, United States, [4]Baylor International Pediatric AIDS Initiative at Texas Children's Hospital, Baylor College of Medicine, Houston, United States, [5]University of Utah, Department of Pediatrics, Salt Lake City, United States
Presenting author email: monica.ann.schwarz@gmail.com

Background: Early diagnosis and treatment of HIV improves patient outcomes and minimizes risk of transmission. Provider-initiated testing and counseling (PITC) is an effective case-finding strategy, but implementation models vary. Malawi Ministry of Health (MOH) guidelines recommend routine opt-out PITC, in line with WHO recommendations for countries with generalized epidemics, but little is known about its implementation. Our objective was to assess PITC implementation in Malawi.

Methods: We conducted a cross-sectional study of PITC implementation at 118 clinics and wards within 12 MOH facilities in central Malawi during June-July 2014. Qualitative data detailing PITC practices was collected through structured interviews with 71 providers who conduct HIV testing at their facility, and characterized using standardized definitions (Figure 1). Quantitative data describing patient visits and HIV tests recorded during 2013 was abstracted from MOH HIV testing reports.



[Figure 1 Definitions of PITC models]

Results: Variable models of PITC were reported across facilities and departments (Table 1). Overall, symptom-based PITC was most commonly reported. Only antenatal and maternity (20/24) departments reported implementing routine opt-out testing. Use of a PITC register varied significantly according to department type.

Only 7.7% (86,657/1,102,802) of patient visits in 2013 included an HIV test. Subgroup analysis of TB and antenatal clinics with available data demonstrated that HIV status was ascertained in 94.3% (5,293/5,615) and 86.8% (26,831/30,961) of patients, respectively.

Providers most commonly cited test kit shortages (71/71 providers), inadequate physical space (58/71), and inadequate number of HIV counselors (32/71) as challenges in PITC implementation. Providers from inpatient units cited the inability to test on weekends (8/16).

	Types of PITC Reported - n (%)			
Department type	Routine opt-out	Routine opt-in	Symptom-based	PITC register in use - n (%)
TB Clinic	5/12 (42)	7/12 (58)	0/12 (0)	12/12 (100)
Antenatal Clinic & Maternity Ward	20/24 (83)	4/24 (17)	0/24 (0)	24/24 (100)
Family Planning Clinic	1/11 (9)	7/11 (64)	3/11 (27)	8/11 (73)
STI Clinic	3/6 (50)	3/6 (50)	0/6 (0)	6/6 (100)
Outpatient Department, Under-5 Clinic, & Immunization Clinic	4/36 (11)	4/36 (11)	28/36 (78)	9/36 (25)
Malnutrition Clinic	7/10 (7)	2/10 (20)	1/10 (10)	5/10 (50)
Adult & Pediatric Inpatient Wards	1/19 (5)	3/19 (16)	15/19 (79)	5/19 (26)
Totals	41/118 (35)	30/118 (25)	47/118 (40)	69/118 (59)

[Table 1 Reported PITC model & use of PITC register]

Conclusions: Various models of PITC concurrently exist at MOH facilities in Malawi. Only antenatal and maternity clinics demonstrated high rates of routine opt-out PITC. The low ratio of facility visits that included an HIV test suggest missed opportunities for HIV testing. However, the high proportion of patients at TB and antenatal clinics with known HIV status suggest routine testing is feasible. These results underscore the need to develop clear, standardized PITC protocols and tools, and to address obstacles of limited health commodities, infrastructure, and human resources.

WEPDD0103

Evaluation of HIV PIMA™CD4 point-of-care test operation by trained non-health workers in rural health centers in Chiradzulu District, Malawi

B. Schramm[1], A. Tayea[2], L. Wolters[2], S. Nicholas[1], C.W. Masiku[3], D.B. Zolowere[4], E. Mhango[5], J.R. Kandulu[5], J.-F. Etard[1,6], I. Amaros[3], E. Szumilin[7], M. Gueguen[7]
[1]Epicentre, Paris, France, [2]Medecins sans Frontieres, Chiradzulu, Malawi, [3]Medecins sans Frontieres, Lilongwe, Malawi, [4]Ministry of Health, Chiradzulu, Malawi, [5]Ministry of Health, Lilongwe, Malawi, [6]Université de Montpellier, UMI 233 Institut de Recherche pour le Développement, Montpellier, France, [7]Medecins sans Frontieres, Paris, France
Presenting author email: birgit.schramm@epicentre.msf.org

Background: CD4 count is essential to identify antiretroviral treatment (ART) eligibility. For over a decade, Médecins Sans Frontières and the Ministry of Health provides ART in 10 rural health centers (HCs) in Chiradzulu District, Malawi. From June 2013, Alere's PIMA™ CD4 point-of-care (POC) test is being implemented in the HCs. Shortage of health care- and laboratory staff is an issue in this setting.
We assessed task-shifting of PIMA CD4 test operation to non-health workers living in the community around the HCs.
Methods: Four non-health workers received a one-week structured training on PIMA CD4 POC operation. Between June 2014 and January 2015, 331 venous blood samples of pre-ART and ART-patients attending routine CD4-testing in 2 rural HCs were included. Each sample was assessed on site with PIMA by a lab technician (LT) and a trained community worker (TCW), and measured with PartecCyflow® counter at district hospital. Kappa-coefficient and percent agreement for CD4-classification below and above relevant thresholds were obtained. Bias and limits of agreement (LOA) were assessed for absolute CD4 counts. PIMA error-rates and failed runs (2 consecutive errors) were recorded and TCW-operator acceptability assessed.
Results: Three-hundred-twenty-eight venous blood samples (85% ART-patients, 68.5% female) were included. Median CD4 count (LT PIMA) was 425 cells/µl (IQR: 323, 570). Error rates were low (LT: 1.2% vs TCW: 2.4%, p= 0.34) and no failed runs occurred. Good agreement was achieved for PIMA results by LTs versus TCWs for CD4 threshold 350 cells/µl (91.7% (CI95%: 88.2-94.5); kappa=0.80)) and 500 cells/µl (91.1% (CI95%: 87.5-93.9); kappa=0.80)). The mean bias (TCW-PIMA minus LT-PIMA) was low (-2.2 cells/µl (LOA: 137.4, -141.9). Bias and LOA comparing PIMA results by LTs or TCW versus Partec was similar (LT-PIMA minus Partec: - 46.4 cells/µl (95.9, -188.8)); TCW-PIMA minus Partec: - 46.5 cells/µl (118.0 -211.0)). TCWs rated PIMA operation as very easy.
Conclusions: Adequately trained community workers delivered CD4 results equivalent to lab technicians with PIMA POC in health center laboratories. Task shifting of simplified CD4 POC-technologies to trained non-health care staff can serve as a key strategy to ensure sustainable provision of CD4-testing in support of ART-initiation in rural facilities.

WEPDD0104

Improving dried blood spot (DBS) transport logistics for early infant diagnosis (EID) in Nigeria: *the SPEEiD model*

N. Ndulue[1], A. Etsetowaghan[1], C. Gabriel[2], J. Ibrahim[3]
[1]Management Sciences for Health, Clinical Unit, Abuja, Nigeria, [2]Management Sciences for Health, Laboratory System Strengthening, Ilorin, Nigeria, [3]Nigerian Postal Service, Expedited Mail Service, Ilorin, Nigeria
Presenting author email: nndulue@msh.org

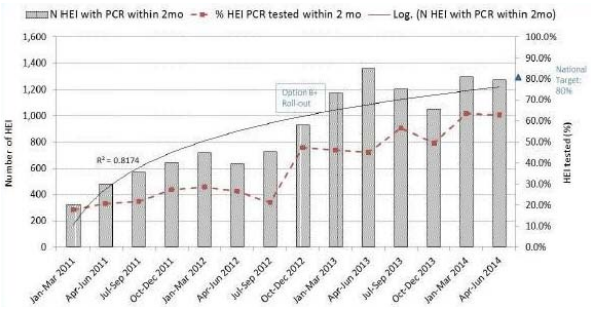
Background: WHO recommends that all children exposed to HIV be tested within 4 to 6 weeks of birth to ensure that all infected infants are identified and initiated on treatment early. One major challenge with EID of HIV in Nigeria remains the absence of standardized logistic sample transfer systems, resulting in long turnaround times between date of sample collection and date of return of result to the mother. To address this challenge, the USAID-funded ProACT project implemented by MSH, pioneered the "Strengthening the Process and Efficiencies for Early infant Diagnosis (*SPEEiD*) model, which involves the transportation of DBS samples from remote HIV clinics to regional PCR labs using the Nigerian Postal Service (NIPOST) Express Mail Service (EMS) platform, which has a network of over 3,900 post offices and agencies spread across the country, ensuring penetrance to remote HIV clinics. The objective of this study was to review the effect of utilizing an innovative DBS transport model in improving DBS transportation.
Methods: We carried out a retrospective analysis of logistic data from 177 samples transferred from 28 PMTCT sites using the *SPEEiD* model over a 12 month period from March 2013 to February 2014 in Kwara state, North Central Nigeria.
Results: A review of the data showed a reduction in turnaround time for return of results from 3-6 months to 3-4 weeks utilizing the *SPEEiD* Model. Results were received for 97% of samples (171/177) transported with this model, compared to 51% previously. The average cost of sample transfer was estimated at between $20-$40 per batch and remains comparatively less expensive to other models by at least 30%.
Conclusions: The MSH *SPEEiD* model remains an indigenous, cost effective, sustainable, and time sensitive sample transfer model which ensures that exposed infants are able to receive their EID test results quickly. This approach may be easily replicated by other partners working in similar resource limited settings, as it provides a practical solution for DBS sample transfer, which remains one of the major challenges affecting EID of HIV in Nigeria.

WEPDD0105

Trends in early infant HIV diagnosis and treatment (EIDT) services in rural South-West Uganda (2011-2014)

J. Seclen-Palacin[1], E. Natumanya[2], L. Nabitaka[3], E. Bitarakwate[2], S. Ismail[1]
[1]Elizabeth Glaser Pediatrics AIDS Foundation, Washington D.C., United States, [2]Elizabeth Glaser Pediatrics AIDS Foundation Uganda, Mbarara, Uganda, [3]Ministry of Health of Uganda, AIDS Control Program, Kampala, Uganda
Presenting author email: jseclen@gmail.com

Background: In Uganda, 39% of HIV exposed infants (HEI) were HIV tested within 2 month and less than 30% of children accessed to ARVs (UNAIDS, 2014) which reveal challenges to reach to EIDT services. Through implementation of Strengthening TB and HIV/AIDS response in Uganda Southwestern Region (STAR-SW) project, EGPAF provides support to districts and sites to strengthen and increase access to EIDTservices. This includes training and mentoring site-based health care workers (nurses, clinicians) on proper utilization of EID guidelines (counseling and testing manuals, treatment protocols), optimizing patient care flow, expanding points of care, strengthening laboratory capacity, utilization of EIDT clinical registers and reporting, and conducting regular data reviews for continuous improvement. This report describes trends of accessing EIDT services under this project.
Methods: Using HIV program data from the Uganda Health System for January 2011 to June 2014, we conducted an EIDT analysis covering all 192 supported sites. Indicators analyzed were number of HIV-positive pregnant women identified during antenatal care, HIV-positive mothers delivered at health institutions, HEI received ARV at birth, exposed infants tested for HIV within two months after birth. ARV uptake and HIV testing coverage were estimated by dividing number of HEI received ARVs at birth and who were tested within two months between HIV-positive pregnant women in ANC, respectively. Descriptive and trends analysis were conducted.
Results: By January 2011, HEI testing coverage was 17.8%, which increased to 47.5% in December 2012. With the rollout of the Option B+ in early 2013, HEI testing continued to increase and reached around 63% in mid-2014 (trend R^2=0.8174). Simultaneously, HEI receiving ARVs at maternity progressively increased over time from 17% (312/1,799) in January 2011 to 32% at the end of 2012, peaking at 48% (966/2,026) in June 2014.



[Figure 1. Trends of EID for HIV in Southwestern Uganda: 2011-2014]

HEI accessing to ARVs	Jan-Mar 2011	Apr-Jun 2011	Jul-Sep 2011	Oct-Dec 2011	Jan-Mar 2012	Apr-Jun 2012	Jul-Sep 2012	Oct-Dec 2012	Jan-Mar 2013	Apr-Jun 2013	Jul-Sep 2013	Oct-Dec 2013	Jan-Mar 2014	Apr-Jun 2014
HIV+ pregnant woman ANC	1799	2325	2611	2357	2499	2392	3418	1958	2550	3008	2126	2121	2039	2026
HEI born at maternity (n)	312	430	513	518	674	700	635	644	816	792	860	813	821	966
HEI on ARV (%)	17%	18%	20%	22%	27%	29%	19%	33%	32%	26%	40%	38%	40%	48%

[Table 1]

Conclusions: HIV testing and ARV uptake for HEI have progressively improved in STAR-SW catchment area. The various site level of support provided by EGPAF seems to have contributed to these results. EGPAF will continue supporting the national and district health systems in further expansion of EIDT services as well as on further analysis of disaggregated data, informing quality improvement interventions, and planning additional operational research studies.

WEPDD0106

Sensitivity of a rapid point of care assay for early HIV antibody detection is enhanced by its affinity for HIV gp41 IgM antibodies

N. Moshgabadi, R. Galli, A. Daly, S.M.S. Ko, M. Zhang, T. Westgard, A. Bulpitt, C.R. Shackleton
Biolytical Laboratories, Richmond, Canada
Presenting author email: n.moshg@gmail.com

Background: HIV-IgM antibody is detectable within 2 weeks following infection and is therefore an important immunoassay target for early HIV antibody detection. The objective of this study is to determine if the proven early HIV antibody sensitivity of the 60 second INSTI HIV-1/HIV-2 Antibody test, is due to its ability to detect HIV-IgM antibodies.
Methods: The INSTI HIV-1 gp41 recombinant antigen was applied to a HIV-IgM ELISA to demonstrate its ability to capture HIV gp41 IgM antibody. This HIV-IgM ELISA assay was run on 6 commercial early seroconversion samples, known to be HIV-IgM positive, and 5 long term HIV positive serum samples. A separate experiment to demonstrate that the dye-labelled recombinant Protein A-based colour developer (CD) used in the INSTI assay hasaffinity to human IgM was conducted. 0.5µg of purified human immunoglobulins (IgM, IgD, IgA, IgE, and IgG) were blotted onto nitrocellulose (NC) and probed with the CD to observe for spot development. Finally, to determine if INSTI performance is affected by IgM removal, IgM was removed by human anti-IgM MicroBeads on 21 early seroconversion samples with known or undetermined levels of HIV-IgM and with 5 samples from long term HIV-positive samples. INSTI results were observed for reduced test spot intensity following IgM removal.
Results: The gp41-based HIV-IgM ELISA was positive for the 6 early seroconversion samples that were known INSTI and HIV-IgM positive, and negative for the 5 long-term HIV positive samples indicating the assay signal was due to HIV-IgM capture by the immobilised gp41 antigen. The dye-labelled recombinant Protein-A used in the INSTI colour developer produced distinct spots for purified IgM, IgA, and IgG blotted on the NC membrane. Following IgM removal from 21 seroconversion samples with known or undetermined HIV-IgM levels, 10/21 samples becameINSTI HIV negative from INSTI HIV positive. In 10/21 samples test spot intensity was reduced by > 50% and 1/21 samples slightly < 50%, while the 5 long term HIV positive samples showed no reduction (Table 1).

	Before IgM removal	After IgM removal			
Number of Seroconversion (SC) samples	INSTI positive	INSTI test dot became negative	INSTI test dot intensity diminished by >%50	INSTI test dot intensity diminished by <%50	No change in INSTI test dot intensity
15 early SC, IgM Positives	15	8	7	-	-
6 early SC, IgM not determined	6	2	3	1	-
5 late SC, IgG	5	-	-	-	5
Total=26	26	10	10	1	5

[Table 1]

Conclusions: The INSTI HIV-1/HIV-2 Antibody Test is shown to detect HIV gp41 specific IgM antibodies in early HIV infection which enhances its utility in early HIV infection.

Wednesday 22 July

Poster Exhibition

Entry (attachment, receptors and co-receptors, penetration and tropism)

WEPEA100

CXCR4 tropic HIV-1 is a cause of but not a result of CD4+ T cell count depression

T. Hayashida, K. Tsuchiya, H. Gatanaga, Y. Kikuchi, S. Oka
National Center for Global Health and Medicine, AIDS Clinical Center, Tokyo, Japan
Presenting author email: thayashi@acc.ncgm.go.jp

Background: CXCR4 tropic HIV-1 (X4 virus) is more likely to be detected in patients with low CD4+ T cell count. However, whether X4 virus is a cause of or a result of CD4 count depression is still unclear. To answer this question, we examined when X4 virus appeared using deep sequencer.
Methods: We enrolled 6 patients, who are hemophiliacs, were infected with HIV-1 at early 1980s, and were antiretroviral therapy (ART) naïve over 20 years. We checked viral sequences (340 bp) around V3 region of HIV-1 *env* using GS Junior and analyzed the data using Amplicon Variant Analyzer. Viral tropisms were predicted by geno2pheno [coreceptor] 2.5 with cutoff value at false positive ratio (FPR)
<5 %. Firstly we checked viral sequences of 6 patients at ART naïve and latest samples. If X4 virus was found, we then checked viral sequences of previous samples to determine when X4 virus appeared. Phylogenetic analysis was conducted by Genetyx software with neighbor-joining method.
Results: X4 viruses were found in 2 patients at the samples of just before starting ART (CD4 counts were 88 and 44 /μL). Other 4 patients did not have X4 virus (CD4 counts were 289, 234, 545, and 363 /μL). The earliest samples containing X4 viruses were, respectively, at 16 months ago (CD4 count was 619 /μL. Population of X4 viruses was 0.9 %. Lowest FPR was 1.7 %.) and at 34 months ago (CD4 count was 221 /μL. Population of X4 viruses was 75.5 %. Lowest FPR was 0.5 %.) from their ART start. After X4 virus appeared, decrease speeds of CD4 count became faster (-403 and -67.6 CD4 count /μL /year) than before (-23.2 and -16.6 CD4 count /μL /year). Phylogenetic analysis showed that viruses made clearly different clusters in 6 each patient. X4 viruses formed subclusters in the clusters of 2 each patient.
Conclusions: X4 viruses emerged while CD4 counts were still high, followed by rapid CD4 count decrease. It suggests X4 virus is a cause of but not a result of CD4 count depression. Phylogenetic analysis shows these X4 viruses emerged by evolution, not by superinfection.

WEPEA101

Deciphering the interactions between the V1V2 domain of the HIV-1 envelope protein gp120 and α4ß7 integrin of the host cell

E. Messina[1], S. Chand[1], W. Alsalmi[1], G. Gao[1], Q. You[1], G. Uritskiy[1], M. Mahalingam[1], N. Ananthaswamy[1], K. Peachman[2], M. Robb[2], M. Rao[3], V. Rao[1]
[1]Catholic University of America, Biology, Washington, DC, United States, [2]Henry M. Jackson Foundation for the Advancement of Military Medicine, USMHRP, Silver Spring, United States, [3]Walter Reed Army Institute of Research, USMHRP, Silver Spring, United States
Presenting author email: messina@cua.edu

Background: Data from the landmark RV144 HIV-1 vaccine trial indicated that antibodies directed to the V1V2 region of the envelope protein, gp120, provided modest protection against HIV infection. The V1V2 region has been reported to interact with integrin α4ß7, which may serve as a co-receptor for HIV. Some studies have demonstrated that V1V2 antibodies are protective against pseudoviruses and block V1V2 binding to α4ß7. Yet, other studies showed that this interaction is not essential for HIV-1 infection. To date, the specificity of V1V2-α4ß7 interaction, which residues are involved, and the role the interactions play in HIV-1 entry, remains unresolved.
Methods: We have constructed a variety of recombinant proteins containing the V1V2 domain from several HIV-1 clades. These include: V1V2 scaffolded to the bacteriophage T4 proteins, Soc (small outer capsid protein), or the 12-mer small terminase protein, gp16, and HIV-1 envelope protomers and trimers. We have also developed a sensitive cell-binding assay using α4ß7-expressing RPMI 8866 B cells, which lack the CD4 receptor. A series of purified V1V2 proteins (both glycosylated and de-glycosylated), glycosylation mutants, and substitution and deletion mutants, have been tested for binding to α4ß7.
Results: The V1V2 recombinant proteins specifically bound to RPMI cells. This interaction was partially inhibited by the α4ß7-specific Act-1 antibody. However, the V1V2 mutants lacking the conserved LDI tripeptide, which was thought to be essential for binding to α4ß7, bound as well or better than the full-length V1V2 domain. Unglycosylated V1V2 scaffolds purified from *E. coli* and de-glycosylated protomers and trimers produced in mammalian cells bound α4ß7 with a 5-20 fold greater affinity than the glycosylated proteins.
Conclusions: We demonstrate specific binding of the V1V2 domain to α4ß7-expressing B cells. However, the specificity determinant appears to be located in the V1 region. Further mutational analysis revealed specific glycosylation patterns within the V1 region that are important for binding. These results lead us to propose a potential new α4ß7 binding site in the V1 loop of the HIV-1 envelope protein gp120, which may have important implications in the design of V1V2-based HIV-1 vaccines.

Reverse transcription and integration

WEPEA102

Investigation of the sequential development of integrase strand transfer inhibitor resistance mutations in HIV

K.R.A. Anstett[1,2], T. Mesplede[1], M. Oliveira[1], V. Cutillas[1,2], M. Wainberg[1,2]
[1]McGill AIDS Center, Lady Davis Institute, Montreal, Canada, [2]McGill University, Microbiology and Immunology, Montreal, Canada
Presenting author email: kaitlin.anstett@mail.mcgill.ca

Background: When treated with the new integrase inhibitor (INI) dolutegravir (DTG), patients previously treated with older INIs have lower response rates than other patient populations but are unable to develop the DTG resistance mutation R263K. We investigated whether the presence of INI resistance mutations affects the emergence of R263K.
Methods: When treated with the new integrase inhibitor (INI) dolutegravir (DTG), patients previously treated with older INIs have lower response rates than other patient populations but are unable to develop the DTG resistance mutation R263K. We investigated whether the presence of INI resistance mutations affects the emergence of R263K.
Results: Each combination reduced the strand transfer activity of INB relative to INB_{R263K} and only $INB_{Q148R/R263K}$ had increased resistance to DTG biochemically. The $NL4.3_{IN(Y143R/R263K)}$ and $NL4.3_{IN(Q148R/R263K)}$ viruses grew very poorly in tissue culture. The $NL4.3_{IN(E92Q/R263K)}$ virus had increased DTG resistance relative to $NL4.3_{IN(E92Q)}$, but the combination negatively impacted infectivity. The addition of N155H to R263K partially restored the infectious defect of $NL4.3_{IN(R263K)}$, while increasing DTG resistance compared to either single mutant. Both $NL4.3_{IN(E92Q)}$ and $NL4.3_{IN(N155H)}$ were also able to select for R263K under DTG pressure. Due to the high compatibility of N155H and R263K, we next investigated whether secondary resistance mutations associated with N155H in response to older INIs would also have a compensatory effect in the N155H/R263K background, and found that T97A, E157Q, and G163R were each able to enhance $INB_{N155H/R263K}$ enzyme performance biochemically.
Conclusions: The combination of INI resistance mutations with R263K does not usually lead to increased fitness or drug resistance. The combination of N155H and R263K, however, does represent a possible mechanism through which resistance may develop.
This combination was recently identified in a patient failing an older INI, and the N155H pathway is increasingly being associated with DTG failure in the clinic. In accordance with this, we have also shown that select secondary mutations common to N155H also have a positive impact on $INB_{N155H/R263K.}$
These results suggest that two prominent DTG resistance pathways are complementary *in vitro.* This will have significant implications for the treatment of HIV-positive individuals as DTG becomes more common in clinical settings.

WEPEA103

Use of amplification refractory mutation system PCR assay as a simple and cost-effective tool to detect HIV-1 drug resistance mutations

A.J. Nanfack[1], L. Agyingi[2], J.J. Noubiap Nzeale[3], J. Ngai[2], V. Colizzi[4], P. Nyambi[1]
[1]University of New York, Pathology, Bronx, United States, [2]Medical Diagnostic Center, Yaounde, Cameroon, [3]Hopital de District d'Edea, Edea, Cameroon, [4]University of Rome Tor Vergata, Surgery and Medicine, Rome, Italy
Presenting author email: a_nanfack@yahoo.fr

Background: The main obstacle to successful antiretroviral therapy (ART) is the emergence and transmission of HIV drug resistance mutations; resistance testing is established by sequencing but its feasibility is limited in resource-constrained settings by high cost,suggesting the need for a sensitive, cost effective, and simplifiedmethod to identify HIV-1 drug resistance (HIVDR) mutations. In this study,the Amplification Refractory Mutation System (ARMS)-PCR, a point mutation assay,was developed and used to investigate the most frequent HIVDR mutations affecting first line ART.

Methods: Samples from 75 HIV-1 infected patients (33 ART-naïve and 42 on ART) living in Cameroon were used to assess the performance of ARMS-PCR assay in its ability to detect M184V, T215Y/F, K103N, and Y181C mutations. For comparison, sequencing of HIV-1 reverse transcriptase was simultaneously performed and discordant samples were tested with Trugene HIV-1 genotyping kit, a FDA-approved genotyping assay.
Results: ARMS-PCR assay was able to detect M184V, T215Y/F, K103N, and Y181C mutations with sensitivity of 96.8%, 85.7%, 91.3%, and 70%, respectively, and specificity of 90.6%, 95%, 100%, and 96.9%, respectively, when compared with sequencing data. The results indicated the highest positive predictive value for K103N (100%) and the highest negative predictive value for M184V (97.5%). Moreover this assay was able to correctly detect the different HIVDR mutations present in a B subtype molecular clone obtained from NIH reagent program. ARMS-PCR efficiently identified mutations in individuals with different HIV-1 clades (CRF02_AG and non-CRF02_AG), different ART and varying HIV-1 viral loads.ARMS-PCR'slimit of detection in serially diluted samples for mutations M184V, T215Y/F, K103N and Y181Cwere < 75 copies/ml, 143 copies/ml, 143 copies/ml and 836 copies/ml, respectively. More so, this approach was more cost-effective than other genotyping assays requiring only $10 to cover reagent cost of one mutation.
Conclusions: The good performance, the cost-effectiveness, and the simplicity of the ARMS-PCR suggest that this assay is a suitable tool to monitor HIVDR patterns. This assay will help improve care and management of HIV-1 infected patients in regions with limited resources and also improve ART programs; Thereby reducing the rate of acquired and transmitted drug resistance.

WEPEA104

Identification of HIV aberrant strains in Cameroon

L. Agyingi[1], A.J. Nanfack[2,3], B. Asaah[1], B. Ngoin[1], C. Kakam[1], D. Munchep[1], J. Ngai[1], P. Nyambi[2]
[1]Medical Diagnostic Center, Yaounde, Cameroon, [2]University of New York, Pathology, New York, United States, [3]Medical Diagnostic Center, Serology, Yaounde, Cameroon
Presenting author email: aglucy2000@yahoo.fr

Background: The identification of many HIV recombinants forms in Cameroon, couple with the fact that HIV -1 Group O, N and P were first identified in this region, makes HIV landscape in this region complicated. Therefore this country is likely to harbor aberrant or/and rare HIV variants.
Methods: Blood specimens were collected from 1,861 persons in 4 regions of Cameroon during HIV voluntary counseling and testing sessions. Samples were screened with HIV rapid tests (Determine HIV1/2, Hexagon HIV1/2) onsite and HIV infected patients were referred to HIV treatmentand care centers.Non-reactive samples to HIV rapid testing were then tested with 15 synthetic peptides derived from the consensus sequences of V3 loop of different HIV and SIV strains to identify aberrant HIV strains circulating in Cameroon. The 15 peptidesused included HIV-1 group: F2, Ncon, Ocon, Obe, Ocm, PFR, PCM, CRF02_AGcm. SIV: CPZus, CPZcam3, CPZant, CPZgab1, CPZcm, GORcm, GORpet.
Results: Out of 1,861 persons screened on the fieldwith rapid tests,114 samples were reactive,giving a HIV prevalence of 6.1%. Out of 500so far screened on V3 peptide ELISA, 25 were reactive (OD≥0.500)toat least one of the 15 peptides tested. Most of the samples reacted to CRF02_AG and F2 peptides with 1.9% and 0.9%, respectively; followed by CPZant with 0.3%. 0.19% of samples reacted to CPZcm, ConP, CPZus, CPZgab1, CPZcam3, ConO and ConN. No sample reacted to ConP, GORpet, GORcm, Pcm, Obe and Ocm. Samples that reacted to at least one of the HIV/SIV V3 peptides will further be tested by PCR using specific primers. Positive samples to PCR will be used in characterizing genetic subtype of the virus infecting the study subjects and identify aberrant HIV-1 strains.
Conclusions: Our preliminary results indicate the possible circulation of aberrant HIV strains in Cameroon and the inability of current available HIV diagnostic tests to efficiently identify all HIV infected persons. Theidentification and characterization of these aberrant HIV variants will lead to the improvement of diagnostic methods, treatment strategies and more importantly set the basis for an efficient HIV vaccinesince.

WEPEA105

Withdrawal of dolutegravir in early phases of HIV-1 infection in tissue culture does not abrogate antiretroviral activity

N. Osman[1,2], T. Mesplede[1], P. Quashie[1,3], M. Oliveira[1], S. Hassounah[1,3], V. Cutillas[1,2], K. Anstett[1,2], M.A. Wainberg[1,2,3]
[1]McGill AIDS Centre, Lady Davis Institute, Jewish General Hospital, Montreal, Canada, [2]McGill University, Microbiology and Immunology, Faculty of Medicine, Montreal, Canada, [3]McGill University, Experimental Medicine, Faculty of Medicine, Montreal, Canada
Presenting author email: nathan.osman@mail.mcgill.ca

Background: Dolutegravir (DTG) has shown greater efficacy than Raltegravir (RAL) in suppressing HIV-1 replication in treatment-experienced individuals. Biochemical experiments studying the dissociative half-lives of these Integrase (IN) Strand-Transfer Inhibitors (INSTIs) showed significant differences between them, and that common mutations involved in resistance against INSTIs were associated with lower dissociative half-lives. However, it remains unknown whether these results also apply to infected cells. Accordingly, we are investigating whether drug removal from INSTI-treated HIV-1 infected cells results in different times to viral rebound depending on the INSTI, and whether the R263K mutation associated with resistance against DTG affects the time to viral rebound.
Methods: MT-2 cells treated with DTG, RAL or MK-2048 were infected with HIV-1_{WT} or HIV-$1_{IN(R263K)}$, and drugs were removed after different times of treatment. Viral replication was monitored by measuring reverse transcriptase (RT) activity in culture fluids. As a control, cells were infected with the different viruses but not treated with INSTIs. Drug controls were obtained by not washing out drug in infected cells after treatment with an INSTI.
Results: We observed a slower increase in RT activity after removal of DTG compared to RAL or a different INSTI termed MK-2048, resulting in an up to 5 days shift in order to reach the same level of RT activity. The incubation time before the drug was removed had an impact on RT activity as well, independently of the drug and virus used. Using HIV-$1_{IN(R263K)}$ did not have any impact on this long-acting DTG effect, suggesting that DTG binding to R263K remains consequential.
Conclusions: These results suggest that the time of residence of INSTIs on IN is a key factor in the activity of these drugs and that the repercussions of an interruption of treatment would be more manageable when using DTG than RAL. These findings underline another benefit of using DTG as part of a first-line regimen and may support strategies that will aid in HIV elimination from latency.

Viral assembly and maturation

WEPEA106

Development of an *in vitro* assay to assess the function of naturally occurring HIV-1 Vpu sequences without codon optimization

M. Soto-Nava[1], T.J. Escamilla-Gómez[1], G. Anmole[2], K. Cobarrubias[2], R. Singh[3], T. Ndung'u[4], S. Ávila-Ríos[1], G. Reyes Terán[1], Z.L. Brumme[2,5], M.A. Brockman[2,5]
[1]National Institute of Respitary Diseases, Research Center for Infections Disease, Mexico City, Mexico, [2]Simon Fraser University, Burnaby, Canada, [3]University of KwaZulu-Natal, Durban, South Africa, [4]University of Cape Town, Cape Town, South Africa, [5]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada
Presenting author email: maribel.soto@cieni.org.mx

Background: Vpu is a highly variable HIV-1 accessory protein that facilitates virion release. Codon optimization is often required to enhance Vpu expression *in vitro* and as a result, little is known regarding the functional diversity of naturally occurring Vpu sequences. We developed an assay to assess Vpu's two most well characterized functions - cell-surface tetherin (BST2/CD317) and CD4 downregulation - in non-codon-optimized subtype B and C sequences.
Methods: Vpu sequences from the HIV-$1_{NL4.3}$ subtype B and HIV-1_{MJ4} subtype C reference strains were PCR-amplified using forward primers located ~100, ~50 and 0 bases upstream of the Vpu start site and a reverse primer 57 bases downstream of Vpu's stop codon, and cloned into the pSELECT-GFP expression vector. Site-directed mutagenesis was used to construct NL4-3 Vpu sequences lacking a native cryptic start/stop motif located 5 bases upstream of Vpu's start codon. A published codon-optimized Vpu sequence and an empty pSELECT-GFP expression vector were used as positive and negative controls. Vpu constructs were transfected into an immortalized CD4+ T cell line, and tetherin or CD4 downregulation assessed by flow cytometry 20 hours later. The downregulation activity of each Vpu construct was compared to that of codon optimized Vpu.
Results: As expected, codon-optimized Vpu displayed robust downregulation of tetherin and CD4 (>8-fold and >7-fold, respectively), which was designated as 100% activity for comparative analyses. In contrast, Vpu clones encoding ~50 or more bases of sequence upstream of the Vpu start site exhibited < 20% ability to downregulate either receptor, regardless of subtype. However, subtype B and C Vpu sequences cloned directly at the Vpu start site exhibited 82% and 77% tetherin downregulation function and 49% CD4 downregulation function for both subtypes. Elimination of the cryptic start/stop motif 5 bases upstream of Vpu in subtype B did not enhance protein function.
Conclusions: Our results indicate that the function of naturally occurring HIV-1 Vpu isolates can be assessed *in vitro* without codon optimization by excluding sequence information upstream of the Vpu start site. This finding opens the possibility of functionally assessing patient-derived Vpu clones.

Transcriptional and gene expression regulation (including regulatory genes)

WEPEA107

HIV-1 Rev regulates the expression of Tat and viral replication via modulation of NAD(P)H: quinine oxidoreductase 1 (NQO1)

S. Lata[1], V. Sood[1], R. Raja[2], A. Banerjea[2]
[1]University College of Medical Sciences and Guru Teg Bahadur Hospital, University of Delhi, Microbiology, Delhi, India, [2]National Institute of Immunology, Virology, New Delhi, India
Presenting author email: snehl5555@gmail.com

Background: HIV-1 encodes two regulatory proteins, Tat and Rev. Tat increases the steady state levels of all viral transcripts. Rev, on the other hand, increases the stability of singly spliced or unspliced HIV-1 genomic RNA and downregulates levels of Tat, Rev and Nef mRNAs resulting in a switch from early Rev-independent to Rev-dependent gene expression associated with late stages of viral life cycle. The regulatory feedback mechanisms governed by Tat and Rev ensure the delicate balance between early and late infection. HIV-1 proteins are also known to interact with one another to modulate various functions; Vif is reported to degrade the Vpr protein and Nef promotes the degradation of Tat. So, we studied the inter-regulation of two regulatory proteins (Tat and Rev) of HIV-1.
Methods: The expression and LTR transactivation activity of Tat was studied in presence of HIV-1 Rev in HEK-293T and CHME3 cells. The destabilization of Tat by Rev was studied by cycloheximide chase assay. RT-PCR analysis was also done. MG132 treatment and ubiquitination assay was performed to check translational regulation of Tat by Rev. The expression of Tat was also checked in presence of NLS or NES deletion mutants of Rev to find out the domain of Rev required for regulation of Tat expression. The expression of NQO1 was studied in presence of Rev in HEK-293T cells.
Results: Rev induced specific degradation of Tat protein and downregulation of HIV-1 replication. Tat degradation was not due to transcription but was at the level of translation involving proteasomal machinery. Nuclear export signal (NES) region of Rev was found to be critical for its ability to degrade Tat protein but have no affect on its interaction with Tat suggesting that it is an interaction independent phenomenon involving host proteins. NQO1 is known to stabilize unstructured proteins and might stabilize the expression of Tat. Rev was decreasing the expression of NQO1. Rev mediated downregulation of Tat via NQO1 degradation was observed to take place predominantly in cytoplasm.
Conclusions: HIV-1 Rev decreases Tat levels by downregulating NQO1. Expression of Tat is downregulated during latency. So, these observations are important to understand HIV-1 biology and latency.

WEPEA108

Analysis of in vivo splice site usage by HIV-1 transcripts through deep sequencing: high diversity of spliced RNA expression patterns and identification of new splice sites

Y. Vega[1], E. Delgado[1], J. de la Barrera[1], C. Carrera[1], A. Zaballos[1], I. Cuesta[1], A. Mariño[2], A. Ocampo[3], C. Miralles[3], S. Pérez-Castro[3], H. Álvarez[2], P. Ordóñez[2], I. López-Miragaya[3], M.M. Thomson[1]
[1]Instituto de Salud Carlos III, Centro Nacional de Microbiología, Majadahonda, Spain, [2]Hospital Arquitecto Marcide, Ferrol, Spain, [3]Complejo Hospitalario Universitario de Vigo, Vigo, Spain
Presenting author email: mthomson@isciii.es

Background: HIV-1 RNAs are generated through a complex splicing mechanism and are classified in 3 major categories; unspliced, singly spliced (SS) and doubly spliced (DS). The complexity of HIV-1 splicing is increased by optional incorporation of noncoding exons and by redundant 3' splice site (3'ss) usage by some RNAs. Knowledge of in vivo HIV-1 splicing patterns is scarce.
Here we analyze in vivo HIV-1 splice site usage through deep sequencing.
Methods: CD4+CD25+ lymphocytes were immunomagnetically separated from peripheral blood mononuclear cells from 19 HIV-1-infected individuals and total RNA was extracted. HIV-1 DS and SS RNAs were amplified separately by RT-PCR in 19 and 12 samples, respectively, using primers recognizing sequences in outer exons common to all RNAs of each category. Deep sequencing was done with 454 GS Junior+ System (Roche). Sequences were identified through alignment with HIV-1 reference sequences generated by all possible combinations of all reported HIV-1 exons, using BWA-MEM. Sequences with ambiguous assignations with BWA-MEM were mapped to the HXB2 genome using Sequence Locator program.
Results: In total, 9,196 and 3,250 sequences derived from HIV-1 DS and SS RNAs, respectively (mean, 484 and 271 per sample), were identified, corresponding to 67 different RNA classes. Mean relative proportions in DS RNAs were nef 70.5%, rev 17.5%, tat 9.7%, vpr 2.3%, and in SS RNAs, env 75.6%, tat 9%, vpr 15.4%, vif 0%. A great diversity of expression patterns was observed, frequently differing from those reported in in vitro infection. Particularly, a substantially greater SS vpr RNA expression than reported was observed in most samples. In 4 samples, 5 unreported 3'ss were identified, 3 used by nef and 2 by rev RNAs. Rev RNAs predominantly used 3'ss A4e in a subtype B sample and A4f in a subtype C sample. RNAs incorporating noncoding exons 2 and/or 3 were predominant in nef, rev, tat and env RNAs in 52.6%, 35.7%, 7.7% and 42%% samples, respectively.
Conclusions: We report the first study on in vivo HIV-1 splicing patterns analyzed through deep sequencing. A great diversity of patterns was observed, frequently discordant from those reported in in vitro infection, and 5 new HIV-1 splice sites were identified.

Intrinsic cellular defences and restriction factors

WEPEA109

Decreased interferon signature in HIV-1 viremic controllers

J. Blanco-Heredia[1], S. Avila-Rios[1], D.F. Nixon[2], G. Reyes Terán[1], R.A. Raposo[2]
[1]Centro de Investigación en Enfermedades Infecciosas, Instituto Nacional de Enfermedades Respiratorias, Mexico City, Mexico, [2]George Washington University, Department of Microbiology, Immunology and Tropical Medicine, Washington, United States
Presenting author email: araposo@gwu.edu

Background: Several host-encoded interferon-inducible antiviral factors suppress HIV-1 replication in a cell-autonomous fashion in vitro. The relevance of these defences to the control of HIV-1 in vivo in humans remains to be elucidated. Recent data from Sandler et al. suggest that administration of interferon to monkeys, and hence the modulation of restriction factor expression at different stages of SIV infection dramatically determines disease outcome. We hypothesized that host restriction factors play a role in disease outcome in chronically HIV-1-infected individuals.
Methods: A total of 99 chronic HIV-1-infected individuals were selected from the cohort at the National Institute of Respiratory Diseases in Mexico City and divided into 3 groups: 1) Low Viremic (VL < 2,000 copies and CD4 >250), 2) High Viremic (VL >10,000 copies and CD4 >250) and 3) Advanced Infection (VL >10,000 copies and CD4 < 250). Twenty HIV-1-uninfected individuals from the same ethnic background were used as a control group. CD4+ T cells were enriched from whole PBMC and the expression of 42 established anti-HIV-1 genes was determined by quantitative real-time PCR.
Results: We consistently detected an overexpression of restriction factors and ISGs in individuals with advanced disease, followed by high viremic individuals ($p < 0.0001$, Krustal-Wallis Test). Low viremic individuals had the lowest expression, even compared to uninfected. The expression of IFITM1, RTF1, TRIM22, RSAD2/Viperin and SLFN11 significantly correlated with VL in individuals with advanced infection ($r>0.43$, $p< 0.05$). Finally, we performed 4-digit HLA typing and found unconventional HLA-B haplotypes to be associated with either control (B*3902) or risk (B*3905) of HIV-1 disease and restriction factor expression profile.
Conclusions: In conclusion, we show evidence for the existence of novel mechanisms associated with protection or risk of HIV disease progression in a previously uncharacterized population with unique immunogenetic characteristics.

WEPEA110

Differential effects of cell-surface CD4 and tetherin on ADCC mediated by non-neutralizing and broadly neutralizing anti-HIV antibodies: the role of Nef and Vpu

T.N.Q. Pham[1], G. Perron[1], É.A. Cohen[1,2]
[1]Institut de Recherches Cliniques de Montréal (IRCM), Montréal, Canada, [2]Université de Montréal, Department of Microbiology, Infectiology and Immunology, Montréal, Canada
Presenting author email: tram.pham@ircm.qc.ca

Background: The advent of monoclonal antibodies capable of broadly neutralizing HIV variants and recent demonstrations in humanized mice of how some of these antibodies can impact latent virus reservoirs in a Fc domain-dependent manner have rejuvenated interests in the area of humoral/innate immunity for HIV cure. HIV accessory proteins Nef and Vpu have been shown to promote escape from ADCC that is mediated by non-neutralizing antibodies by down-regulating CD4 and BST2/Tetherin. Indeed, the HIV receptor CD4 is down-modulated by both proteins, while BST2, which retains progeny virions at the cell surface, is down-regulated by Vpu. In doing so, the virus ensures that ADCC-mediating epitopes, including those transitionally exposed upon CD4-Env interactions, remain unmasked. Here, we:
(1) delineated mechanistically the relative contributions of CD4 and BST2 to ADCC;
(2) ascertained whether this mode of immune evasion is relevant to broadly neutralizing antibodies; and
(3) assessed whether latently infected T cells, upon reactivation, are susceptible to ADCC.

Methods: Primary CD4+ T cells or T cells expressing only CD4, BST2, or both were infected with CCR5-tropic wild-type HIV or those deficient of Nef, Vpu or both proteins. Infected T cells were examined by flow cytometry for Env recognition by anti-HIV Env antibodies and susceptibility to ADCC.
Results: Shielding of infected T cells from ADCC induced by non-neutralizing antibodies is primarily dependent on Nef-induced CD4 down-regulation. BST2 provides a modulatory role. In marked contrast, BST2 down-modulation is crucial to prevent exposure of epitopes that are recognized by neutralizing antibodies, especially 10E8 and PG9. In fact, CD4 accumulation at the surface of infected cells was linked to significantly reduced Env recognition and ADCC by the PGT121 family. Further, T cells that are latently infected with *nef- vpu-* HIV were more susceptible to ADCC upon reactivation.
Conclusions: Non-neutralizing and broadly neutralizing anti-HIV antibodies can mediate efficient ADCC if relevant epitopes are exposed, although CD4 and BST2 contribution to this process is markedly different between these two classes of antibodies. Approaches aimed at neutralizing ADCC evasion by HIV Nef and Vpu would be important to the development of more robust anti-HIV responses and effective shock-and-kill strategies against latently infected cells.

WEPEA111

PKR as a restriction factor during HIV-1 infection counteracted by virus-induced cellular mechanisms

A. Daher[1], S. Burugu[1,2], G. Clerzius[1,3], E. Shaw[1,3], E. Chukwurah[4], R. Radetskyy[1,2], R.P. Labbé[1,2], J.-P. Routy[3,5], R.C. Patel[4], A. Gatignol[1,2,3]
[1]Lady Davis Institute for Medical Research, Montreal, Canada, [2]McGill University, Microbiology and Immunology, Montreal, Canada, [3]McGill University, Medicine, Div. Experimental Medicine, Montreal, Canada, [4]University of South Carolina, Biological Sciences, Columbia, United States, [5]McGill University Health Centre, Hematology, Montreal, Canada
Presenting author email: anne.gatignol@mcgill.ca

Background: Several cellular restriction factors control the replication of HIV. Many have their activity controlled by viral proteins, but for several, no virally-encoded counteracting factor has been identified. Several restriction factors are induced by interferon (IFN), showing an interplay between innate and intrinsic immunity. The IFN-induced protein kinase RNA-activated (PKR) represses the expression of several viruses and acts as a potent HIV-1 inhibitor. PKR phosphorylates the α subunit of the translation initiation factor eIF2α and consequently inhibits protein synthesis. We showed that PKR is activated at the beginning of HIV-1 infection in peripheral blood mononuclear cells (PBMCs) followed by a deactivation due, in large part, to cellular mechanisms involving the TAR RNA Binding protein (TRBP), the adenosine deaminase (ADAR1) and the PKR activator (PACT). ADAR1 expression is induced during HIV-1 replication and PACT becomes a PKR inhibitor in HIV-expressing cells (Burugu et al., Virus Res. 2014, 193:65). Our objective is to elucidate the HIV-induced mechanisms involving ADAR1 and PACT, which prevent PKR to act as a restriction factor in HIV-replicating cells.
Methods: We compared the activation of PKR and the expression of PKR, ADAR1 and PACT in PBMCs of non-infected, HIV-infected naïve patients and HIV-infected treated patients by western blots. We performed immunoprecipitations of HIV-infected cells with PKR, ADAR1 and PACT antibodies to identify the HIV-induced multiprotein complex that inhibits PKR activation. We expressed PKR, ADAR1 and PACT in vitro to determine their direct interactions and their activity on PKR activation.
Results: We observed an inverse correlation between PKR activation and ADAR1 expression in HIV-infected patients. Immunoprecipitations using HIV-1 infected cells showed an enhanced multiprotein complex between PKR, ADAR1 and PACT correlated with PKR deactivation. We also observed a direct interaction between ADAR1 and PACT. By in vitro reconstitution, we observed that ADAR1 and HIV proteins are required for the change of PACT function on PKR activation.
Conclusions: PKR is a restriction factor that has the potential to prevent HIV replication. The multiprotein complex formed by ADAR1, PACT and HIV proteins counteracts PKR activation in HIV-infected cells, which likely contributes to viral persistence in patients.

Type I Interferons (viral inhibition, immunomodulatory functions)

WEPEA112

Comparison of gene expression profile between human and macaque dendritic cells infected with virus carrying or not Vpx-loaded particles and assessment of their pathogenic impact

E. Calonge[1], M. Bermejo[1], I. Mangeot[2], N. Gonzalez[1], M. Coiras[1], L. Jimenez[1], J. Garcia-Perez[1], R. Legrand[2], J. Alcami[1]
[1]Centro Nacional Microbiologia, ISCIII, Inmunopatologia de SIDA, Majadahonda, Spain, [2]Institute of Emerging Diseases and Innovative Therapy (IMETI-CEA), Immunovirology Department (SIV), Paris, France
Presenting author email: ecalonge@isciii.es

Background: Dendritic cells (DC) are antigen presenting cells that play a central role in the regulation of the immune response and whose functions depend on their stage of differentiation. Besides, DCs are characterized by a highly restrictive environment to HIV-1 replication. Susceptibility of DC to infection by different lentivirus is related with the presence of the Vpx protein that overcomes restriction due to SAMHD1. Current findings suggest that productive infection of immature-DC (IDC) is detected by sensor proteins that activate Interferon-mediated responses that interfere with viral propagation and decrease virulence. However, few data have been provided about mature DC (MDC) infection.
Methods: To get a better insight into the pathogenic consequences of DCs infection we analyzed changes in gene expression with a whole genome microarray when IDC or MDC were productively infected using Vpx-loaded HIV-1 particles. Based on microarray data we performed additional studies using qPCR to analyze transcriptomic changes provoked by infection of human and macaque IDC and MDC in restrictive (HIV-1) and productive (HIV-1+Vpx, HIV-2 and SIVmac) conditions
Results: Strong differences in gene expression were found according to DC differentiation and type of infection. Whereas in IDC productive HIV infection strongly induced class-I-interferon-stimulated-genes such induction was not produced in MDC. In contrast a sharp decrease in CXCR3-binding chemokines was observed when MDC were infected with Vpx-loaded particles and this reduction resulted in decreased trans-infection of CD4 lymphocytes and decline of viral reservoirs. Similar patterns of gene expression were found when dendritic cells were infected with HIV-2 and SIV that naturally express Vpx from their genomes.
Overall these results suggest that, paradoxically, restriction of HIV-1 infection in DCs results in increased virulence through different mechanisms. In IDC, restrictive infection avoids sensing and induction of interferon-mediated responses whereas in MDC the production of CXCR3 binding chemokines is not modified in the absence of productive infection leading to lymphocyte attraction to the immune synapse , enhancement of HIV-1 trans-infection and an increase in viral reservoirs size.
Conclusions: Our data confirm previous observations and propose new pathogenic mechanisms to understand how restriction of HIV-1 replication in DC favors viral dissemination and increased virulence in infected host.

NK cells and dendritic cells

WEPEA113

A pseudo-glycodendrimer inhibits DC-SIGN-mediated HIV trans-infection and interferes with DC-SIGN signal

A. Berzi[1], S. Ordanini[2], M. Masetti[1], M. Biasin[1], D. Trabattoni[1], A. Bernardi[2], M. Clerici[3,4]
[1]University of Milan, Department of Biomedical and Clinical Sciences L. Sacco, Milan, Italy, [2]University of Milan, Department of Organic and Industrial Chemistry, Milan, Italy, [3]University of Milan, Department of Pathophysiology and Transplantation, Milan, Italy, [4]Don C. Gnocchi Foundation, IRCCS, Milan, Italy
Presenting author email: michela.masetti@unimi.it

Background: DC-SIGN is involved in the initial stages of mucosal HIV infection. DC-SIGN, by binding mannosylated residues (high mannose glycan) on HIV gp120, mediates trans-infection of CD4 T cells. Furthermore HIV interaction with DC-SIGN subverts its normal immune-activating functions shifting the Th1/Th2 balance towards a Th2 response that favours the persistence of the virus. HIV binding to DC-SIGN induces intracellular signalling pathways that trigger activities required to viral replication and promote immunosuppressive responses by interfering with TLR signalling. Pseudo-mannosylated compounds were synthesized in the attempt to compete with the binding of DC-SIGN to HIV gp120 and interfere with the immunosuppressive DC-SIGN signalling.

Methods: A hexavalent pseudo-glycodendrimer (PM26) able to interact selectively with DC-SIGN was synthesized. The ability of PM26 to inhibit HIV-1 trans-infection was assessed in cellular models based on DC-SIGN expressing B-THP-1 cells. To study the effects of PM26 on DC-SIGN signal, gene expression profile after treatment of human monocyte-derived DCs with PM26 in presence/absence of TLR agonist (LPS and Poly:IC) was evaluated. The cytotoxicity of the compound was also assessed.
Results: PM26 abrogated almost completely (>98%) the transmission of different HIV strains (Bal, Du174) to CD4 T cells at 1 µM, with an IC50 of 25 nM.Treatment of DCs with PM26 in presence/absence of LPS or Poly:IC strongly increased the expression of cytokines that regulate innate immunity, such as IL-1β, IL-6, TNFα and IL-12. Interestingly, an upregulation of IRF8, involved in the regulation of IL-12 expression, was observed. PM26 also induced IFNγ and CCL3, CCL4 and CCL7. TAPBP, involved in antigen presentation, and TLR9, were up regulated as well. In contrast, the compound did not augment IL-10, CCR5, CXCR4 and DC-SIGN expression. No toxicity was observed at the concentrations tested in the cellular assays.
Conclusions: The pseudo-glycodendrimer PM26 inhibits HIV-1 trans-infection by competing with the binding of the virus to DC-SIGN. Furthermore, PM26 both alone and in synergy with TLR agonist stimulates early immune responses that contribute to counteract HIV infection and activate adaptive immunity. These features make the compound a potential candidate for the development as topical microbicide.

WEPEA114

Investigation of which NK cell populations expressing or not NKG2A, KIR2DL3 or KIR3DL1 are activated by autologous HIV-infected CD4 T cells

I. Lisovsky[1,2], G. Isitman[1,2], R. Song[1,2], S. DaFonseca[2], B. Lebouché[2,3,4], J.-P. Routy[1,2,3], J. Bruneau[5,6], N. Bernard[1,2,3]
[1]McGill University, Medicine, Montreal, Canada, [2]Research Institute of the McGill University Health Centre, Montreal, Canada, [3]Chronic Viral Illness Service, McGill University Health Centre, Montreal, Canada, [4]McGill University, Department of Family Medicine, Montreal, Canada, [5]Centre de Recherche du Centre Hospitalier de l'Université de Montréal, Montreal, Canada, [6]Université de Montréal, Department of Family Medicine, Montreal, Canada
Presenting author email: irene.lisovsky@mail.mcgill.ca

Background: Carriage of certain NK cell receptor (NKR)/HLA ligand pairs is associated with slow time to AIDS in HIV$^+$ subjects and protection from infection in HIV-exposed seronegative subjects, implicating NK cells in HIV control. NK cells acquire functional potential through licensing, which requires engagement of inhibitory NKRs (iNKRs), such as NKG2A, KIR2DL3 (2DL3) and KIR3DL1 (3DL1) by their ligands. NKG2A interacts with HLA-E presenting leader peptides from HLA-I proteins, 2DL3 and 3DL1 interact with HLA-C1 and Bw4$^+$ HLA-A/B antigens, respectively. Functional responses of NKG2A$^+$ and 2DL3$^+$ NK cells and the impact of NKG2A, 2DL3 and 3DL1 expression on NK responses to iCD4 cells are currently unknown. Here, we examined the functional profiles of the eight possible NKG2A$^{+/-}$2DL3$^{+/-}$3DL1$^{+/-}$ populations responding to autologous HIV infected CD4 (iCD4) cells.
Methods: We studied 20 HIV-negative subjects. Responses to HIV were assessed by co-culture of NK cells with autologous iCD4 cells. Flow cytometry was used to gate on NKG2A$^{+/-}$2DL3$^{+/-}$3DL1$^{+/-}$ populations and detect all possible Boolean combinations of CD107a, IFNγ, and CCL4 functional subsets.
Results: iCD4 induced differential frequencies of NKG2A$^{+/-}$2DL3$^{+/-}$3DL1$^{+/-}$ populations with total-responsiveness, tri-functional, CD107a$^+$IFNγ$^+$, IFNγ$^+$CCL4$^+$ and IFNγ$^+$ response profiles ($p \leq 0.02$). The frequency of functional responses to iCD4 of NKG2A$^+$2DL3$^+$ populations were higher than that of NKG2A$^-$2DL3$^+$ NK cells ($p \leq 0.01$). Co-expression of 3DL1 on either NKG2A$^-$2DL3$^+$ or NKG2A$^-$2DL3$^+$ NK cells did not modulate their responsiveness to iCD4. A lower frequency of NKG2A$^-$2DL3$^+$ from HLA-C1 than C2/C2 carriers responded to iCD4 while NKG2A co-expression eliminated this difference.
Conclusions: These investigations suggest that 3DL1 has a minimal impact on NK cells functionality to iCD4. In contrast, 2DL3 has an impact on functionality which is enhanced by NKG2A co-expression. 2DL3$^+$ NK cells from carriers of the ligand for 2DL3 are less responsive to iCD4 than those from carriers lacking the 2DL3 ligand (HLA-C2/C2$^+$). Co-carriage of NKG2A and 2DL3 abolishes the suppression of 2DL3$^+$ NK function in NK cells from HLA-C1 carriers. These data suggest that the NKG2A receptor has an important role in modulating NK cell mediated anti-HIV immune responses.

WEPEA115

Enhanced capacity of NK-cells from carriers of the protective KIR3DS1 homozygous genotype to inhibit HIV replication in autologous infected CD4 T cells

N. Bernard[1,2,3], R. Song[1,2], I. Lisovsky[1,2], J. Bruneau[4]
[1]Research Institute McGill University Health Centre, Medicine, Montreal, Canada, [2]Division of Experimental Medicine, McGill University, Montreal, Canada, [3]Chronic Viral Illness Service, McGill University Health Centre, Montreal, Canada, [4]Centre de Recherche du Centre Hospitalier de l'Université de Montréal, Family Medicine, Montreal, Canada
Presenting author email: nicole.bernard@mcgill.ca

Background: In previous studies we identified 2 genotypes encoding Natural Killer (NK) cell receptors with and without their putative HLA ligands that are associated with protection from HIV infection. NK cells from carriers of the Killer Immunoglobulin-like Receptor (KIR) *3DL1* high expression allele genotype with *HLA-B*57* (** h/*y+B*57)* inhibited HIV replication in autologous HIV infected CD4+ T cells more potently than those from carriers of control genotypes such as *HLA-Bw6* homozygotes (hmz). Here we investigated whether carriers of the other protective *KIR3DL1/S1* genotype, *KIR3DS1* (*3DS1*) hmz, also have an enhanced capacity to inhibit HIV replication in autologous cells
Methods: 22 HIV$^-$ subjects were studied: *3DS1* hmz with no alleles encoding the putative HLA-B*80I ligand for this receptor (n=7), *3DS1/L1* heterozygotes who were *80I positive (n=9) and *Bw6hmz* (Bw6 antigens do not interact with 3DS1 or 3DL1) (n=6). Isolated CD4$^+$ T cells were activated for 4 days and infected at a multiplicity of infection of 0.01 with $HIV_{JR\text{-}CSF}$. Purified NK cells and iCD4 cells were co-cultured for up to 10 days. On days 3, 7 and 10 supernatants were tested for p24 levels. Results were reported as percent inhibition of p24 in the presence versus absence of NK cells.
Results: NK cells from carriers of the *3DS1* hmz genotype inhibited HIV replication more potently than those from *Bw6hmz* and these differences were significant on days 3 and 7 ($p < 0.05$, Mann-Whitney test). The level of inhibition of HIV replication in autologous iCD4 cells was similar to that seen by NK cells from carriers of *3DL1/S1+*80I and *h/*y+B*57* genotypes previously shown to inhibit HIV replication better than NK cells from carriers of the receptor or ligand alone or neither or from Bw6 hmz.
Conclusions: NK cells from subjects positive for the activating 3DS1 receptor and negative for the licensing KIR/HLA 3DL1+*80I are able to suppress HIV replication in autologous iCD4 cells. This activity may be a mechanism underlying the association of the 3DS1 hmz genotype with protection from HIV infection.

WEPEA116

DNA methylation analysis of natural killer cells during HIV-1 infection

L. Soares[1], M. Espíndola[1], F. Zambuzi[1], L. Lima[1], C. Fontanari[2], V. Bollela[1], F. Frantz[2]
[1]Faculdade de Medicina de Ribeirão Preto - USP, Ribeirão Preto, Brazil, [2]Faculdade de Ciências Farmacêuticas de Ribeirão Preto - USP, Ribeirão Preto, Brazil
Presenting author email: luanasisoares@hotmail.com

Background: In HIV infection, several dysfunctions associated with natural killer (NK) cells have been reported which increase the susceptibility of infected individuals to opportunistic infections. In this way, our aim is to characterize the phenotype and function of NK cells from untreated HIV-1+ patients and correlate to epigenetic changes in these cells.
Methods: Control samples were obtained from healthy blood donors (n=20) and HIV-1$^+$ patients (n=21) from Hospital das Clínicas de Ribeirão Preto. Plasma levels of proinflammatory molecules were determined by Multiplex Platform and ELISA. NK cell frequency was determined by flow cytometry. NK cell was obtained by magnetic separation and its function was evaluated by cytotoxicity assay. Also, cytokines were quantified in the supernatant of the cytotoxicity assay by Multiplex Platform. DNA was purified from NK cells and global DNA methylation was measured by ELISA.
Results: Plasma levels of proinflammatory cytokines were increased in HIV-1 infected individuals with significant increasing of TNF-α (15.43 ± 9.675 pg/mL) and IP-10 (1871 ± 2074 pg/mL). Also, the molecular inflammatory markers CD14s and CD163s were significantly increased. NK cell frequency was decreased in HIV-1 patients (7.973 ± 5.294) compared to control (11.65 ± 6.247). NK cell subpopulations ($CD56^{bright}CD16^-$ and $CD56^{dim}CD16+$) were also decreased in HIV-1 patients. Otherwise, the percentage of the non-functional NK subpopulation ($CD3^-CD56^-CD16^+$) was significantly increased in HIV-1 patients (8.443 ± 9.08). Furthermore, NK from HIV-1 infected patients showed lower percentage of cytotoxicity compared to control group and IFN-g production by NK cells was decreased in the HIV group (0.698 ± 0.7486 pg/mL). The percentage of global DNA methylation of NK cells was similar between the groups, however it was observed higher DNA methylation in NK cells from HIV-1 patients (47.48 ± 20.47) with advanced disease (pVL > 10,000 copies/mL, < 200 CD4$^+$ T cells/µL).
Conclusions: Our data, obtained from HIV-1 patients, clearly showed systemic immune activation and impaired NK cell function that could contribute to the well-described state of immunosupression. Also, the higher percentage of global DNA methylation in HIV-1+ patients with advanced disease could be correlated to the worst prognostic, remaining to be determined which specific genes are downregulated by this alteration.

WEPEA117

NK cells expressing self-inhibitory KIR2DL receptors exhibit a reduced capacity to inhibit HIV-1 replication in vitro

C. Körner[1], C.R. Simoneau[1], M. Granoff[1], B. Corleis[1], E. Scully[1], D.S. Kwon[1,2], S. Jost[1], M. Altfeld[1,3]
[1]Massachusetts General Hospital, Ragon Institute of MGH, MIT and Harvard, Cambridge, United States, [2]Massachusetts General Hospital, Division of Infectious Diseases, Boston, United States, [3]Heinrich Pette Institute, Leibniz Institute for Experimental Virology, Virus Immunology, Hamburg, Germany

Background: Acquisition and maintenance of NK cell function is mediated by inhibitory killer-cell immunoglobulin-like receptors (KIR) through the interaction with HLA class I molecules, a process termed "licensing". HLA-C expression levels have been associated with differential outcomes of HIV-1 infection. In addition, we recently showed that HLA-C group haplotypes were associated with increased frequencies of NK cells expressing the respective self-inhibitory receptors KIR2DL1 (HLA-C2) and KIR2DL3 (HLA-C1) and maintenance of a licensed phenotype in primary HIV-1 infection, indicating a potential role of HLA-C-mediated licensing of NK cells in HIV pathogenesis. However, it remains unclear whether the increased functional competence of licensed NK cells directly translates into increased inhibition of viral replication or protection against HIV-1. Therefore, we investigated the antiviral capacity of KIR2DL1+ and KIR2DL3+ NK cells in the context of the underlying HLA-C haplotype.
Methods: Primary NK cells derived from HIV-1-negative individuals (N=16) were used to test the ability of NK cells to inhibit HIV-1 replication in vitro. FACS-sorted KIR2DL1+ and KIR2DL3+ NK cells were co-cultured with HIV-1-infected autologous CD4+ T cells for 7 days. In addition, primary bulk NK cells were co-cultured with HIV-1-infected autologous CD4+ T cells for 7 days in the presence of αKIR2DL1, αKIR2DL3, αKIR3DL1 to block KIR/HLA interaction or αCD56 as a control. Viral RNA was quantified in the collected supernatant to monitor NK-cell-mediated inhibition of HIV-1 replication.
Results: NK cells expressing self-inhibitory KIR2DL receptors displayed a reduced ability to inhibit HIV-1 replication in vitro as compared to bulk NK cells or NK cells lacking self-inhibitory KIR2DL receptors (p=0.02). Blockade of self-inhibitory KIRs was associated with improved antiviral capacity (p=0.016) while blockade with αCD56 or KIR antibodies not matching donor HLA class I molecules did not affect inhibition of HIV-1 replication by NK cells (p=0.67). Moreover, levels of viral inhibition correlated with the frequency of NK cells expressing self-inhibitory KIRs in blocking experiments (rs=0.62, p=0.01).
Conclusions: Our results showed that the ability of NK cells to directly inhibit HIV-1 replication was limited by the expression of self-inhibitory KIR2DL molecules, and that blocking of inhibitory KIRs on NK cells can unleash the antiviral activity of these cells.

Monocytes and macrophages

WEPEA118

Functional impairments of macrophages derived from HIV-1+ patients are partially reversed after beginning of HAART

L. Lima[1], M. Espíndola[1], L. Soares[1], F. Zambuzi[1], V. Brauer[1], C. Fontanari[1], V. Bollela[2], F. Frantz[1]
[1]Universidade de São Paulo, Laboratório de Imunologia e Epigenética, Ribeirão Preto, Brazil, [2]Universidade de São Paulo, Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto, Ribeirão Preto, Brazil
Presenting author email: frantz@fcfrp.usp.br

Background: Over 30 years passed since the HIV was isolated and associated with AIDS development. Although in this period the researches and the clinical use of antiretroviral drugs changed dramatically the outcome of millions of infected patients around the world, many aspects of infection and therapy remain poorly explored. Besides of well-marked CD4+ T cells commitment, macrophages are also chronically infected and play a key role during the disease progression. These cells can be activated in classical (M1) or alternative (M2) patterns and when they are infected exhibit several functional impairments, which can be associated with immune failure. Our aim was to evaluate the effect of Highly Active Antiretroviral Therapy (HAART) on cytokines, chemokines released on supernatant, in addition to mRNA expression after *in vitro* stimulation of macrophages with LPS or β-glucan.
Methods: Mononuclear CD14+ cells were isolated from peripheral blood samples and differentiated using M1 or M2a conditioned medium. After six days in culture, LPS or β-Glucan were added to the cells during 24 hours and the supernatant was collected to cytokines and chemokines quantification using a multiplex platform. Here we evaluated cells from health blood-donors (*n=15*), HIV-1+ non-treated patients (*n=8*) or under regular therapy (HIV-1+ plus HAART; *n=15*).
Results: M1 and M2a macrophages derived from HIV+ plus HAART fail to restore the IL-6, IL-12, IL-10, TNF-α, RANTES and MCP-1 released levels after LPS or β-Glucan stimuli when compared to control group. Interestingly, we did not observe nitric oxide release in M1 or M2a supernatant after PAMPs stimulation. Futher, the CCL3 and IP-10 expression in HIV-1+ plus HAART-derived macrophages was higher than observed in control group. In all the samples, *Arg-1* expression was not detected, even under PAMPs stimulation.
Conclusions: HAART protocols exert a differential impact in the profile of cytokines and chemokines released by macrophages after PAMPs stimulation. The evaluation of therapy effectiveness based on macrophage functions may be helpful to understanding the immunologic state of patient and prevent the occurrence of opportunistic infections.

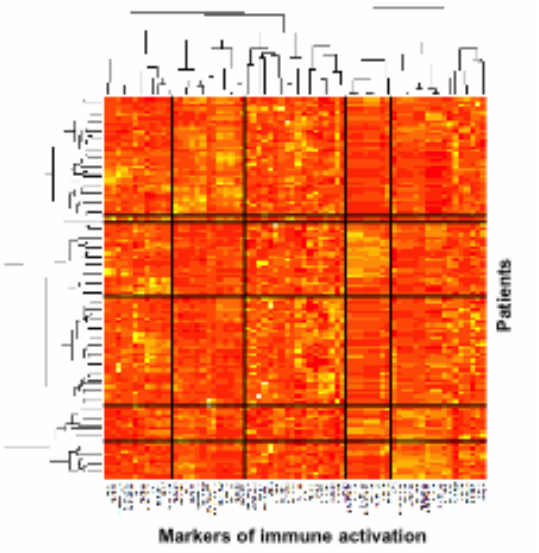
Mechanisms underlying systemic immune activation and inflammation

WEPEA119

HIV-1-infected patients under suppressive cART present with various patterns of persistent immune activation: the ACTIVIH study

C. Psomas[1,2], M. Younas[3], R. Cézar[4], C. Merle[1], N. Atoui[1], E. Tuaillon[1,5], C. Fernandez[1], V. Le Moing[1,2], C. Barbuat[6], E. Nogue[7], N. Nagot[7], C. Reynes[8], R. Sabatier[8], P. Portales[9], J.-F. Eliaou[9], E. Delaporte[1,2], J. Reynes[1,2], P. Corbeau[3,4]
[1]Academic Hospital of Montpellier, Infectious Diseases Department, Montpellier, France, [2]UMI 233, IRD Montpellier University, Montpellier, France, [3]Montpellier University, Institute of Human Genetics, Montpellier, France, [4]Academic Hospital of Nîmes, Immunology Department, Nîmes, France, [5]Academic Hospital of Montpellier, Microbiology Department, Montpellier, France, [6]Academic Hospital of Nîmes, Infectious Diseases Department, Nîmes, France, [7]Academic Hospital of Montpellier, Department of Medical Informatics, Montpellier, France, [8]University of Montpellier 1, Laboratory of Industrial Physics and Treatment of Information, Montpellier, France, [9]Academic Hospital of Montpellier, Immunology Department, Montpellier, France
Presenting author email: c-psomas@chu-montpellier.fr

Background: HIV-1 infection induces a global immune activation fuelled by several causes. Immune activation is reduced under combination AntiRetroviral Therapy (cART), but usually not abolished. In the ACTIVIH study, we analyzed whether persistent immune activation is qualitatively the same for all successfully treated patients or whether different patterns of immune activation may be identified.
Methods: ACTIVIH is a cross-sectional and observational study. HIV-1-infected adults (>45 years) under cART were included if their CD4 count was over 200 /mm3, and their viral load below 50 copies/ml for at least 2 years. We measured in 89 patients 55 cell surface and soluble markers of inflammation, and CD4+
T cell, CD8+ T cell, B cell, NK cell, monocyte, neutrophil, and endothelial activation. We clustered the dataset with two independent hierarchical clustering analyses using respectively correlation and Euclidean distance to measure proximities/distances between markers and patients.



[Heatmap Markers of Immune Activation]

Results: We identified 6 main groups of patients presenting with very different patterns of immune activation that may be clustered in 5 groups of markers (Figure). Using ANOVA results corrected by False Discovery Rate for multiple testing, more than 80% of markers were on

average significantly different for at least one group of patients with regards to the other ones ($p < 0.05$). Two groups of patients presented with a statistically significant increase in almost all markers of immune activation comparatively to the other groups. By contrast, one group had low levels of immune markers. The four other groups presented with intermediate, specific profiles of immune activation. For example one of these subgroups presented with CD4+ and CD8+ T cell activation, and another one with monocyte and NK cell activation.

Conclusions: Successfully treated patients are not equal in terms of persistent immune activation. These different patterns of immune activation may be the consequence of different causes, and may result in different comorbidities. A better understanding of the links between causes, patterns, and consequences of immune activation might lead to the identification of predictive markers of specific comorbidities, and facilitate an immunosuppressive therapeutic approach tailored to each patients group.

CP and MY contributed equally to the study.

WEPEA120

The different patterns of immune activation in virologic responders are linked to various causal factors

M. Younas[1], R. Cézar[2], C. Merle[3], C. Fernandez[3], N. Atoui[3], E. Tuaillon[3,4], V. Le Moing[3,5], C. Barbuat[6], C. Dunyach[7], J.-P. Lavigne[7], E. Nogue[8], N. Nagot[8], C. Reynes[9], R. Sabatier[9], P. Portales[10], C. Psomas[3,5], J.-F. Eliaou[10], J. Reynes[3,5], P. Corbeau[1,2], K.C. Psomas[3,11]

[1]Montpellier University, Institute of Human Genetics, Montpellier, France, [2]Academic Hospital of Nîmes, Immunology Department, Nîmes, France, [3]Academic Hospital of Montpellier, Infectious Diseases Department, Montpellier, France, [4]Academic Hospital of Montpellier, Microbiology Department, Montpellier, France, [5]UMI 233, IRD Montpellier University, Montpellier, France, [6]Academic Hospital of Nîmes, Infectious Diseases Department, Nîmes, France, [7]Academic Hospital of Nîmes, Microbiology Department, Nîmes, France, [8]Academic Hospital of Montpellier, Department of Medical Informatics, Montpellier, France, [9]University of Montpellier 1, Laboratory of Industrial Physics and Treatment of Information, Montpellier, France, [10]Academic Hospital of Montpellier, Immunology Department, Montpellier, France, [11]Institute of Human Genetics, Montpellier, France

Presenting author email: c-psomas@chu-montpellier.fr

Background: By measuring 55 cell surface and soluble markers of inflammation, and CD4+ T cell, CD8+ T cell, B cell, NK cell, monocyte, neutrophil, and endothelial activation in 89 patients, we have recently shown in the ACTIVIH study that HIV-1-infected adults aviremic under combination antiretroviral therapy present with 6 different patterns of immune activation. Immune activation may be fuelled by residual viral production, microbial translocation, coinfections, CD4 lymphopenia, immunosenescence and a deficit in Treg function. In this study, we questioned whether the diversity of the patterns of immune activation we observed might be the consequence of the diversity of these causes.

Methods: To answer this question, we analyzed in these patients putative causes of their immune activation. To this aim, we quantified markers of causal factors, i.e. their CD4 count and residual viremia, their plasma level of bacterial DNA, their level of CD4+ and CD8+ T cell (CD57+, eventually CD28- and CD27-) and NK cell (CD57+) senescence, as well as the frequency of their total (CD4+C25hiFoxP3+CD127lo) and activated (CD4+C25hiFoxP3hiCD127loCD45RA-) Treg cells. We also determined if they were coinfected with Epstein-Barr virus, cytomegalovirus, and/or hepatitis A/B/C virus. We looked for significant differences in these markers of causal factors between the different patterns of immune activation using ANOVA for quantitative causes and chi-square test for qualitative ones.

Results: We found no correlation between either residual viremia, microbial translocation, or coinfection and immune activation. By contrast, CD4 count, the frequency of Treg cells, and the senescence of NK and

T cells were significantly linked to immune activation. In the joint figure, the level of the markers of each of these causes of immune activation is indicated for each group of patients (the darker the higher). Interestingly, the levels of these markers of causes were highly variable in-between the patients groups.

Conclusions: Our data suggest that the diversity of the patterns of immune activation observed in virologic responders might be the consequence of the diversity of the causes of this activation. A diagnosis of the causes of immune activation in each patient might lead to a specific etiologic therapy.

CP, PC and MY contributed equally to the study.

	Patients group					
	1	2	3	4	5	6
CD4 count						
CD57+ NK cell count						
%Treg cell						
%activated Treg cell						
CD57+ CD4+ T cell count						
CD57+ CD28-CD4+ T cell count						
%CD57+ CD4+ T cell						
%CD57+ CD28-CD4+ T cell						
%CD57+ CD28-CD27-CD4+ T cell						
CD57+ CD28-CD27-CD4+ T cell count						
CD57+ CD8+ T cell count						
CD57+ CD28-CD8+ T cell count						
CD57+ CD28-CD8+CD27- T cell count						
%CD57+ CD8+ T cell						
%CD57+ CD28-CD8+ T cell						
%CD57+ CD28-CD27-CD8+ T cell						
% CD57+ NK cell						

[Causes of Immune Activation]

WEPEA121

Elevated levels of circulating nucleosomes in HIV-infected women: cause or consequence of chronic immune activation?

S. Desai[1], K. Weber[2], R. Ronquillo[1], G. Lei[1], A. Landay[1], M. Cohen[2]

[1]Rush University Medical Center, Chicago, United States, [2]John H. Stroger Jr. Hospital of Cook County, Chicago, United States

Background: Circulating DNA is present in plasma/serum, mainly complexed with histones as nucleosomes. The detection of nucleosomes is representative of cell death from apoptosis or necrosis. Inflammation induced pyroptosis and activation induced apoptosis is associated with enhanced cell death in HIV infection. We hypothesize; higher circulating nucleosomes levels will be associated with cell death in HIV infected subjects contributing to inflammation/activation.

Methods: We studied 44 individuals from the Women's Interagency HIV Study (25 HIV+ antiretroviral (ARV) naïve with CD4 >350cell/mm^3; and 19 socio-demographically matched HIV negative controls). Immune activation (HLADR+CD38+) and apoptosis (intracellular Caspase-3) markers were assessed in PBMCs using multi-parametric flow-cytometry and inflammation markers [Tumor Necrotic Factor-Receptor- II (TNFR-II), & IL-6] were measured in paired plasma using ELISA. Circulating nucleosomes (c-Nucs) were quantified in plasma using Cell Death Detection Plus-ELISA to detect histone-associated DNA fragments (mono-nucleosomes and oligonucleosomes). Differences between groups were detected using t-test and associations between markers determined by Spearman's correlation coefficients.

Results: HIV+ve group had mean (SD) CD4 numbers 654 (269) and viral load with mean (SD) 17,036 (30,359) HIV RNA copies/mL. Significant differences were observed between HIV+ve compared to HIV-ve subjects in c-Nucs levels [Mean AU (SD) 48.24(27.81) vs. 28.37 (25.56) resp., p=0.02]; TNFR-II [Mean pg/mL (SD) 3392 (1796) vs.1630 (605) resp., p< 0.001]; CD8 T cell activation [% CD8 HLADR+CD38+ (SD) 9.75 (7.70) vs.2.48 (2.56) resp., p< 0.001] and CD8 T cell Caspase-3 [% (SD) 4.98 (3.74) vs.2.24 (1.02), p=0.003].

c-Nucs inversely correlated with CD4 Numbers (p=0.047, r= -0.300). Elevated c-Nucs levels were significantly associated with CD8 T cell activation (p=0.039, r=0.3117). Inflammation markers TNFR- II and IL-6 did not significantly correlate with c-Nucs. Importantly, c-Nuc levels significantly correlated with Caspase-3 expression in activated CD4 (p=0.014, r=0.367) and CD8 T cells (p=0.036, r= 0.316), programmed to undergo activation induced cell death by apoptosis.

Conclusions: Circulating nucleosomes correlated with activation induced cell death in HIV infected women. Circulating nucleosomes can stimulate the innate and adaptive immune system in HIV infection, keeping it chronically activated.

Mechanisms of T cell depletion and reconstitution

WEPEA122

HIV-infected individuals with suboptimal CD4 restration despite suppressive antiretroviral therapy exhibit altered CD4+ T cell subsets and escalated both CD4+ and CD8+ T cell exhaustion

K. Fujimoto[1], M. Kosugi-Kanaya[1], M. Kanaya[1], J. Sugita[1], M. Onozawa[1], D. Hashimoto[1], T. Endo[1], T. Kondo[1], S. Hashino[2], T. Teshima[1]

[1]Hokkaido University Graduate School of Medicine, Department of Hematology, Sapporo, Japan, [2]Hokkaido University, Health Care Center, Sapporo, Japan

Background: Poor immunological recovery despite virological successful antiretroviral therapy (ART) is partially explained by persistent immune activation, whereas the mechanism for defective immune restoration has not been fully clarified. We conducted T cell subset analysis in HIV-controlled patients with ART.

Methods: Peripheral blood mononuclear cells were isolated from 74 HIV-infected patients under suppressive ART for at least 2 years and analyzed the expression of markers related to activation (IL-7Rα, CD38), senescence (CD57), exhaustion (PD-1, CTLA-4, Tim-3, LAG-3, 2B4), apoptosis (Fas) and thymic function (CD31) on CD4+ and CD8+ T cell subsets: naïve (CD45RA+CCR7+), central memory (CM:CD45RA-CCR7+), effector memory (EM:CD45RA-CCR7-), terminally differentiated effector (CD45RA+CCR7-) and regulatory (CD4+CD25++CD127dim, Treg) T cells. Patients with at least 500 CD4+ T cells/mm^3 were categorized as complete responders (CR), whereas residual patients were categorized as incomplete responders (IR).

Results: Twenty-eight patients were classified as IR, and 46 patients as CR. CD4 count at the beginning of ART were lower in IR than CR (126 vs 221/mm^3, p=0.0107). The proportion of naïve CD4+ T cells was decreased (33.9 vs 41.6%, p=0.0442) and that of EM CD4+ T cells was increased (11.8 vs 8.5%, p=0.0168). Total number of CD8+ T cells was lower (692 vs 895/mm^3,

p=0.0151), while no proportion of CD8+ T cells was altered. In CD4+ T cells, the expressions of PD-1 and Fas were higher in CM subset (PD1; 55.1 vs 49.1%, p=0.0408 and Fas; 194.3 vs 162.7 MFI, p=0.0461). Meanwhile, in CD8+ T cells, the expressions of CD57 and 2B4 were upregulated, and IL-7Rα was downregulated in the all subsets (CD57; 302.3 vs 201.3 MFI, p=0.0461, 2B4; 64.6 vs 48.5 MFI, p=0.0498, IL-7Rα; 58.4 vs 69.8%, p=0.0112). The surface expression of CTLA-4 in whole T cells was faint but was significantly reduced in the all subsets in CD8+ T cells (11.0 vs 16.8%, p=0.0333) and also tended to be downregulated in Treg subset (14.6 vs 22.6%, p=0.0831).
Conclusions: Our findings suggest that, even under prolonged and fully suppressed ART, immune exhaustion in both CD4+ and CD8+ T cells can lead to an impairment of CD4+ T cell restoration. However, CTLA-4 might regulate immune reconstitution in a different manner.

WEPEA123

HIV-1 group M subtypes display differential rates of CD4 T cell decline

C. Venner[1], I. Nankya[2], E. Arts[1]
[1]*University of Western Ontario, Microbiology and Immunology, London, Canada,* [2]*Joint Clinical Research Centre, Kampala, Uganda*
Presenting author email: cvenner2@uwo.ca

Background: HIV-1, the etiological agent of AIDS, can be categorized into evolutionarily distinct clades. The most prevalent of these clades is Group M (Major) which can be further subdivided into 9 subtypes: A-D, F-H, J and K. The predominant viral subtypes of the epidemic in Sub-Saharan Africa are A, D and C, with subtype C making up more than 50% of global infections alone. Unfortunately, despite their importance in global health, these subtypes are studied far less frequently relative to subtype B, the predominant viral subtype in North America and Europe. This study sought to compare rates of pathogenesis between these understudied subtypes in a natural history cohort.
Methods: A cohort of HIV positive Zimbabwean and Ugandan women with known dates of infection had their CD4+ memory T-cell and viral loads monitored every three months post-infection. Subtype was determined via PCR of the viral envelope. All analyses were done using Generalized Estimating Equations (GEEs, n=302) and Generalized Linear Models (GLMs, n=68).
Results: These data showed distinct patterns of T-cell subset decline between HIV subtypes. Infection with a subtype C virus shows a significantly slower rate of cell decline in both total CD4+ cells as well as in CD4+ memory subsets compared to subtypes A and D (p< 0.01 and p< 0.003 respectively). Additionally, subtype C infections demonstrate a significantly longer time to viral load set point with no difference in total viral load at set point relative to subtypes A and D (p=0.009 and p< 0.001 respectively). Finally, acute early viruses (within 3 months of infection) were isolated from this cohort and their viral envelopes were cloned into a reporter virus for ongoing work on infection in human primary PBMCs.
Conclusions: Disease stemming from infection by an HIV subtype C virus progresses at a diminished rate compared to subtypes A and D. Preliminary studies suggest that similar patterns are also true for viral entry; subtype C viruses enter at a reduced rate relative to subtypes A and D.

Pathogenesis in gut, lymphoid tissues and bone marrow

WEPEA124

Flow virometry: envelope heterogeneity on individual HIV-1 virions

A. Arakelyan[1], W. Fitzgerald[1], D. King[2], V. Barreto-de-Souza[1], S. Zicari[1], J.-C. Grivel[1], R.J. Shattock[2], L. Margolis[1]
[1]*National Institute of Child Health and Human Development/NIH, Bethesda, United States,* [2]*Imperial College, London, United Kingdom*
Presenting author email: margolis@helix.nih.gov

Background: The ability of HIV to infect depends on the presence of "functional" spikes of envelope spike glycoproteins (Env) of non-covalently linked gp120-gp41 heterodimers. However, other non-functional Env conformations, including uncleaved precursors (gp160), aberrant oligomers, monomers and gp41 stumps devoid of gp120 are also thought to be displayed on virions. The extent to which functional and non-functional forms of Env are co-displayed on individual virions requires development of new techniques to analyze individual virions.
Methods: We have applied a new nanoparticle-based technique, "flow virometry", to probe the conformation of Envs on the surface of individual particles using a panel of anti-Env antibodies that discriminate between different conformations of these molecules. HIV-1 virions of BaL and SF162 strains were captured with 15 nm magnetic nanoparticles (MNPs) coupled to one of several monoclonal antibodies recognizing particular conformations of Env. Captured virions were then stained with fluorescent anti-Env antibodies different from the capture antibody and separated from free antibodies on a magnetic column. A range of antibodies targeting various Env forms were used and their representation on individual viral particles was assessed.
Results: We demonstrated a non-uniform distribution of functional and non-functional Envs within a viral population, where differential patterns of antibody staining revealed virion populations that were homogenous or mosaic with respect to functional and various non-functional forms of Env. Also, we identified extra-cellular vesicles (EVs) that carry gp120 and affect HIV infection. The presence of various functional and non-functional Envs corresponds to ability of HIV-1 to infect TZM-bl cells and human tissues ex vivo.
Conclusions: Flow virometry allowed the evaluation of the distribution of functional and non-functional spikes on individual virions to establish the relationship between the number of variously conformed Env molecules and infectivity of virions. We showed that what we call "HIV suspensions" are mixtures of true viruses carrying gp120 in different conformations, EVs carrying gp120, and intermediates between viruses and EVs, all important for HIV infection. Analysis of individual virions is important for understanding of HIV transmission, pathogenesis and for development of anti-HIV-1 vaccines, which must neutralize all functional spikes irrespective of their viral context.

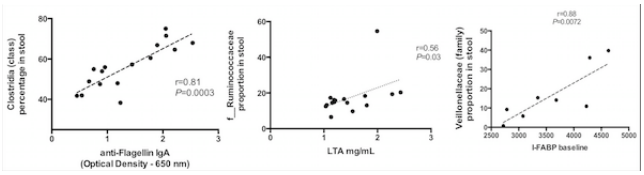
Microbial translocation and microbial dysbiosis

WEPEA125

Serum-derived bovine immunoglobulin (SBI)-induced changes in stool microbiota correlate with levels of microbial translocation (MT) and reduced mucosal damage

D.M. Asmuth[1], L. Ursell[2], N.G. Sandler[3], B. Siewe[4], T.R. Ziegler[5], A.T. Gewirtz[5,6], A. Albanese[7], P. Troia-Cancio[1], A. Landay[4], D.C. Douek[8], R. Knight[9]
[1]*University of California Davis School of Medicine, Internal Medicine/Infectious Diseases, Sacramento, United States,* [2]*University of Colorado at Boulder, Department of Chemistry and Biochemistry, Boulder, United States,* [3]*University of Texas Medical Branch, Galveston, United States,* [4]*Rush University, Chicago, United States,* [5]*Emory University, Atlanta, United States,* [6]*Georgia State University, Atlanta, United States,* [7]*Veterans Administration Hospital of Northern California, Mather, United States,* [8]*National Institute of Health, Human Immunology Section, NIAID, Bethesda, United States,* [9]*University of California San Diego, San Diego, United States*
Presenting author email: david.asmuth@ucdmc.ucdavis.edu

Background: SBI is a medical food that improves HIV enteropathy and increases CD4+ T-cell density in duodenal GALT. These studies sought to identify microbiome correlates of the effect of SBI on HIV enteropathy and MT.
Methods: 8 subjects (pts) on suppressive ART with HIV enteropathy received SBI (EnteraHealth, Ankeny, IA) 5 gms/day for 8 weeks (wks) and 5 continued for 48 wks. 16S rDNA from the stool were sequenced using Illumina MiSeq Sequencer and processed using the QIIME pipeline. Serum lipoteicoic acid (LTA), from gram-positive cell walls, anti-flagellin IgA (aFlig-A), and I-FABP, released from damaged enterocytes were measured by ELISA. Bacterial 16S rDNA from serum was quantitated by qPCR. Median values and nonparametric analysis are reported.
Results: There were no treatment effects on LTA and 16s rDNA levels, but I-FABP fell in 4/5 subjects who finished 48 wks of SBI and aFlig-A declined in 6/8 pts (*P*=0.15). The Bacteroidetes/Firmicutes ratio, which is low in obesity, increased in 6/8 pts from 0.27 to 0.55 (*P*=0.11). Clostridiales (order) fell in 6/8 from 56.6% to 51.4% (**P**=NS). Clostridiales correlated with aFlig-A (r=0.81, *P*=0.0003). At the family level, Ruminococcaceae correlated with LTA (r=0.59, *P*=0.03), and Veillonellaceae correlated with I-FABP baseline and end of treatment levels (r=0.76, *P*=0.001)(see figure below). 16S rDNA correlated with Clostridiaceae as well as Enterobacteriaceae (r=0.55, *P*=0.03, and r=0.69, *P*=0.004, respectively).
Conclusions: SBI for 8 wks improved symptoms of HIV enteropathy and had a modest impact on stool microbiota, largely in anaerobic taxa within the order Clostridiales. Ruminococcaeae are an enterotype associated with obesity phenotype and Veillonellaceae are an oral pathogen causing gingovitis and abscesses. These data suggest that different families of Clostridiales play separate roles in pathogenic findings related to HIV enteropathy and MT.



[Clostridia correlates of MT]

WEPEA126

Influence of HIV infection and antiretroviral therapy on the immune status and microbial translocation in HIV-infected children in Vietnam

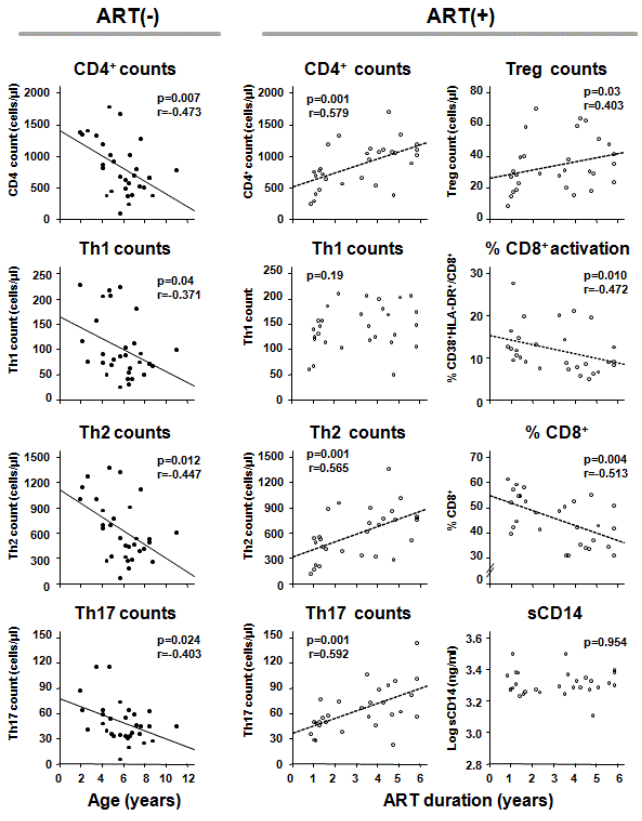
X. Bi[1], A. Ishizaki[1], L.V. Nguyen[2], K. Matsuda[3], H.V. Pham[2], C.T.T. Phan[2], K. Ogata[3], T.T.T. Giang[2], T.T.B. Phung[2], T.T. Nguyen[2], M. Tokoro[4], A.N. Pham[2], D.T.K. Khu[2], H. Ichimura[1]
[1]Kanazawa University, Department of Viral infection and International Health, Kanazawa, Japan, [2]National Hospital of Pediatrics, Hanoi, Vietnam, [3]Yakult Central Institute for Microbiological Research, Tokyo, Japan, [4]Department of Parasitology, Kanazawa, Japan
Presenting author email: bixiuqiong@hotmail.co.jp

Background: The destruction of CD4+T-cells particularly Th17 subset in the gut-associated lymphoid tissue, intestinal microbial translocation, and chronic systemic immune activation are reported as the main pathogenesis of HIV infection. A few studies on these in children have been reported. This study aimed to investigate the influence of HIV infection and antiretroviral therapy (ART) on the immune status and the microbial translocation in HIV-infected Vietnamese children.

Methods: This was a cross-sectional study carried out in the National Hospital of Pediatrics in Hanoi, Vietnam in May 2012. Blood samples were collected from 60 HIV-infected children [HIV(+), age 2.0-11.0 years, male/female 26/34]: 31 without ART [ART(-)] and 29 with ART [ART(+), ART duration 0.8-5.8 years], and 20 HIV-uninfected children [HIV(-), age 2.0-8.3 years, male/female 8/12], and analyzed immunologically and bacteriologically. ART(+) children were treated with AZT/3TC/NVP (8), d4T/3TC/NVP (7), AZT/3TC/EFV (6), d4T/3TC/EFV (4) and other drug combinations (4). The cells were defined as: Th1 ($CXCR3^+CCR6^-CD4^+$), Th2 ($CXCR3^-CCR6^-CD4^+$), Th17 ($CXCR3^-CCR6^+CD4^+$), Treg (regulatory T, $CD25^{high}CD4^+$), activated $CD8^+$ ($CD38^+HLA\text{-}DR^+CD8^+$). Mann-Whitney test and Spearmen correlation was done using SPSS-v19 with p< 0.05 considered significant.

Markers	HIV(+)ART(-) n=31	HIV(+)ART(+) n=29	HIV(-) n=20	ART(-) vs HIV(-)	ART(+) vs HIV(-)	ART(-) vs ART(+)
CD4+ count (cells/µl)	698	894	1050	0.003	0.018	>0.05
Th1 count (cells/µl)	80	147	135	0.003	>0.05	0.002
Th2 count (cells/µl)	537	553	821	0.016	0.009	>0.05
Th17 count (cells/µl)	45	58	109	<0.001	<0.001	0.016
Treg count (cells/µl)	14	30	48	<0.001	0.004	<0.001
% CD8+/lymphocytes	43.4	44.7	31.4	<0.001	<0.001	>0.05
CD8+ count (cells/µl)	1368	1212	1101	>0.05	>0.05	>0.05
% activated CD8+	27.5	10.2	12.9	<0.001	>0.05	<0.001
sCD14 (ng/ml)	1637	1964	1413	0.009	<0.001	<0.001

[Comparison of markers in different groups]



[Correlation analysis in ART(-) and ART(+)]

Results: Compared with HIV(-) group, ART(-) had significantly lower $CD4^+$/Th1/Th2/Th17/Treg counts, significantly higher proportions of activated $CD8^+$ cells, $CD8^+$ cell percentages in lymphocytes and sCD14 in plasma. The decrease of $CD4^+$/Th1/Th2/Th17 counts correlated significantly with the children's age (HIV infection period) in ART(-). Bacterial 16S/23S rRNA was not detected in whole blood samples but the rDNA was detected in plasma of ART(-) (25.8%) and HIV(-) (15%) (p=0.49). In ART(+), the increase of $CD4^+$/Th2/Th17/Treg counts correlated significantly with ART duration, but Th1 counts were restored to the Th1 level of HIV(-) after about 1 year of ART; the proportion of activated $CD8^+$ cells and the $CD8^+$ percentages in lymphocytes declined significantly with the ART duration, but sCD14 level in plasma showed no significant change. ART(+) had significantly lower viral load than ART(-).

Conclusions: In children, HIV infection reduced $CD4^+$/Th1/Th2/Th17/Treg counts, enhanced $CD8^+$ cell activation and sCD14 level in plasma. ART restored $CD4^+$/Th1/Th2/Th17/Treg counts, suppressed $CD8^+$ activation, but showed little influence on sCD14 levels. HIV infection tended to increase microbial translocation but not significantly.

WEPEA127

TLR2 stimulation acts synergistically with acetate stimulation to promote HIV-1 infection of CD4 + T cells

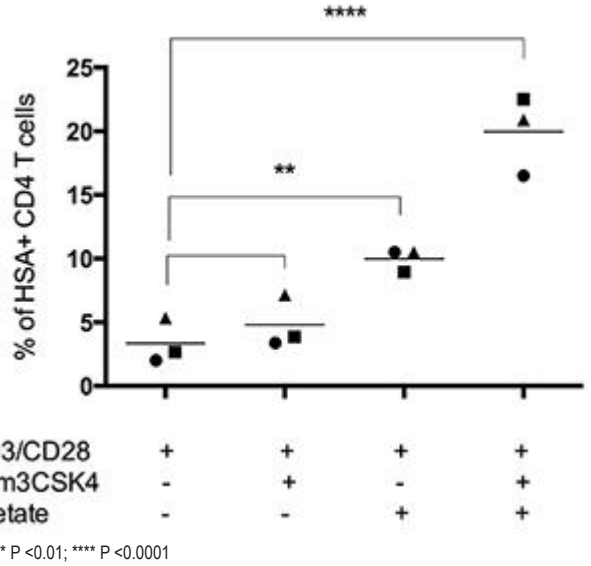
J.-F. Bolduc, M. Ouellet, M.J. Tremblay
Université Laval, Québec, Canada
Presenting author email: jean-francois.bolduc@crchul.ulaval.ca

Background: Following primary infection, HIV-1 breaches the integrity of gut and/or female genital tract mucosal epithelial barrier allowing bacterial translocation. Those anaerobic microorganisms may stimulate CD4+ T cells (T4 cells) through Toll-like receptor (TLR) and the production of short-chain fatty acids.
In this study, we investigated the effect of acetate combined, or not, to TLR2 ligation on the susceptibility of T4 cells to HIV-1 infection.

Methods: Primary human resting T4 cells were stimulated for 72h with anti-CD3/CD28 antibodies +/- acetate and Pam3CSK4 (TLR2 ligand). Cells were then infected with the R5 HIV-1-based reporter virus NL4-3-Bal-IRES-HSA for 72h. The effect of acetate +/- Pam3CSK4 stimulations on T4 cells' susceptibility to HIV-1 infection was then analyzed by flow cytometry where the percentage of productively infected T4 cells expressing HSA was evaluated and confirmed by p24 ELISA. The effect of acetate +/- Pam3CSK4 stimulations on cell distribution, proliferation and activation and on the relative susceptibility of CCR6+/- T4 cells to HIV-1 infection were analysed by flow cytometry to explain the correlation between those stimulations and T4 cells' susceptibility to HIV-1 infection.

Results: Acetate and acetate/Pam3CSK4 stimulations induced respectively a 3-fold and a 6-fold increase in the percentage of infected (HSA+) T4 cells compared to controls (n=3). This was reflected on viral p24 production as assessed by ELISA (n=3). However, neither acetate nor acetate/Pam3CSK4 stimulations affect cell distribution (n=3), proliferation (n=4) and the relative susceptibility of CCR6+/- T4 cells to HIV-1 infection (n=3). Most importantly, acetate and acetate/Pam3CSK4 stimulations increase cell activation as reflected by a significant increase in CD69 and CD154 cell surface expression.

Conclusions: We suggest that acetate stimulation plays a significant role in early HIV-1 infection by increasing cell activation. We also propose that this augmentation of T4 cells' susceptibility to HIV-1 infection induced by acetate stimulation may be synergistically enhanced by TLR2 ligation. These results highlight the possible importance of early interactions between HIV-1 and female genital tract/gut microbiota where bacteria act via the production of short-chain fatty acids and/or their pathogen-associated molecular patterns.



n = 3; ** P <0.01; **** P <0.0001
[Summary results_Acetate_TRL2L_JFB]

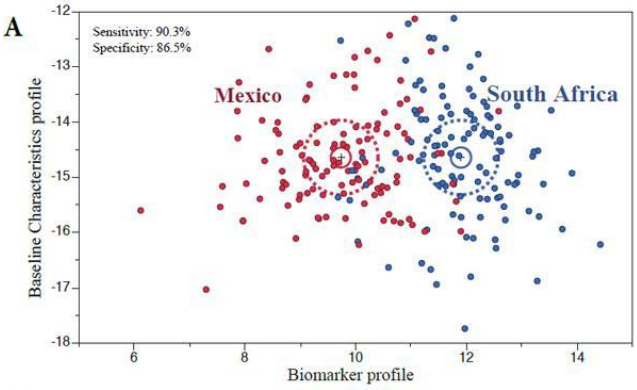
Mechanisms underlying immune reconstitution inflammatory syndrome (IRIS)

WEPEA128

Ethnicity impacts inflammatory and coagulation profile in HIV patients

M. Manion[1], R. DerSimonian[1], W. Gu[1], B. Andrade[2], A. Rupert[3], L. Musselwhite[4], J. Sierra-Madero[5], P. Belaunzaran-Amudio[5], I. Sanne[6], M. Lederman[7], I. Sereti[1]
[1]National Institutes of Health, Bethesda, United States, [2]FioCruz, Salvador, Brazil, [3]Leidos Biomedical Inc, Reston, United States, [4]Duke Global Health Institute, Durham, United States, [5]Instituto Nacional de Ciencias Medicas y Nutricion, Mexico City, Mexico, [6]University of Witwatersrand, Johannesburg, South Africa, [7]Case Western Reserve University, Cleveland, United States
Presenting author email: isereti@niaid.nih.gov

Background: Biomarkers of inflammation and coagulation are independent predictors of morbidity and mortality in HIV infected patients. Multiple studies have investigated biomarkers in HIV study cohorts, however whether ethnicity or country has an effect on those biomarkers is unknown. We aimed to investigate the influence of ethnicity/country on biomarker levels in HIV infected patients at similar stages of HIV infection.
Methods: Cryopreserved baseline plasma specimens were analyzed using ELISAs, electrochemiluminescence, and enzyme-linked immunofluorescence assay from two hundred sixty seven ART naïve patients with CD4 < 100 cells/ul, participating in the CADIRIS trial from clinical sites in Mexico (N= 124) and South Africa (N=128). Sparse canonical correlation was performed to demonstrate the distribution of biomarkers between the two countries (Figure 1a). Median levels of biomarkers from each site were compared with Wilcoxon rank-sum test, and then these variables were subsequently adjusted using multivariate analysis (Figure 1b).



B

Biomarkers from CADIRIS study based upon country of origin

	Mexico	South Africa	P-value
Fibrinogen (mg/dL)	723 [448, 1300]	1229 [715, 1945]	<0.0001
IFN-γ (pg/mL)	4.09 [2.20, 7.41]	2.19 [1.17, 5.58]	0.034
IL-8 (pg/mL)	11.80 [7.77, 18.13]	5.79 [3.40, 8.31]	<0.0001
IP 10 (pg/mL)	2575 [439, 1780]	1691 [999, 2693]	<0.0001
Leukotriene B4 (pg/mL)	10.20 [10.20, 37.17]	47.84 [16.50, 76.57]	<0.0001
P-selectin (ng/mL)	48.49 [37.2, 64.71]	64.65 [50.05, 82.57]	<0.0001
% Protein S	3550 [3037, 3960]	4376 [3658, 5430]	<0.0001
Vitamin D (ng/mL)	7.72 [4.44, 13.36]	10.42 [6.9, 17.09]	0.026
sCD40 L (pg/ml)	586 [227, 1096]	1157 [870, 1716]	<0.0001

Figure 1.

A) Sparse Canonical Correlation: The x-axis gives the score in the biomarker profile while the y-axis gives the score in the baseline characteristics. Data on biomarkers were inputted after logaritimic transformation. Data points were labeled based on the two diagnostic classes South Africa or Mexico. Small circles denote 95% confidence region estimated to contain the mean of a group. Ellipses denote the regions estimated to contain 50% of the class clusters.

B) Biomarkers (Medians and IQR) that differed significantly by country when adjusted for baseline characteristics.

[Figure 1]

Results: Baseline patient characteristics that differed significantly between Mexico and South Africa included age (35 vs. 38 years, p=0.006), gender (12% vs. 54% female, p<0.0001), CD4 count (31 vs. 37 cells/ul, p=0.034), hemoglobin (13 vs. 12 g/dL, p=0.03), AIDS defining illness (79% vs. 43% of patients, p<0.0001), and prevalence of active TB (17% versus 28% of patients, p=0.0404). Baseline plasma HIV viremia and CD8 T cells did not differ significantly. After adjusting for baseline characteristics, patients from the Mexican cohort had higher levels of IFN-γ, IL-8, and IP-10 whereas patients from South Africa had higher levels of vitamin D, fibrinogen, LTB4, P-selectin, protein S, and sCD40 ligand.
Conclusions: Our data suggest that inflammatory and coagulation biomarkers may vary significantly by region or ethnicity and that country-specific data may be needed in studies using biomarkers as predictors or clinical trial end points. Further studies are needed to evaluate how these differences may also contribute to HIV pathogenesis and prognosis in diverse populations.

Central nervous system

WEPEA129

Cell-to-cell transmission of HIV from lymphocytes to astrocytes via a unique, CXCR4-dependent mechanism

G.-H. Li[1], C. Anderson[1], L. Jaeger[1], T. Do[2], E. Major[3], A. Nath[1]
[1]NIH/NIDS, Section of Infection of the Nervous System, Bethesda, United States, [2]NIH/NCI, Laboratory of Cell Biology, Bethesda, United States, [3]NIH/NIDS, Laboratory of Molecular Medicine and Neuroscience, Bethesda, United States
Presenting author email: guanhan.li@nih.gov

Background: HIV reservoir in the brain represents a major barrier for curing HIV infection. As the most abundant, long-lived cell type, astrocytes play a critical role in maintaining the reservoir; however the mechanism of infection remains unknown. Here, we determine how viral transmission occurs from HIV-infected lymphocytes to astrocytes by cell-to-cell contact.
Methods: Human astrocytes were exposed to HIV-infected lymphocytes and monitored by live-imaging, confocal microscopy, transmission and 3-demesional electron microscopies. A panel of receptor antagonists was used to determine mechanism of viral entry. An in vitro BBB model was established to test the migration of HIV-infected lymphocytes.
Results: We found that cell-to-cell contact resulted in efficient transmission of X4- or X4R5-using viruses from T lymphocytes to astrocytes. In co-cultures of astrocytes with HIV-infected lymphocytes, the interaction occurred through a dynamic process of attachment and detachment of the two cell types. Infected lymphocytes invaginated into astrocytes or the contacts occurred via filopodial extensions from either cell type, leading to formation of virological synapses. In the synapses, budding of immature or incomplete HIV particles from lymphocytes occurred directly onto the membranes of astrocytes. This cell-to-cell transmission could be almost completely blocked by anti-CXCR4 antibody and its antagonist, but only partially inhibited by CD4, ICAM1 antibodies. Furthermore, SDF-1 that can be secreted from astrocytes in patients with HIV-associated neurological diseases significantly triggered the migration of HIV-infected lymphocytes across the BBB.
Conclusions: Cell-to-cell transmission was mediated by a unique mechanism by which immature viral particles initiated a fusion process in a CXCR4-dependent, CD4-independent manner. These observations have important implications for developing approaches to prevent formation of HIV reservoirs in the brain.

Mechanisms underlying co-morbidities in ARV treated individuals

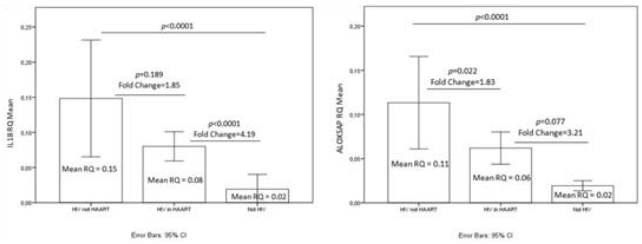
WEPEA130

IL18 and ALOX5AP mRNA levels are increased in HIV-infected individuals despite the use of HAART

L. Ibáñez[1], P.S. Velli[2,3], R. Font[2,3], A. Jaén[1], J. Royo[2,3], D. Irigoyen[2,3], A. De La Sierra[2,3], M. Cairó[2,3], D. Gallardo[4], D. Dalmau Juanola[1,2,3]
[1]Fundació Docència i Recerca MútuaTerrassa, Terrassa, Spain, [2]Hospital Universitari MútuaTerrassa, Terrassa, Spain, [3]Universitat de Barcelona, Barcelona, Spain, [4]Universitat Autonoma de Barcelona, Bellaterra, Spain
Presenting author email: ddalmau@mutuaterrassa.cat

Background: Persistent inflammation is thought to be related to a high prevalence of HIV-associated comorbidities. It has been shown that HAART introduction diminishes the levels of inflammatory proteins in HIV-infected individuals, but not to the levels observed in non-infected subjects. However, the transcriptional involvement of blood cells in HIV-related inflammation is still uncertain.
The purpose of our study was to test if the mRNA levels of 9 genes involved in inflammation (*CX3CR1, IL8, CXCL2, LTA, IL6, ALOX5, ALOX5AP, IL18* and *CCL5*) are affected by HAART treatment in blood cells of HIV-infected subjects.
Methods: This cross sectional study included 142 treated HIV-infected individuals, 31 untreated HIV-infected individuals and 19 uninfected controls. RNA was extracted from blood white cells using standard methods. Relative quantification of mRNA levels (RQ) was performed using quantitative PCR methodology. Results were analyzed with the ΔΔCt method using *ACTB* as Housekeeping gene.
Mann-Whitney U and Kruskal-Wallis tests were performed to study the variations of mRNA levels. Statistical analyses were conducted using SPSS and Expression Suite Statistical Packages.
Results: mRNA levels of *ALOX5AP* and *IL18* were found significantly different when comparing the three groups (HIV untreated, HIV treated and uninfected controls). Increased *ALOX5AP* and *IL18* mRNA levels were observed when comparing HIV-untreated and HIV-treated

individuals, although only *ALOX5AP* mRNA levels reached statistically significant values. *IL18* and *ALOX5AP* mRNA levels were lower in uninfected controls compared with HIV-treated subjects. Only *IL18* mRNA levels reached statistically significant values.



[Gene Expression versus ART treatment Status]

Conclusions: Alterations in mRNA levels of genes involved in the inflammatory pathway were observed in HIV-treated subjects in comparison with uninfected controls. However, the mRNA levels in HIV-treated patients were markedly inferior to those observed in HIV-untreated subjects, highlighting the possible benefits of earlier introduction of HAART. Further studies are needed for a better understanding and control of the inflammatory pathway.

Viral mechanisms of HIV/SIV persistence and latency

WEPEA131

Low frequency of HIV rebound after antiretroviral treatment interruption

M. Pinkevych[1], D. Cromer[1], M. Tolstrup[2], D. Cooper[3], S. Lewin[4,5], O. Søgaard[2], T. Rasmussen[2], S. Kent[4], A. Kelleher[3], M. Davenport[1]
[1]UNSW Australia, Sydney, Australia, [2]Aarhus University Hospital, Denmark, Norway, [3]Kirby Institute, Sydney, Australia, [4]Doherty Institute for Infection and Immunity, The University of Melbourne, Melbourne, Australia, [5]Alfred Hospital and Monash University, Melbourne, Australia
Presenting author email: m.davenport@unsw.edu.au

Background: HIV persists in latent reservoirs and produces viral rebound upon interruption of antiretroviral therapy (ART). Understanding the temporal kinetics of viral recrudescence upon interruption of ART is important for current curative strategies aimed at achieving ART-free viral remission.
Methods: We have analysed clinical data on time to viral rebound after ART-interruption from four independent patient cohorts totaling 100 patients. This includes patients treated with a variety of ART regimes, treated at different stages of HIV infection (including primary infection, n = 59), treated with latency reversing agents (n=9) and monitored regularly for viral recrudescence early after ART-interruption. We fitted a model of exponential distribution of time to recrudescence to each cohort to estimate the average frequency of viral recrudescence that would be required to produce the observed distribution of time-to-infection. The same approach was also applied to data on viral rebound in macaques treated early in infection.
Results: The time between ART-interruption and viral detection varied widely amongst different patients. However, within all patient cohorts, time to detection followed an exponential distribution. Fitting the distribution of time-to-detection, we derived an average frequency of viral recrudescence of once every 6 days (range 5.1 - 7.6 days between the four cohorts). This rate is over 30 times lower than previous estimated and suggests that a reduction in the reservoir size of around 61-fold would be required to extend the average time-to-recrudescence to about one year. Analysis of the time-to-recrudescence in a cohort of SIV infected macaques treated early in infection reveals an average frequency of reactivation events of once every 1.7 days - over three times more frequent than in HIV infection in humans.
Conclusions: Previous studies have suggested that HIV reactivates from latency around five times per day, based on indirect estimates of rates of acquisition of drug resistance under ART. We estimate a frequency of reactivation that is 30 times lower (once every 6 days), based on analysis of time to recrudescence. This has important implications for how much the latent reservoir will need to be reduced to produce significant remissions after ART-interruption.

WEPEA132

Dynamic imaging of intracellular glutathione redox potential of HIV-1 infected macrophages and its exploitation by *Mycobacterium tuberculosis* through its lipids

M. Munshi[1], A. Bhaskar[1], S. Jameel[2], A. Singh[1]
[1]Indian Institute of Science, Department of Microbiology and Cell Biology, Bangalore, India, [2]International Centre for Genetic Engineering and Biotechnology, Virology, New Delhi, India
Presenting author email: mohsinmunshi@yahoo.com

Background: Oxidative stress plays an important role in HIV-1 pathogenesis. Several markers of oxidative stress including glutathione, thioredoxins, cysteine, *etc* were found to be altered in HIV-1 infected patients. Conventional measurements of oxidative stress upon HIV-1 infection are either based on redox dyes or invasive technologies, thereby introducing oxidation artifacts and preclude dynamic measurements. In this study, we have utilized a novel non-invasive technology based on genetically encoded redox biosensors, to measure redox potential of HIV-1 infected macrophages in real-time.
Methods: Since intracellular levels of oxidized (GSSG) and reduced glutathione (GSH) are used as indicator of cellular redox potential, we non-invasively tracked glutathione redox potential (*E*GSH) of HIV-1 infected macrophage cell line (U1) using a highly sensitive and specific bioprobe, Grx1-roGFP2. We report precise measurements of *E*GSH in sub-cellular compartments during HIV-1 infection. We also measured *E*GSH during HIV-1 activation from latency using lipids isolated from different clinical strains of *M.tuberculosis*. We performed oxidative stress and antioxidant defense pathway-focused human gene expression-array during latent and reactivation phase of HIV-1 infection using U1 and its uninfected counterpart U937 cells. Lastly we performed qRT-PCR analysis using selected set of oxidative stress genes on RNA isolated from the PBMCs of HIV-1 infected symptomatic individuals.
Results: We show that the steady-state *E*GSH of cytosol and mitochondria in both HIV-1 infected (U1) and uninfected (U937) macrophages was highly reduced (i.e. -310 mV to -320 mV). In contrast, activation of HIV-1 replication induces significant oxidative shift in the *E*GSH (~-240 mV) of mitochondria and cytosol. We found that *E*GSH of U1-cells dynamically responds to pro-apoptotic signal, H2O2, to modulate resistance towards oxidative stress and apoptosis. Importantly, we show that bioactive-lipids synthesized by clinical drug-resistant isolates of *M.tuberculosis* reactivate HIV-1 through modulation of intracellular *E*GSH. Finally, the expression analysis of U1 and patient PBMCs demonstrated a major recalibration of cellular redox homeostatic pathways during persistence and active replication of HIV-1.
Conclusions: Since redox signaling is believed to play an important role in HIV-1 reactivation and progression to AIDS, we believe that this technology will open up fresh avenues of research pertaining to the development of novel intervention strategies against HIV-1 infection.

WEPEA133

Histone deacetylase inhibitors alter the accumulation of spliced HIV mRNA: implications for virus production

T.M. Mota[1,2], F. Wightman[2,3], K.Y. Cheong[2], H.K. Lu[2], J.L. Anderson[2,3], A. Solomon[2,3], D.F. Purcell[1,2], S.R. Lewin[2,3]
[1]University of Melbourne, Department of Microbiology and Immunology, Melbourne, Australia, [2]University of Melbourne, Peter Doherty Institute for Infection and Immunity, Melbourne, Australia, [3]Alfred Hospital and Monash University, Department of Infectious Diseases, Melbourne, Australia

Background: Clinical trials in HIV-infected patients on antiretroviral therapy with histone deacetylase inhibitors (HDACi) have demonstrated an increase in cell-associated unspliced (CA-US) HIV RNA, variable changes in plasma HIV RNA and no change in the number of latently infected cells. We aimed to define the effects of latency reversing agents (LRAs) on HIV mRNA splicing.
Methods: Resting CD4+ T cells isolated from the blood of HIV-negative individuals were treated with the chemokine CCL19 and infected with wild type $HIV^{NL4.3}$ to establish latency (n=5). Latently infected CCL19-stimulated cells were then cultured with vorinostat, romidepsin, JQ1, romidepsin+JQ1 or PMA/PHA, all in the presence of an integrase inhibitor (L8). Cells and supernatant were harvested at 6, 24, 48, and 72 hours. Reverse transcriptase (RT) was quantified in supernatant and CA-US and multiply spliced (MS) HIV RNA were quantified by real time qPCR.
Results: In latently infected CCL19-treated CD4+ T-cells, stimulation with PMA/PHA led to a significant exponential increase in both US-RNA and MS-RNA, and by 48 hours reached a mean fold increase above baseline of 80-fold for US-RNA and 56-fold for MS-RNA (p=0.03 for both, relative to DMSO). There was a significant increase in RT in supernatant following stimulation with PMA/PHA but no change following any LRA (n=2). In contrast, following stimulation with each LRA, there was only a modest increase in CA-US RNA that was not statistically significantly different from DMSO (p=0.56). MS-RNA increased transiently (mean 2.7-fold change at 6hr with romidepsin) and then significantly declined over time following treatment with romidepsin and romidepsin+JQ1 (p=0.02 and 0.002 respectively), with a mean fold reduction by 72 hours compared to baseline of 0.15-fold and 0.17-fold respectively (p=0.02 for both compared to DMSO) in the absence of any cellular cytotoxicity.

Conclusions: In this in vitro model of latency, PMA/PHA and the potent HDACi romidepsin had strikingly different effects on the accumulation of US-RNA, MS-RNA and virus production. While successful HDACi agents yield small increases in US-RNA, synergistic strategies that achieve a larger accumulation of MS RNA may result in enhanced release of latent HIV.

WEPEA134

Purging HIV-1 from latent reservoirs using human methyltransferase inhibitors

S. Samer[1], L.B. Giron[1], M.S. Arif[1], T.M. Oshiro[2], M.C.A. Sucupira[1], A. Duarte[2], R.S. Diaz[1]
[1]Federal University of Sao Paulo, Medicine, Sao Paulo, Brazil, [2]University of Sao Paulo, Dermatology, Sao Paulo, Brazil
Presenting author email: sadia.samer1@gmail.com

Background: Histone lysine methylation is one of the most robust histone modifications, with central role in conferring epigenetic control to the chromatin template. Latent HIV proviruses are silenced as a result of deacetylation and methylation of histones located at the long terminal repeats (LTRs). Thus the chromatin remodeling plays a major role in chromatin-mediated repression or expression of the HIV-1 promoter. Here, we evaluated the potential of two histone methyl transferase inhibitors (HMTIs) namely Chaetocin and BIX-01294 in reactivating HIV-1 from latency.
Methods: We used CD8T-cells depleted PBMCs isolated from 15 HIV$^+$ HAART-treated patients with undetectable viral load over a period 4 years. We measured HIV-1 recovery in ex-vivo cell cultures first activated by PHA for one day and then treated with chaetocin and BIX-01294 and cultivated in RPMI medium supplemented with IL-2 and fetal bovine serum while CD8$^+$ T-cells depleted PBMCs activated with PHA and then cultivated in RPMI medium supplemented with IL-2 and fetal bovine serum were used as control samples.
Results: HMTIs induced purging in 11 out of 15 subjects. Second day after treatment with the drugs, culture supernatants were tested for viral load using qPCR and the results revealed HIV-1 emergence from day 3rd -day 29th (median 09 days) with viral load from 2.2 log10 to 6.0 log10 (median of 5.7). To find a correlation between PBMC proviral load and culture positivity, qPCR was done. Proviral load varied from 28.51 to 515.90 (median=91; mean=144.21). The results showed that culture positivity is independent of proviral load, CD4+T cell nadir, time of viral laod below detection limits and antiretroviral scheme.
Conclusions: As part of an attempt to HIV eradication in human hosts, it would be important to overcome HIV latency, one of the major obstacles towards the sterilizing HIV cure. We showed here that these non-administrable HMTIs may provide a therapy to purge the dormant HIV-1 from reservoirs possibly in combination with other chromatin remodeling drugs. Therefore, clinical grade HMTIs should be synthesized or screened and evaluated to exploit their HIV reactivation potential.

Host cellular factors and latency

WEPEA135

Immunological markers associated with HIV persistence during ART identified by iterated conditional random forests analysis

R. Fromentin[1], C.M. Ramirez[2], G. Khoury[3], E. Sinclair[4], F.M. Hecht[4], S.G. Deeks[4], R.P. Sekaly[5], S.R. Lewin[3,6], N. Chomont[1,7]
[1]CRCHUM, Montreal, Canada, [2]University of California Los Angeles, Department of Biostatistics, Los Angeles, United States, [3]Alfred Hospital and Monash University, Department of Infectious Diseases, Melbourne, Australia, [4]University of California San Francisco, Department of Medicine, San Francisco, United States, [5]Case Western Reserve University, Department of Pathology, Cleveland, United States, [6]The University of Melbourne, Doherty Institute for Infection and Immunity, Melbourne, Australia, [7]Université de Montréal, Department of Microbiology, Infectiology and Immunology, Montreal, Canada
Presenting author email: fromentin.remi@gmail.com

Background: The persistence of latently infected cells and residual levels of viral production contribute to HIV persistence and immune activation in HIV infected individuals on suppressive antiretroviral therapy (ART) and represent major barriers to HIV eradication. We hypothesized that HIV persistence on ART was associated with markers of T-cell activation, homing and proliferation.
Methods: Expression of activation/proliferation markers, chemokines receptors, immune checkpoints and their ligands were measured by flow cytometry on PBMCs isolated from 48 HIV-infected subjects on ART for >3 years with HIV viral load < 50 copies/ml and with a CD4 count >350 cells/µL. Two virological markers of HIV persistence were determined by quantitative (q)PCR: the frequencies of CD4 T cells harboring integrated HIV DNA and cell associated unspliced (CA-US) HIV RNA . Chemokines, gamma-c cytokines and sCD14 were quantified in plasma. More than 600 variables were analyzed by fuzzy forests to identify novel biomarkers associated with HIV persistence and that predict low reservoir size. Briefly fuzzy forests first separates the variables into modules that have a similar correlation structure to account for network effects and then performs recursive feature elimination random forests to find the top parameters that are predictive of the outcome.
Results: Using fuzzy forests, we identified the top 100 variables of importance/predictors that were most strongly associated with high frequency of CD4 T cells harboring integrated HIV DNA or CA-US HIV RNA. High CA-US RNA was strongly associated with activating IFN signaling pathway in T cells (pSTAT1-3). High frequency of cells harboring integrated HIV DNA was associated with low CD4 count (p=0.0015) as expected but also with higher frequency of cells expressing markers of proliferation/activation (including expression of 2B4, LAG3, TIGIT on central memory CD4 T cells, p=0.0057, p=0.0016, p=0.0106 respectively and HLA-DR and CD38 on CD8 T cells, p=0.019 and p=0.0252 respectively).
Conclusions: Current assays that measure virus persistence are associated with different immunological pathways. CA-US RNA, a surrogate marker of active viral transcription, was associated with the STAT1-3 downstream of type I interferon signaling pathway while the number of latently infected cells was associated with markers of T-cell activation, proliferation and exhaustion.

WEPEA136

Transcriptional profiling identifies RORC and PPARG as two major mechanisms regulating HIV permissiveness in primary Th17 cells

Y. Zhang[1,2], D. Planas[1,2], A. Cleret-Buhot[1,2], J.-P. Goulet[3,4], P. Monteiro[1,2], A. Gosselin[1,2], V. Sue Wacleche[1,2], M.-A. Jenabian[5], J.-P. Routy[6,7], E. Haddad[8], R.-P. Sekaly[9], P. Ancuta[1,2]
[1]CHUM-Reseach Centre, Montreal, Canada, [2]Université de Montréal, Department of Microbioloy, Infectiology and Immunology, Montreal, Canada, [3]CARTaGENE, Université de Montréal, Montreal, Canada, [4]Research Centre Ste-Justine Hospital, Montreal, Canada, [5]Université du Québec à Montréal, Biological Sciences and BioMed Research Centre, Montreal, Canada, [6]McGill University Health Center, Division of Hematology, Montreal, Canada, [7]McGill University Health Centre, Chronic Viral Illness Service and Research Institute, Montreal, Canada, [8]Vaccine and Gene Therapy Institute, Port St Lucie, United States, [9]Case Western Reserve University, Cleveland, United States
Presenting author email: zhangyw927@gmail.com

Background: Th17 cells are major players in mucosal immunity. Th17 cells are highly permissive to HIV infection, while Th1 cells are relatively resistant. As a consequence, Th17 are depleted in HIV-infected subjects and their frequency is partially restored under antiretroviral therapy. Our recent studies demonstrated persistence of HIV reservoirs in CD4+ T-cells expressing the Th17 marker CCR6 in ART-treated subjects. To identify molecular mechanisms of HIV permissiveness in Th17 cells, we performed a genome-wide analysis of gene expression in Th17 *vs.* Th1 cells.
Methods: Th17 (CCR4+CXCR3-CCR6+) and Th1 (CCR4-CXCR3+CCR6-) subsets were sorted by flow cytometry and stimulated *via* CD3/CD28 Abs. The expression of 47,000 probe-sets was tested using the Illumina BeadArray technology. Transcripts were classified by biological functions using *Gene Set Variation Analysis* and *Gene Ontology*. Real-time RT-PCR and fluorescence microscopy were used to validate differential gene expression. RNA interference was used to evaluate the role of top-modulated genes in regulating HIV permissiveness. Cytokine production and proliferation was measured by flow cytometry. HIV infection-integration was quantified by HIV-p24 ELISA and nested real-time PCR.
Results: HIV permissiveness in Th17 *vs.* Th1 was regulated by both entry and post-entry mechanisms. Among 2,533 "present calls", 1,335 and 1,198 probe-sets were upregulated and downregulated, respectively, in Th17 *vs* Th1 cells. Genes associated with T-cell differentiation (RORC, KLF2, ARNTL), TCR signaling (ZAP-70, Lck, MAP3K4), activation/apoptosis (PTPN13), and HIV replication (PPARG) were upregulated in Th17 *vs.* Th1 cells. Genes down regulated in Th17 *vs.* Th1 cells and previously linked to HIV resistance included CCR5-binding chemokines and IFN-induced molecules. HIV permissiveness in Th17 *vs.* Th1 cells was associated with high sensitivity to TCR triggering, increased proliferation potential, and superior NF-κB DNA-binding activity. RORC RNA interference decreased HIV replication, while PPARG silencing induced opposite effects.
Conclusions: Our study reveals a unique molecular signature for HIV-permissive Th17 cells and identifies RORC and PPARG as major positive and negative regulators, respectively, of HIV replication in these cells. Novel therapeutic strategies aimed at interfering with Th17-specific transcripts may limit HIV replication and reservoir persistence, while preserving the beneficial role of Th17 cells in mucosal immunity.

WEPEA137

Modulation of HERV family expression after treatment with HDAC inhibitors

M. de Mulder Rougvie[1], P. Brailey[1], R.A. Saraiva Raposo[1], D. Sengupta[2], H.A. Michaud[3], F. Leal[1], C.E. Ormsby[4], R.B. Jones[5], M. Ostrowski[6], D.F. Nixon[1]
[1]George Washington University, Microbiology, Immunology and Tropical Medicine, Washington, United States, [2]University of California San Francisco, Department of Experimental Medicine, San Francisco, United States, [3]Institut de Recherche en Cancérologie de Montpellier, Equipe Immunité et Cancer, Montpellier, France, [4]Instituto Nacional de Enfermedades Respiratorias, Centro de Investigaciones en Enfermedades Infecciosas, Mexico City, Mexico, [5]Massachusetts Institute of Technology and Harvard University, Ragon Institute, Boston, United States, [6]University of Toronto, Department of Immunology, Toronto, Canada
Presenting author email: mdemulder@gwu.edu

Background: Human Endogenous Retroviruses (HERVs) comprise about 8% of the human genome. Some autoimmune diseases and cancers have been associated with the expression of HERV-K, which is the most recently integrated family of endogenous retroviruses. The production of HERV-K derived proteins in HIV infected cells provides a potential target for HIV eradication. Latently HIV infected remain as the major obstacle for HIV eradication. Use of histone deacetylase inhibitors (HDACis) to induce HIV expression in resting cells is a promising strategy for HIV latency reversal.
Methods: In this study we quantified the reactivation of five different families of HERVs by three non-selective HDACis (Vorinostat, Panobinostat and Romidepsin) in a latently HIV-1 T-cell model.
Results: After a 5-hour pulse with each HDACis, Vorinostat (1000nM), Panobinostat (50nM) and Romidepsin (50nM), we detected a 23.8%, 32.1% and 58.9% reactivation of HIV-1, respectively by measuring intracellular KC57 expression by flow cytometry. We also detected an increase in the gene expression of tested HERV families (R, K, H and P), with Panobinostat having the strongest ability to induce expression HERV-K. Further analysis within the HERV-K family, revealed that the pol gene was the most expressed gene compared to gag and env.
Conclusions: These data demonstrate the dynamic regulation of HERV expression after treatment with HDACis and future HIV-1 therapeutic strategies should consider the influence of the reactivation of endogenous retroviruses in infected cells.

Cellular and tissue reservoirs of HIV/SIV

WEPEA138

Distinct HIV genetic populations in effector memory T cells after prolonged therapy

E. Lee[1,2], B. Hiener[1,2], P. Bacchetti[3], W. Shao[4], E. Boritz[5], D. Douek[5], M. Somsouk[6], P. Hunt[6], R. Fromentin[7], S.G. Deeks[6], F.M. Hecht[6], N. Chomont[7], S. Palmer[1,2]
[1]Westmead Millennium Institute for Medical Research, Centre for Virus Research, Westmead, Australia, [2]University of Sydney, Sydney Medical School, Sydney, Australia, [3]University of California San Francisco, Department of Epidemiology and Biostatistics, San Francisco, United States, [4]Leidos Biomedical Research, INC, Frederick National Laboratory for Cancer Research, Frederick, United States, [5]National Institutes of Health, Immunology Laboratory, Vaccine Research Center, National Institute of Allergy and Infectious Diseases, Bathesda, United States, [6]University of California San Francisco, Department of Medicine, San Francisco, United States, [7]Vaccine and Gene Therapy Institute of Florida, Port Saint Lucie, United States
Presenting author email: eunok.lee@sydney.edu.au

Background: The effect of prolonged antiretroviral therapy (ART) on the genetic composition of persistent HIV in cellular reservoirs is unknown. We examined the genetic makeup of HIV DNA sequences within T-cell subsets from peripheral blood and gut tissue of persons on ART for >15 years.
Methods: Using single-proviral sequencing, we isolated HIV DNA from naïve, stem cell memory (T_{SCM}), central (T_{CM})-, transitional (T_{TM})- and effector (T_{EM})-memory and homing CD4+ T-cells (expressing CCR6, CXCR5 or both markers) sorted from peripheral blood and total CD4+ T-cells sorted from rectal biopsies. Samples were collected from 6 subjects on ART for >15 years: 3 who initiated therapy during early infection and 3 during chronic infection. Hypermutants, drug resistance mutations and identical sequences were identified by phylogenetic analysis. We used the tat/rev induced limiting dilution assay (TILDA) to measure the frequency of cells with inducible multiply spliced HIV RNAs (msRNAs).
Results: In subjects treated during chronic infection, T_{EM} contained genetically distinct HIV populations, often clonal in nature, compared to other cells. In one subject all HIV sequences (n=62) from T_{EM} were hypermutants and 82% clonal, whereas all other T-cell subsets had significantly fewer identical HIV DNA hypermutants (p=< 0.0001-0.001). Another subject, with a history of sequential ART regimens, had wildtype HIV sequences in T_{EM} (92%) and more drug resistant HIV in other T-cell subsets (p=< 0.0001-0.0004). T_{EM} from the third chronic subject contained 73% clonal drug resistant HIV sequences whereas the other cells had only 7-15% (p=< 0.0001-0.0002). In one subject treated during early infection, 44% of all HIV sequences were hypermutant: 56% in T_{EM} and 86% in CD4+ T-cells from rectal biopsies. All subjects had inducible HIV msRNAs in memory T-cell subsets as measured by TILDA but msRNAs were lower in T_{EM} from individuals containing hypermutant populations.
Conclusions: The distribution of HIV genetic material among memory subsets varied dramatically across the cohort after prolonged ART. T_{EM} are marked by clonal expansions which may reflect random antigen-driven cellular proliferation and expansion. Enrichment of hypermutant HIV in T_{EM} suggests new infection events during proliferative bursts are attenuated by cellular restriction factors and/or by death of cells expressing replication competent virus.

WEPEA139

Progressive contraction of the latent HIV reservoir around a core of less-differentiated CD4+ memory T cells

S. Jaafoura[1], M.G. De Goer De Herve[1], E.A. Hernandez-Vargas[2], H. Hendel-Chavez[1], M. Abdoh[1], M.C. Mateo[1], R. Krzysiek[3,4], M. Merad[5], R. Seng[6], M. Tardieu[1,4], J.F. Delfraissy[1,4,7], C. Goujard[4,5,7], Y. Taoufik[1,4]
[1]INSERM U 1012, Le Kremlin Bicetre, France, [2]Helmholtz Centre for Infection Research, Braunschweig, Germany, [3]INSERM U 996, Clamart, France, [4]Faculté de Médecine, Université Paris-Sud, Le Kremlin Bicetre, France, [5]Institut Gustave Roussy, Department of Medicine, Villejuif, France, [6]INSERM U 1018, Le Kremlin Bicetre, France, [7]Hopitaux Universitaires Paris-Sud, Department of Internal Medicine, Le Kremlin Bicetre, France
Presenting author email: salma.jaafoura@u-psud.fr

Background: HIV can persist within a small pool of long-lived resting memory $CD4^+$ T cells infected with integrated latent virus. This latent reservoir involves several memory $CD4^+$ T-cell subsets at distinct differentiation stages with different phenotypic and functional properties, forming distinct sub-reservoirs. Precise immunological characterization of the latent reservoir, including the size of each sub-reservoir, is important for the complex challenge of 'therapeutic purging'. The relative size of each sub-reservoir may depend on its decay rate and may therefore vary according to the time on ART. Here, we determined the decay rates of latently infected resting memory subsets.
Methods: We conducted a cross-sectional study on 45 strictly selected homogeneous patients. Inclusion criteria were: plasma virus load undetectable for 24 to 189 months without any viral blip and a CD4 T cell count higher than 500/ mm^3 of blood.
Highly purified memory CD4 T-cell subsets were sorted: stem cell memory CD4 T cells (T_{SCM}), central memory CD4 T cells (T_{CM}), effector memory CD4 T cells (T_{EM}), and an additional subset with an intermediate phenotype (T_{IM}). Integrated HIV DNA was quantified in these cells by ALU-gag PCR. To take into account inter-patient variability, we performed a mathematical modeling (Monte Carlo algorithm).
Results: Our results suggest a progressive reduction of the size of the blood latent reservoir around a core of less-differentiated memory subsets (central memory (T_{CM}) and stem cell-like memory (T_{SCM}) $CD4^+$ T cells). This process appears to be driven by the differences in initial sizes and decay rates between latently infected memory subsets. Our results also suggest an extreme stability of the T_{SCM} sub-reservoir, the size of which is directly related to cumulative plasma virus exposure before the onset of ART.
Conclusions: Latently infected T_{CM} and T_{SCM} should be a priority target for therapeutic strategies. Our results stress the importance of early initiation of effective ART to limit the size of the T_{SCM} sub-reservoir.

WEPEA140

Quantification and replication competency of HIV-1 following latency disruption in CD4+ T cells

J. Hataye[1], J. Casazza[1], D. Ambrozak[1], E. Boritz[1], T. Yamamoto[2], D. Douek[1], R. Koup[1]
[1]National Institute of Allergy and Infectious Diseases, Vaccine Research Center, Bethesda, United States, [2]Osaka University, World Premier International Immunology Frontier Research Center (IFReC), Osaka, Japan
Presenting author email: jason.hataye@nih.gov

Background: The size of the latent reservoir in a patient with ART induced HIV suppression can be estimated by viral outgrowth in a limiting dilution culture of activated CD4+ T cells. A culture well containing HIV is typically detected with p24 ELISA, but recently HIV RNA RT-PCR has been shown to be more sensitive. This allowed us to determine the proportion of cells producing viral RNA that resulted in replication competent virus.
Methods: Resting memory CD4+ T cells from 9 virally suppressed patients were stimulated with beads coated with antibodies against CD2, CD3, and CD28, and plated in limiting dilution in two conditions: 1) 100,000 MOLT-4/CCR5 cells per well and IL-2 were added on day 1 to facilitate viral outgrowth, or 2) the reverse-transcriptase inhibitor efavirenz was present immediately on day 0 to suppress viral replication, with no exogenous cells or IL-2 added. Culture media was collected and replaced every 4 days, and the viral RNA isolated and then quantified by real time HIV *gag* RT-PCR. The frequency of HIV RNA producing cells was estimated using the R package for Extreme Limiting Dilution Analysis.

Results: The frequency of HIV RNA producing cells following latency disruption was strongly correlated under viral outgrowth vs. viral suppression conditions. In most positive wells under viral suppression, viral RNA was detectable by day 4; some were followed by an increase while others decreased. In some outgrowth wells, the amount of HIV RNA on days 8 and 12 greatly exceeded that in comparable wells in the suppression assay. Culture supernatant from positive outgrowth wells was used to infect new cultures of activated, allogeneic CD4+ T cells. In 2 experiments, each utilizing a different donor, 35%(27/78) and 14%(11/78) of original positive outgrowth wells supported viral growth.
Conclusions: While HIV *gag* RNA RT-PCR with a concentrated viral suppression culture was as sensitive for quantifying the frequency of HIV RNA producing cells as a viral outgrowth assay, much HIV RNA recovered in the outgrowth wells, including many wells that had increasing amounts of viral RNA over time, did not represent replication-competent virus.

WEPEA141

T cell immunity in testicular tissue of ART-treated HIV-infected subjects: results from the Orchid study

M.-A. Jenabian[1], K. Vyboh[2], P. Brassard[3], M. Bélanger[3], N. Chomont[4], P. Ancuta[4], J.-P. Routy[2,5]
[1]Université du Québec à Montréal (UQAM), Department of Biological Sciences and BioMed Research Centre, Montreal, Canada, [2]McGill University Health Centre, Chronic Viral Illness Service and Research Institute, Montreal, Canada, [3]Metropolitan Centre for Plastic Surgery, Montreal, Canada, [4]University of Montreal and CHUM Research Centre, Department of Microbiology and Immunology, Montreal, Canada, [5]McGill University, Division of Hematology, Montreal, Canada
Presenting author email: jenabian.mohammad-ali@uqam.ca

Background: HIV persistence in anatomical reservoirs is a major hurdle in HIV eradication. Testis represent a neglected but nonetheless important viral anatomical reservoir as it constitutes an immune privileged site. We assessed T-cell distribution in testis versus blood in HIV-infected individuals receiving suppressive ART.
Methods: Testicular tissue and blood samples were collected from virally suppressed individuals (n=6) on ART for at least 6 months prior to surgery and uninfected controls (n=10) who underwent elective orchiectomy for gender reassignment. T-cells were purified using CD3 microbeads from freshly isolated testicular interstitial cell suspensions. T-cell subsets, CCR5 and ectonucleotidases (CD39 and CD73) expression, T-cell activation, and frequency of regulatory T-cells (Tregs) were assessed using multicolor flow cytometry.
Results: Lower proportions of CD4 T-cells among total T cells were found in testis versus blood, in both HIV- and HIV+ subjects (37±9.5% *vs.* 80±9.4% and 29.2±7,4% *vs.* 73±11.5%; p< 0.001).
A decrease in naïve and an increase in effector-memory T-cell subsets were observed in testis compared to PBMCs in both groups (p< 0.001). Importantly, up to 77 fold increases in the CCR5 expression on testicular CD4 and CD8 T-cells were observed when compared to blood (CD4 HIV-: p< 0.0001, CD4 HIV+: p=0.003, CD8 HIV-: p=0.0005, CD8 HIV+: p=ns). Increased T-cell immune activation (CD38/HLA-DR co-expression) in testis was observed in HIV+ individuals. A higher expression of immunosuppressive $CD39^+$ Tregs was found in testis of both HIV- and HIV+ subjects compared to blood (64±22% *vs.* 37±27%, p=0.002 and 62.9±11,5%, *vs.* 42.6±10%,
p< 0.001). A massive increase in the proportion of testicular CD73+ memory CD8 T-cells in HIV- and HIV+ subjects *versus* blood was also observed (24.6±13.2 *vs.* 77.4±4% and 13.8±4 *vs.* 67.6±14.6%,
p< 0.001).
Conclusions: For the first time, our results indicate an increase in the proportion of effector memory T-cells, CCR5 expression on T-cells and higher expression of ectonucleotidases in testicular tissue when compared to blood regardless of HIV status. However, virally suppressed subjects on ART had elevated levels of testicular T-cell immune activation when compared to HIV- controls. Collectively, these findings demonstrate the contribution of distinctive T-cell distribution in testicular tissue as anatomical reservoirs for HIV persistence.

WEPEA142

Extracellular ATP induces the rapid release of HIV-1 from virus containing compartments of human macrophages

F. Graziano[1,2], M. Desdouits[3], L. Garzetti[4], P. Podini[5], M. Alfano[4], R. Furlan[5], P. Benaroch[3], G. Poli[1,2]
[1]San Raffaele Scientific Institute, AIDS Immunopathogenesis Unit, Milan, Italy, [2]San Raffaele University, Milan, Italy, [3]Institut Curie, Centre de Recherche, Paris, France, [4]San Raffaele Scientific Institute, Milan, Italy, [5]San Raffaele Scientific Institute, Department of Neuroscience, Milan, Italy
Presenting author email: graziano.francesca@hsr.it

Background: The human immunodeficiency virus type-1 (HIV-1) infects CD4+ T lymphocytes and myeloid cells, in particular tissue macrophages. In comparison to T cells, infected macrophages differ both in terms of decreased to absent cytopathicity and for actively accumulating new progeny HIV-1 virions in Virus Containing Compartments (VCC). For these reasons, infected macrophages are believed to act as "Trojan horses" carrying infectious particles to be released upon cell death or functional stimulation.
Methods: The U937-derived chronically HIV-1 infected promonocytic cell line U1 was differentiated into macrophage-like cells (D-U1 cells) by PMA in the presence of urokinase-type plasminogen activator to favor virion retention in intracellular vacuoles and then shortly exposed to extracellular (e) ATP to induce their release. Primary human monocyte-derived macrophages (MDM) of HIV-1 seronegative donors were infected either with an R5 HIV-1 strain or with a VSVg-pseudotyped vector expressing eGFP. Both D-U1 cells and MDM were stimulated with eATP to induce the release of virions from VCC. Live imaging analysis was used to study the morphological effects of eATP on HIV-1 infected macrophages.
Results: Short term (5-30 min) eATP stimulation induced massive membrane blebbing and a rapid release of mature HIV-1 infectious virions from primary human MDM infected *in vitro* in the absence of cell death. The same phenomenon was reproduced in chronically infected D-U1 cells. Virion release was associated with a depletion of intracellular virions, as measured by intracellular p24 Gag staining and by visual imaging. Pharmacological inhibition of the microvesicle release pathway and of the ATP receptor (R) P2X7 prevented eATP-induced virion release from both acutely infected MDM and D-U1 cells.
Conclusions: Short (min) eATP stimulation induces the release of HIV-1 virions in both primary MDM and in D-U1 cells, via interaction with P2X7R and in the absence of significant cytopathicity. Pharmacologic interference with the microvesicle release pathway and with the P2X7R prevented this effect suggesting that they could represent novel exploitable targets for interfering with the reservoir of HIV-1 virions of infected tissue macrophages.

WEPEA143

CTLA-4-expressing memory CD4+ T cells are critical contributors to SIV viral persistence

C. McGary[1], S. Paganini[1], B. Cervasi[1], X. Yu[2], M. Lichterfeld[2], G. Silvestri[1], M. Paiardini[1]
[1]Emory University, YNPRC, Atlanta, United States, [2]Ragon Institute, Boston, United States
Presenting author email: cmcgary@emory.edu

Background: Understanding the immunophenotype and anatomic location of latently infected cells represents a critical challenge in designing a cure for HIV. Among memory CD4+ T-cells, those expressing co-inhibitory receptors (Co-IRs) are strong candidates for being enriched in latent HIV, given their negative regulatory function and upregulation on T-cells following HIV infection. However, little is known regarding the dynamics of T-cells expressing multiple Co-IRs following suppressive ART and their contribution to the HIV/SIV reservoir, particularly in tissues.
Methods: We investigated the relationship between the level of Co-IR expression on memory CD4+ T-cells and their level of latent virus in 10 ART-treated, SIV-infected rhesus macaques (RMs). RMs initiated a 5-drug ART regimen 6-8 weeks after SIVmac251 infection, which was maintained until plasma viremia was < 60 copies/mL for at least 3 months. Blood and tissue levels of memory CD4+ T-cells expressing multiple Co-IR (PD-1, CTLA-4, TIM-3, 2B4, TIGIT) were longitudinally analyzed by flow cytometry. Memory CD4+Co-IR+ subsets were sorted twice during viral suppression based on their expression of PD-1, CTLA-4, and TIM-3, to quantify levels of cell-associated SIV-DNA and RNA.
Results: The majority of memory CD4+ T-cells from the blood, GI tract, lymph node, and spleen expressed multiple Co-IRs, specifically PD-1 and CTLA-4, and their frequencies remained stable or increased during SIV infection, even with suppressive ART. Following 1 month of viral suppression, both memory CTLA-4+(PD-1-) and PD-1+(CTLA-4-) CD4+ T-cells harbored significantly higher levels of SIV-DNA in the LN. Yet, after 3 months of suppression, only CTLA-4+ CD4+ T-cells, in the absence of other Co-IRs, were significantly enriched in SIV-DNA in the PBMCs, compared to Co-IR(-) cells, and in the LN, demonstrating the specific persistence of this virally infected subset. Furthermore, this subset did not express high levels of SIV-RNA, which suggests that these CTLA-4+ cells likely harbor latent SIV.
Conclusions: Despite comprising a small frequency of memory CD4+ T-cells, CTLA-4+ T-cells represent a novel subset of virally enriched cells that may critically contribute to persistence in ART-suppressed individuals. These findings highlight the benefit of therapeutically blocking both CTLA-4 and PD-1 to target a large fraction of the HIV reservoir.

Measurement of HIV/SIV reservoirs

WEPEA144

Defining the unique biomarkers of latently infected T cells

M. Tyagi[1], B. Aiamkitsumrit[1], S. Nekhai[2], M. Bukrinsky[1], G. Simon[1]
[1]George Washington University, Medicine, Washington, DC, United States, [2]Howard University, Medicine, Washington, DC, United States
Presenting author email: tmudit@email.gwu.edu

Background: A critical issue in developing therapeutic approaches to HIV eradication is the identification of latently infected cells. Unfortunately, as yet there is no biomarker that distinguishes latently infected resting T cells from uninfected resting T cells. Research in developing means to identify such latently infected cells has been complicated by the fact that the number of latently infected cells in a single patient is extremely small such that it has not been possible to isolate latently infected cells in sufficient numbers in order to characterize these cells.
Methods: To overcome this limitation, we have developed a primary CD4+ T cell based *ex vivo* model system of HIV latency. The unique advantage of our model is that it allows us to generate a large and pure population of latently infected primary CD4+ T cells. This approach has provided sufficient material to characterize these cells and define the unique phenotypic characteristics (biomarkers) of latently infected cells. We compared the proteome of cell membranes from both latently infected and uninfected resting T cells. Differentially expressed protein(s) on latently infected T cells can be used as biomarkers.
Results: By cell membrane proteome analysis we have identified 17 putative biomarker proteins that are either predominantly or exclusively expressed on the surface of latently infected cells. We are currently in the process of evaluating these individual proteins for their potential to act as latency biomarkers. Preliminary results appear to be promising as one of the proteins FS1 predominantly express on the surface of latently infected T cells. These results as well as analysis of other biomarker proteins will be further discussed.
Conclusions: In order to cure AIDS, eradication of HIV is essential and to eradicate HIV, elimination of latent virus is necessary. However, to selectively kill latent viruses, we need to know specific characteristics of cells that harbor latent viruses, in order to avoid the killing of uninfected bystander cells. Unfortunately, the biomarkers of latently infected cells have not been defined. Thus finding the unique biomarkers of latently infected cells is an initial step in developing a strategy for HIV eradication and curing AIDS.

WEPEA145

Cell-associated HIV-1 unspliced to multiply spliced RNA ratio at 12 weeks ART correlates with markers of immune activation and apoptosis and predicts the CD4$^+$ T cell count at 96 weeks ART

A. Pasternak, M. Scherpenisse, B. Berkhout
Academic Medical Center of the University of Amsterdam, Medical Microbiology, Amsterdam, Netherlands
Presenting author email: a.o.pasternak@amc.uva.nl

Background: Incomplete restoration of CD4$^+$ T-cell count during virologically successful antiretroviral therapy (ART) is a major predictor of morbidity and mortality. For better understanding of HIV-1 pathogenesis and improved design of curative strategies, it is important to determine whether the degree of HIV-1 persistence, measured at baseline or early on ART, can predict subsequent immunological response to the long-term therapy and whether viral persistence is associated with host biomarkers of immune dysfunction.
Methods: Total and episomal (2-LTR circles) HIV-1 DNA, unspliced and multiply spliced (total and tat/rev) cell-associated HIV-1 RNA, as well as markers of CD4$^+$ and CD8$^+$ T-cell activation, proliferation, senescence, apoptosis, exhaustion, thymic migration, and CD4$^+$ and CD8$^+$ T-cell subsets (naïve, central memory, effector memory, transitional memory), were longitudinally measured in a cohort of 28 HIV-infected patients at 0, 12, 24, 48, and 96 weeks of virologically suppressive ART.
Results: No baseline HIV-1 marker was predictive of CD4$^+$ T-cell count at 96 weeks of ART. However, at 12 weeks of ART, cell-associated HIV-1 unspliced to multiply spliced-total (US/MS) RNA ratio strongly negatively correlated with both absolute CD4$^+$ T-cell count at 96 weeks of ART (rho=-0,56, P=0,004) and with relative increase in CD4$^+$ T-cell count between baseline and 96 weeks of ART (rho=-0,55, P=0,004). US/MS RNA ratio at 12 weeks ART was not associated with baseline CD4$^+$ T-cell count. Moreover, US/MS RNA ratio at 12 weeks ART strongly positively correlated with markers of CD4+ T-cell activation (CD4$^+$/CD38$^+$/HLA-DR$^+$: rho=0,63, P=0,001) and apoptosis (CD4$^+$/Annexin-V$^+$/FAS$^+$: rho=0,59, P=0,002).
Conclusions: We observed that US/MS RNA ratio at 12 weeks ART positively correlated with immune activation and apoptosis and predicted lower CD4$^+$ T-cell count at 96 weeks ART. Because HIV life cycle involves a temporal shift from the production of multiply spliced to the production of unspliced RNA species, higher US/MS RNA ratio in a patient might reflect the higher frequency of HIV-infected cells in the later stages of viral life cycle, which is characterized by expression of viral proteins and presentation of antigens. Such cells could exert pressure on the host immune system, causing persistent immune activation and apoptosis and contributing to poor immunological response to ART.

WEPEA146

Defective HIV-1 proviruses in the latent reservoir can be transcribed and translated following latency reversal

R. Pollack[1], Y.-C. Ho[1], K. Bruner[1], R. Siliciano[1,2]
[1]Johns Hopkins University, Medicine, Baltimore, United States, [2]Howard Hughes Medical Institutes, Baltimore, United States
Presenting author email: rpollac5@jhmi.edu

Background: Despite long-term highly active anti-retroviral therapy (HAART), human immunodeficiency virus-1 (HIV-1) persists as integrated proviruses, primarily in resting memory CD4+ T cells and remains the major barrier to cure. The vast majority of these proviruses are defective, containing either large internal deletions or extensive APOBEC-mediated G-to-A hypermutations. We recently discovered that many of these defective proviruses have intact promoter regions. Whether these proviruses can become transcriptionally active during the "shock-and-kill" strategies, which attempts to reverse latency and eliminate the latent reservoir, remains unknown. Further, it remains unclear whether these defective proviruses can be recognized and eliminated by the host immune responses following activation. Therefore, defective proviruses may complicate the measurement of the latent reservoir using RNA-based quantification during latency reversal trials with a potential role in immune activation.
Methods: To understand the role of defective viral genomes in viral transcription, proviral sequences defective in *gag*, *tat* and *rev* were generated by site-directed mutagenesis of the NL4-3 reference strain. To reconstruct near-full-length defective proviruses from the resting CD4+ T cells of HIV-1-infected individuals under suppressive HAART we isolated proviruses through limiting dilution PCR and synthesized them by *de novo* gene synthesis. Primary CD4+ T cells were transfected with these proviruses by nucleofection and activated by CD3/CD28 co-stimulation. After DNase treatment, cell-associated HIV-1 RNA was measured by quantitative RT-PCR and HIV Gag protein expression was measured by flow cytometry.
Results: Defective proviruses including hypermutated sequences with intact *tat* and/or *rev* genes can produce HIV-1 RNA at lower levels following CD3/CD28 co-stimulation. These defective proviruses are capable of producing HIV-1 viral proteins at measurable but lower levels than the NL4-3 reference strain.
Conclusions: Defective HIV-1 proviruses in the resting CD4+ T cells can be transcribed and translated following stimulation. In future latency reversal trials, these defective proviruses should be considered in determining the efficacy of treatments. In addition, a thorough investigation of the *in vivo* impact of defective viral transcripts and truncated proteins should be considered before defective proviruses can be determined as non-pathogenic.

WEPEA147

HIV-1 transcription is stable during frequent longitudinal sampling in aviremic patients on ART: implications for HIV cure research

S. Leth, R. Nymann, S. Jørgensen, T.A. Rasmussen, L. Østergaard, P.W. Denton, M. Tolstrup, O.S. Søgaard
Aarhus University Hospital, Department of Infectious Diseases, Aarhus N, Denmark
Presenting author email: steffenleth@gmail.com

Background: Reversal of latency is currently being investigated in studies aiming to reduce the HIV-1 reservoir. To best evaluate the effect of such clinical interventions in HIV-1 eradication trials, it is essential that the longitudinal dynamics of HIV-1 transcriptional activity, as well as the HIV-1 reservoir size, be fully characterized. To address this need, we conducted a longitudinal, observational cohort study that enrolled aviremic, HIV-1 patients at Aarhus University Hospital, Denmark.
Methods: Inclusion criteria were CD4+ T-cell count >200/µL, 2 most recent viral load measurements < 19 HIV-1 copies/mL and at least 2 year on ART. For all participants, monthly blood samples were collected over six consecutive months. HIV-1 transcription as measured by cell-associated unspliced HIV-1 RNA (CA-US HIV-RNA) and the size of the viral reservoir as measured by total HIV-1 DNA (tHIV-DNA) were quantified in unfractionated CD4+ T cells using digital droplet PCR.
To calculate the longitudinal variation in these outcome measures, we first determined the absolute mean values of CA-US HIV-RNA and tHIV-DNA for each individual over the six visits. Then, we determined the fold-change of the absolute values from each of the six visits relative to that mean. Finally, we determined the maximum fold-change from the absolute mean value for each patient and calculated a maximum fold-change with 95% CI for the study population.
Results: During the study period (November-2013 to August-2014) we enrolled 25 patients, including 8 females and 17 males (Table-1). Each participant completed the 6-month study. The mean maximum fold change in CA-US HIV-RNA was 1.49 (95% CI: 1.32-1.65; max. 2.30). The mean maximum fold change in tHIV-DNA was of 1.30 (95%CI: 1.16-1.44; max. 2.50).

Gender	
Male, n (%)	17 (68%)
Female, n (%)	8 (32%)
Age (years), median (range)	49 (31-79)
Ethnicity	
Caucasian, n (%)	23 (92%)
African Danish, n (%)	2 (8%)
Months since HIV-1 diagnosis, median (range)	90 (26-321)
Months from HIV-1 diagnosis to ART initiation, median (range)	7,0 (0-138)
Months on ART, median (range)	78 (25-206)
Months with HIV RNA <50 copies per mL, median (range)	71 (15-172)
Nadir CD4+ count (10e6 cells/L), median (range)	240 (0-710)
Baseline CD4+ count (10e6 cells/L), median (range)	650 (240-1750)
Pre ART viral load (copies/ml) log10, median (range)	4, 74 (2,76-6,23)
ART regimen	
2xNRTI +NNRTI, n (%)	9 (36%)
2xNRTI + protease inhibitor, n(%)	11 (44%)
1xNRTI + protease inhibitor, n(%)	1 (4%)
2xNRTI + 1xNNRTI + protease inhibitor, n(%)	1 (4%)
2xNRTI + integrase inhibitor, n (%)	2 (8%)
1xNRTI + 1xNNRTI + integrase inhibitor, n (%)	1 (4%)

[Table 1. Baseline characteristics n=25]

Conclusions: HIV-1 transcription and reservoir size, as measured by CA-US HIV-RNA and tHIV-DNA, exhibited only minor fluctuations during the study period in aviremic HIV-1 patients. These data provide the first insights into the natural variation over time of CA-US HIV-RNA, a primary outcome measure in HIV-1 latency reversal trails. Furthermore, these data confirm the significance of previously observed increases in transcriptional activity during treatment with latency reversing agents and provide a solid foundation for both design and interpretation of future latency reversal trials.

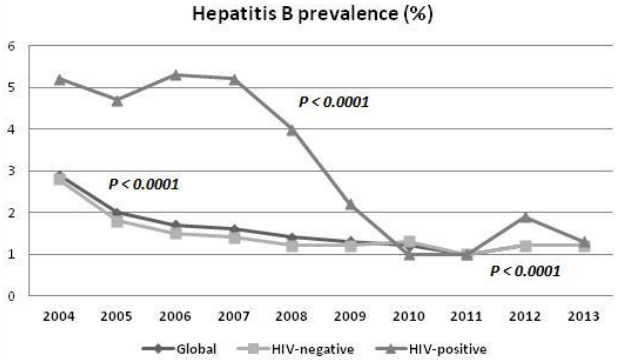
Hepatitis (excluding hepatitis C)

WEPEB313

Serial prevalence of HBV-HIV coinfection in Madrid in the period 2004-2013

A. Díaz-De Santiago[1], S. Serrano[1], C. Gómez-Ayerbe[1], S. Bañón-Escandell[1], E. Loza[2], C. Quereda[1], J.L. Casado[1], A. Moreno[1], M.J. Pérez-Elías[1], S. Moreno[1]
[1]Ramon y Cajal University Hospital, Infectious Diseases, Madrid, Spain, [2]Ramon y Cajal University, Microbiology, Madrid, Spain
Presenting author email: ddsalbertorubio@hotmail.com

Background: Hepatitis B virus (HBV) infects more than 400 million people worldwide and is a common cause of liver disease and liver cancer. In Europe about 14 million people are chronically infected with HBV and thirty-six thousand people die each year from HBV-related causes. Due to common transmission routes HIV/HBV coinfection is higher than in general population. In Spain the proportion of HIV-positive patients coinfected with HBV varies from 3 to 5%. We evaluated the serial prevalence of HIV/HBV coinfection across all risk groups for HIV infection at our Healthcare Area in Madrid (Spain).
Methods: We examined the serial prevalence of HBV infection in HIV-infected/uninfected subjects using data from the Microbiology Department registry of our tertiary hospital (Australian antigen test). Risk factors for HIV/HBV coinfection were analyzed in 676 newly HIV-positive diagnosed subjects at our centre during the study period by logistic regression analysis.



[HBV prevalence (2004-2013)]

Results: The prevalence of HBV infection in the overall population decreased from 2.45% (95%CI, 2.28-2.61) in 2004-05 to 1.19% (95%CI, 1.09-1.29) in 2012-13, *P* <0.0001. HIV/HBV coinfection decreased from 4.99% (95%CI, 4.03-6.11) in 2004-05 to 1.61% (95%CI, 1.11-2.26) in 2012-13, *P* <0.0001, and the prevalence of HBV infection among HIV-negative subjects decreased from 2.32% (95%CI, 2.15-2.41) in 2004-05 to 1.17% (95%CI, 1.07-1.28) in 2012-13, *P* <0.0001. Among HIV-infected subjects the trend from 2004 to 2013 among each risk group was: IDU, 8.57% to 0%, *P* =0.65; MSM, 3.63% to 7.01%, *P* =0.68; heterosexual, 8.92% to 0%, *P* =0.57. The single factor associated with HIV/HBV coinfection was a high HIV RNA: OR 1.74 (95%CI, 1.0004-3.021, *P* =0.0498).
Conclusions: The prevalence of HIV/HBV coinfection decreased in Madrid between 2004 and 2013, becoming similar to the prevalence of hepatitis B in HIV-negative subjects and general population at the end of the study period.

WEPEB314

Lamivudine (3TC) with or without tenofovir disoproxil fumarate (TDF) for treatment of hepatitis B in HIV-HBV co-infected treatment-naïve patients

Y. Li[1], J. Xie[1], Y. Han[1], H. Wang[1], W. Lv[1], T. Zhu[1], Z. Qiu[1], Y. Li[1], X. Song[1], S. Du[1], F. Guo[1], C. Thio[2], T. Li[1]
[1]Peking Union Medical College Hospital, Department of Infectious Diseases, Beijing, China, [2]Johns Hopkins University, Department of Medicine, Baltimore, United States
Presenting author email: liyijia07@mails.thu.edu.cn

Background: Chronic hepatitis B virus (HBV) co-infection occurs in 10-14% of HIV-infected Chinese patients. Although TDF+3TC is recommended for treatment of HIV-HBV co-infected patients, TDF is unavailable or expensive in some resource-limited areas; thus 3TC monotherapy for hepatitis B is given. Therefore, it is important to compare the efficacy of 3TC-based antiretroviral therapy (ART) against HBV with that of TDF+3TC-based ART in HIV-HBV co-infected patients.
Methods: We compared HBV treatment response in 132 HIV-HBV co-infected treatment-naïve patients (HCV uninfected) from our HIV Chinese cohorts (n=61 from cohorts using 3TC and n=71 from cohorts using TDF+3TC). Plasma HBV DNA levels were determined pre-treatment and week 48 of treatment. Poisson regression with robust error variance was used to estimate relative risks (RRs) for HBV DNA suppression (<20 IU/ml). Variables with P values lower than 0.15 in either stratum were included in multivariate analyses. Age, sex, and routes of transmission were also adjusted for in multivariate analyses.
Results: The majority of the subjects were HBV e antigen (HBeAg)-negative (n=93, 70.5%) and were distributed equally in the 3TC and the TDF+3TC groups (P=0.26). Pre-treatment, median HBV DNA was 3.54 logIU/ml (interquartile range [IQR] 1.89-7.98 logIU/ml) in 3TC group and 3.49 logIU/ml (IQR 2.46-6.69 logIU/ml) in 3TC+TDF group (P=0.76). In both groups over half of the subjects had pre-treatment HBV DNA <20,000IU/ml (54.1% in 3TC and 57.7% in TDF+3TC group, P=0.67). After 48 weeks of treatment, 68.9% of patients in 3TC group versus 88.7% of patients in TDF+3TC group achieved HBV viral suppression (P=0.005). However, in patients with baseline HBV DNA<20,000 IU/mL, HBV viral suppression rates were similar in these two therapy groups (Table). In stratified multivariate regression, TDF use (RR 1.78, P=0.031) and baseline HBV DNA (per 1 log increase in IU/ml, RR 0.77, P=0.001) were associated with HBV viral suppression only when baseline HBV DNA>20,000 IU/ml (Table).

Stratum	Factors	HBV viral suppression to <20 IU/ml [n (%)]	Crude RR (95%CI)	Adjusted RR(95%CI)
Baseline HBV DNA <20,000 IU/ml	ART			
	-- 3TC-based	32 (97.0)	Reference	Reference
	-- TDF+3TC-based	40 (97.6)	1.01 (0.93-1.09)	1.02 (0.92-1.13)
	Baseline HBV DNA (per 1 logIU/ml increase)	NA	1.00 (0.97-1.03)	1.00 (0.97-1.04)
Baseline HBV DNA >20,000 IU/ml	ART			
	-- 3TC-based	10 (35.7)	Reference	Reference
	-- TDF+3TC-based	23 (76.7)	2.15 (1.25-3.68)	1.78 (1.06-2.99)
	Baseline HBV DNA (per 1 logIU/ml increase)	NA	0.76 (0.66-0.88)	0.77 (0.65-0.90)

[Factors associated with HBV viral suppression]

Conclusions: This study suggests that 3TC monotherapy is efficacious in HIV-HBV co-infection when baseline HBV DNA<20,000 IU/ml. Studies with long-term follow-up are warranted to confirm this conclusion.

WEPEB315

Analysis of current costs and target prices for entecavir, to treat hepatitis B worldwide

D. Gotham[1], A. Hill[2], G. Cooke[1], S. Bhagani[3], J. Fortunak[4], J. Cohn[5], I. Andrieux-Meyer[6]
[1]Imperial College, Faculty of Medicine, London, United Kingdom, [2]Liverpool University, Pharmacology, London, United Kingdom, [3]Royal Free Hospital School of Medicine, HIV/AIDS, London, United Kingdom, [4]Howard University, Chemistry and Pharmaceutical Sciences, Washington, United States, [5]University of Pennsylvania, Division of Infectious Diseases, Philadephia, United States, [6]University Hospital, Infectious Diseases, Geneva, Switzerland
Presenting author email: microhaart@aol.com

Background: In 2013, an estimated 686,000 people died from Hepatitis B infection worldwide. Mass treatment programmes for Hepatitis B will require drugs available at very low costs. International treatment guidelines recommend first-line monotherapy with either entecavir or tenofovir. While the basic patent on tenofovir expires in 2017/8, entecavir is already generic in several countries, including USA. The chemical structure of entecavir is closely related to abacavir, which costs <$200 per person-year in low-income countries at the dose of 600mg OD, versus 0.5mg OD for entecavir.
Methods: The clinical efficacy, chemical structures, daily doses, routes of chemical synthesis, costs of raw materials and patent expiry dates were analysed for entecavir and tenofovir. Costs of sustainable, generic production were calculated for entecavir, and compared with published originator and generic prices worldwide. Target prices assumed at least 5 million people with chronic HBV treated worldwide (less than 3% of worldwide HBV epidemic).
Results: With a daily dose of 0.5mg, one year's supply of entecavir treatment requires 0.18g of Active Pharmaceutical Ingredient (API) per person, estimated to cost $4/year, based on quotations of API production from generic suppliers. With an additional $20 per year for formulation / packaging and a 50% profit margin, entecavir was estimated to cost a minimum of $36 per person-year, substantially lower than current originator and generic prices (Figure). Entecavir is no longer under patent protection in the USA, China, Brazil and South Africa, with European expiry in 2017. Given differences in daily dosing, production volumes for entecavir would be 600 times lower than tenofovir DF (300mg OD), offering significant logistical advantages.

Country	BMS / Generic price	Price per year (US$)
USA	BMS	$15,111
France	BMS	$7,046
United Kingdom	BMS	$6,826
USA	Generic	$6,127
Thailand	BMS	$2,441
China	Generic	$1,258
Brazil	BMS	$1,161
India	Generic	$427
Minimum estimate	Generic	$36

[Price of entecavir per person-year (US$)]

Conclusions: Mass treatment for Hepatitis B with generic entecavir could be achieved with very low costs (minimum $36 per person-year) in high-, middle- and low-income countries. There would be no patent restrictions to mass generic production of entecavir in most countries. However these low prices could only be achieved if volume demand increases to at least 5 million people treated with entecavir worldwide. Use of entecavir could avoid the renal and bone toxicities from long-term use of tenofovir, which is also still patented in many countries.

WEPEB316

Five-year long-term follow-up of serological responses to vaccination with two versus three doses of hepatitis A virus vaccine in HIV-infected patients receiving combination antiretroviral therapy

W.-C. Liu[1], C.-H. Wu[1], L.-H. Chang[1], Y.-C. Su[1], L.-H. Su[1], Y.-T. Tseng[2], A. Cheng[3], S.-Y. Chang[4], C.-C. Hung[2]
[1]National Taiwan University Hospital, AIDS Center, Internal Medicine, Taipei, Taiwan, Province of China, [2]National Taiwan University Hospital, Internal Medicine, Taipei, Taiwan, Province of China, [3]National Taiwan University Hospital Hsin-Chu Branch, Department of Internal Medicine, Hsin-Chu, Taiwan, Province of China, [4]National Taiwan University College of Medicine, Department of Clinical Laboratory Sciences and Medical Biotechnology, Taipei, Taiwan, Province of China

Background: Whether vaccination with three doses of hepatitis A virus (HAV) vaccine, administered at week 0, week 4, and week 24, may achieve more durable serological responses than with two doses administered at week 0 and week 24 remains unknown in HIV-infected patients receiving combination antiretroviral therapy.
Methods: Between June, 2009 and December, 2010, 365 HIV-infected MSM aged 18 to 40 years who were seronegative for HAV were enrolled to receive two doses of HAV vaccine (1440 ELISA units) (n=140) or three doses (n=225). Antibody titers were determined at weeks 24 and subsequently every 24 weeks for a total of 5 years. Anti-HAV antibody titers were determined with the use of a commercially available enzyme-linked immunosorbent assay (ELISA) method. Seropositivity for HAV was defined as an anti-HAV antibody titer >=20 mIU/mL. The generalized estimating equations (GEE) to account for the interdependence among observations were used to compare mean response rate to different HAV doses, with adjustments made for clinical characteristics such as cART coverage, baseline and follow-up CD4 count as well as PVL.
Results: Throughout the 5-year longitudinal follow-up, patients receiving 3 doses of HAV had statistically significantly higher geometric concentrations of anti-HAV antibody than those receiving 2 doses (1.9 vs 1.7 $\log_{10}$ mIU/ml at two through five years of follow-up), so were the rates of seropositivity for HAV (84.1 vs 80.3% at year 2; 86.8% vs 76.6% at year 3; 84.7 vs 77.3% at year 4; and 85.5 vs 77.1% at year 5). In multivariate analysis using GEE approach to define the factors associated with persistent serological responses between the second to the fifth years of follow-up, vaccination with 3 doses of HAV (adjusted odds ratio, 1.71; 95% CI, 1.02-2.85; *P*=0.04) and CD4≧350 cells/mm^3 at time of vaccination (AOR, 2.65; 95% CI, 1.55-4.40; *P*=0.0003) were significantly associated with persistent serological responses.
Conclusions: HIV-infected patients received three doses of HAV vaccine at CD4≧350 cells/mm^3 achieved a more durable serological response than those who received two doses five years following vaccination in the era of combination antiretroviral therapy.

WEPEB317

Prevalence of hepatitis B and delta among HIV-1, HIV-2 and dually reactive patients: a multi-country cross-sectional survey in West Africa

P.J. Coffie Ahuatchi[1,2], B.K. Tchounga[1,3], A. Inwoley[4], E. Messou[2,5], S.P. Eholie[1,2], A. Sawadogo[6], D. Minta[7], F. Dabis[3], D.K. Ekouevi[1,3,8]
[1]Programme PACCI, Site de Recherche ANRS, Abidjan, Cote D'Ivoire, [2]Service des Maladies Infectieuses et Tropicales, CHU de Treichville, Abidjan, Cote D'Ivoire, [3]Université de Bordeaux, ISPED, Centre INSERM U 897- Epidémiologie-Biostatistique, Bordeaux, France, [4]Centre de Diagnostic et de Recherche sur le SIDA et les Affections Opportunistes, CHU de Treichville, Abidjan, Cote D'Ivoire, [5]Centre de Prise en Charge de Recherche et de Formation, CePReF-Aconda-VS, Abidjan, Cote D'Ivoire, [6]Hôpital de Jour, Service des Maladies Infectieuses et Tropicales, CHU Souro Sanou, Bobo Dioulasso, Burkina Faso, [7]Centre de Prise en Charge des Personnes Vivant avec le VIH, Hôpital du Point G, Bamako, Mali, [8]Université de Lomé, Département des Sciences Fondamentales et Santé Publique, Lome, Togo
Presenting author email: boris.tchounga@yahoo.fr

Background: HIV and hepatitis virus co-infection may impact disease progression and made the treatment of each infection or both challenging. In West Africa where HIV-1 and HIV-2 circulate, the epidemiology of hepatitis B virus (HBV) and delta (HDV) co-infection is not well described. This study aimed at estimating the prevalence of HBV and HDV among West African HIV-V- 1 and HIV-2-infected patients in care.
Methods: A cross-sectional survey was conducted from March to December 2012 in Burkina Faso, Côte d'Ivoire and Mali within the International epidemiological Database to Evaluate AIDS (IeDEA) HIV-2 cohort. All HIV-infected patients >=18 years, screened as HIV-2 according to national algorithms, on ART or not, who attended participating HIV clinics during the study period were eligible. Blood samples were collected and tested for HIV discrimination (Immuno-CombII HIV-1&2-BiSpot Alere/Orgenics), HBV (monolisa HBs Ag ULTRA Biorad®) and HDV Ab (anti-HDV ETI-AB-DELTAK-2).
Results: A total of 825 patients participated in this study: 118 were confirmed HIV-1 (14.3%), 306 HIV-2 (37.1%), 119 HIV-1&2 dually infected (14.4%) and 285 remained of undetermined status. The median age was 47 years (inter-quartile range [IQR] 40-53) and 60.6% were women; median CD4 cell count was 472 cells/mm^3 (IQR: 294-646) (70.2% on ART, 94.1% of them receiving a PI-based regimen). Median follow up was 3.2 years [IQR 1.2-6.3]. The overall prevalence of HBs Ag was 8.9% (95% CI 7.0-11.0; n=73), including 11 patients (15.1%) antibody-positive to HDV. HBs Ag prevalence did not differ by country (p=0.28) or HIV-type (p=0.64), but was significantly higher in males (11.4%) than in females (7.2%) (p=0.045). Among the 73 patients with positive HBs Ag, 56 (76.7%) were on ART, all of them receiving lamivudine or emtricitabine; 17 of them (30.4%) were also receiving tenofovir. In multivariate analysis, young age < 30 years old (aOR 4.13, 95% CI 1.65-10.38) and male gender (aOR 1.85, 95% CI 1.10-3.03) were associated with positive HBs Ag.
Conclusions: HBV and HDV co-infections are common in West African HIV infected patients of all types. Although tenofovir is becoming increasingly available, there is a need to screen HBV and HDV co-infections to better target their use.

Human papillomavirus

WEPEB318

Comparison of anal cytology and human papillomavirus infection between HIV-positive and HIV-negative men in Taiwan

S.-H. Cheng[1,2], C.-Y. Cheng[1], F.-Y. Chu[3], Y.-M. Hsueh[4]
[1]Taoyuan General Hospital, Infectious Diseases, Taoyuan, Taiwan, Province of China, [2]Taipei Medical University, School of Public Health, Taipei, Taiwan, Province of China, [3]Far Eastern Memorial Hospital, Department of Clinical Patholgoy, New Taipei City, Taiwan, Province of China, [4]Taipei Medical University, School of Medicine, College of Medicine, Taipei, Taiwan, Province of China
Presenting author email: shuhsingcheng@gmail.com

Background: Men who were infected with human immunodeficiency virus (HIV), especially men who have sex with men (MSM), are at increased risk of developing anal cancer. To our knowledge, anal cytology and human papillomavirus (HPV) detection were not widely adopted in Taiwanese HIV care providers. The aim of this study was to explore the difference of anal cytology and HPV detection among HIV-positive and HIV-negative men.
Methods: Between March 2013 and December 2014, HIV-infected men who attended the outpatient clinics of Taoyuan General Hospital, Taiwan, had been enrolled voluntarily. HIV-negative men who had experienced unsafe sex and counseled for HIV test, had been enrolled for comparison. All of the subjects completed the self-administered questionnaire. Anal swabs were collected for thin-preparation anal cytology and linear array HPV genotyping testing.
Results: Totally 496 subjects were enrolled. There were 288 subjects who were HIV-infected, and 208 subjects who tested HIV negative. Their mean ages were 30.6 years. Among them, 75% of HIV-infected men and 30.3% of HIV-negative men were tested any HPV positive (P< .001). And, there were 59.7% of HIV-positive men and 22.1% of HIV-negative men having oncogenic HPV (P< .001). HPV type 6, 11, 16 and 51 were commonly encountered genotypes. Anal cytology yielded atypical squamous cells with undetermined significance or higher grades (ASCUS+) in 20.8% of HIV-positive men and 4.7% of HIV-negative men (P< .001). In multivariate analysis, HIV infection (odds ratio [OR], 2.34; 95% confidence interval [CI], 1.04-5.24), history of sexually transmitted infections (STIs) (OR, 2.24; 95% CI, 1.09-3.75), number of oncogenic HPV types (OR, 1.35; 95% CI, 1.09-1.67), number of nononcogenic HPV types (OR, 1.24; 95% CI, 1.03-1.49), and MSM (OR, 5.58; 95% CI, 1.02-20.49) were correlated significantly with anal cytology yielding ASCUS+.
Conclusions: Our data indicates that HIV-infected men who were MSM, having past history of STIs and being infected with various types of HPV were prone to have anal cytological abnormalities. Large scale of anal screening would be suggested for anal cancer prevention.

WEPEB319

Genital shedding of Epstein Barr virus (EBV) is associated with higher prevalence and persistence of anal human papilloma virus (HPV) in HIV-infected men on antiretroviral therapy (ART)

S. Gianella Weibel[1], C.C. Ginocchio[2], D.M. Smith[1], E.S. Daar[3], M.P. Dube[4], R.H. Haubrich[1], S.R. Morris[1], and the CCTG Study Group
[1]University of California San Diego, Medicine, La Jolla, United States, [2]North Shore-LIJ Health System, Lake Success, United States, [3]Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, Torrance, United States, [4]University of Southern California Keck School of Medicine, Los Angeles, United States
Presenting author email: gianella@ucsd.edu

Background: Several studies described the co-occurrence of EBV and HPV in pharyngeal and cervical malignancies. We investigated if genital EBV shedding is associated with prevalence and persistence of HPV in HIV-infected men who have sex with men (MSM) on suppressive ART (<500copies/ml).
Methods: 131 HIV-infected MSM were followed for 12 months and screened for multiple co-infections at several sites, including seminal EBV DNA by RT-PCR, and mRNA from the E6/E7 oncogenes for 14 high-risk HPV types (16/18/31/33/35/39/45/51/52/56/58/59/66/68) by Aptima in semen, rectum and pharynx. Primary analysis tested if seminal EBV shedding was associated with increased HPV prevalence at baseline using univariate tests and multivariable logistic regression. In participants with detectable rectal HPV (baseline), we tested if presence of genital EBV shedding at baseline also predicted reduced HPV clearance by log-rank test. Possible confounders (number of sex partners, CD4 count and plasma HIV RNA [< 50copies/ml or 50-500copies/ml]) were included in the final model if p< 0.05 in univariate analysis.
Results: Baseline prevalence of HPV was: rectal 44% (N=54/121); pharynx 3.8% (N=5/131); semen 7.1% (N=7/98). Seminal EBV shedding was detected in 27% (N=36/131). At baseline, EBV shedding was associated with more than double the prevalence of detectable rectal HPV mRNA (71.4% for EBV shedders versus 33.3% for non-shedders, p< 0.01). There was no significant difference in detectable HPV in pharynx (2.9% versus 4.2%, p=1.00), and semen (11.5% versus 5.6%, p=0.38) between groups. In multivariable models, the odds ratio (OR) of positive rectal HPV was significantly higher in subjects with compared to without EBV shedding after accounting for CD4 count and plasma HIV of 50-500copies/ml (adjusted OR: 3.5 [95%CI: 2.3-5.3]; CD4 and HIV RNA, both p>0.05). In those with detectable rectal HPV at baseline, we found increased persistence of HPV over 12 months of follow-up (measured as time to first negative HPV test) in the EBV shedding group (p< 0.01).
Conclusions: Seminal EBV shedding was associated with an increased risk of having detectable rectal HPV in a cohort of HIV-infected MSM on suppressive ART. Future studies should examine how co-infection with EBV and HPV may act synergistically in pathogenesis of ano-rectal cancer in HIV-infected individuals.

WEPEB320

Lower immune response in HIV-positive girls to the quadrivalent human papillomavirus vaccine

J. Brophy[1], A. Bitnun[2], J. Raboud[3], E. Moses[4], S. Blitz[5], L. Samson[6], N. Lapointe[7], S. Dobson[8], D. Money[8]
[1]University of Ottawa, Department of Pediatrics, Ottawa, Canada, [2]University of Toronto, Department of Pediatrics, Toronto, Canada, [3]University of Toronto, Toronto, Canada, [4]Women's Health Research Institute, Vancouver, Canada, [5]University Health Network, Toronto, Canada, [6]University of Ottawa, Ottawa, Canada, [7]University of Montreal, Montreal, Canada, [8]University of British Columbia, Vancouver, Canada
Presenting author email: jbrophy@cheo.on.ca

Background: The quadrivalent human papillomavirus vaccine (qHPV) is approved for use in HIV-negative (HIV-) adolescents and leads to high rates of seroconversion. There is limited information on the immune response in HIV-positive (HIV+) girls/adolescents.
Methods: Participants were given 3 doses of qHPV at months 0, 2 and 6. Antibody levels to HPV 6, 11, 16, 18 were measured pre-vaccine and post-vaccine at months 7, 12, 18 and 24 by the Merck cLIA assay. HIV- girls of the same age who received 3 doses of qHPV vaccine in a separate study served as controls. Post-vaccination geometric mean titers (GMT) of HIV+ and HIV- girls were compared. Seroconversion was defined as achieving serotype-specific cut-offs for positivity of 20, 16, 20, and 24 mMU/mL for HPV 6, 11, 16, and 18, respectively.
Results: Participants were given 3 doses of qHPV at months 0, 2 and 6. Antibody levels to HPV 6, 11, 16, 18 were measured pre-vaccine and post-vaccine at months 7, 12, 18 and 24 by the Merck cLIA assay. HIV- girls of the same age who received 3 doses of qHPV vaccine in a separate study served as controls. Post-vaccination geometric mean titers (GMT) of HIV+ and HIV- girls were compared. Seroconversion was defined as achieving serotype-specific cut-offs for positivity of 20, 16, 20, and 24 mMU/mL for HPV 6, 11, 16, and 18, respectively.

			HIV Positive Age 9-13		HIV Negative Age 9-13	
Month	HPV Type	Number	GMT	Number	GMT	P Value
7	16	32	4924 (3402-7128)	251	7640 (6561-8896)	<0.01
	18	31	703 (408-1212)	252	1703 (1489-1946)	<0.0001
	6	32	844 (546-1304)	248	1856 (1571-2192)	<0.001
	11	32	971 (651-1468)	251	2096 (1869-2350)	<0.0001
24	16	21	688 (374-1264)	186	1739 (1519-1992)	<0.0001
	18	20	71 (31-164)	187	267 (219-324)	<0.0001
	6	21	122 (60-249)	186	359 (315-410)	<0.0001
	11	21	114 (57-229)	186	422 (369-483)	<0.0001

[Geometric Mean Titres of HIV+ and HIV- age 9-13]

Conclusions: A statistically significant lower peak GMT and a more rapid antibody decline was observed in HIV+ girls compared to HIV- girls of the same age. Ongoing monitoring of the efficacy and effectiveness of qHPV in this population is needed.

WEPEB321

Should we consider anal cancer screening in women living with HIV? Results from the EVVA study on anal intraepithelial neoplasia prevalence and acceptability of screening

E. Kaufman[1], A. de Pokomandy[1,2], C. de Castro[2], M. Munoz[1,2,3], B. Lessard[1,2,4], M.-H. Mayrand[5], L. Charest[3], M. Auger[6], V. Marcus[6], A. Burchell[7], M. Klein[2], F. Coutlée[2,8]
[1]McGill University, Faculty of Medicine, Family Medicine Department, Montreal, Canada, [2]McGill University Health Centre (MUHC), Chronic Viral Illness Service, Montreal, Canada, [3]Clinique Médicale l'Actuel, Montreal, Canada, [4]Clinique Médicale du Quartier Latin, Montreal, Canada, [5]Centre Hospitalier de l'Université de Montréal (CHUM), Department of Obstetrics & Gynecology, Montreal, Canada, [6]McGill University Health Centre (MUHC), Pathology Department, Montreal, Canada, [7]Ontario HIV Treatment Network, Toronto, Canada, [8]Centre Hospitalier de l'Université de Montréal (CHUM), Department of Microbiology & Infectious Diseases, Montreal, Canada
Presenting author email: eckauf@gmail.com

Background: Many experts recommend screening for anal cancer in people living with HIV (PLHIV), given disproportionately high rates of this cancer in this population. Various tools can be considered for screening, but their acceptability is necessary for screening programs to be successful. The EVVA study (Evaluation of HPV, HIV and AIN in women) was conducted in Montreal, Canada, to measure the prevalence of AIN and assess the acceptability of screening in women living with HIV (WLHIV).
Methods: EVVA is an ongoing cohort study of 150 WLHIV. Study visits include cervical/anal HPV testing and cervical/anal cytology every 6 months for 2 years. A systematic HRA was performed at baseline and 2 years in all women, and an acceptability questionnaire was completed at the last visit (or at study withdrawal).
Results: At time of analysis, 150 women had completed the baseline visit and 59 had completed the acceptability questionnaire. Participants' mean age was 47 (range 34-67). Prevalent high-grade AIN was identified in 20 women (13%, 95% Confidence Interval:8.3-19.8). Regarding acceptability**,** 78% (46/59) considered routine anal cancer screening in WLHIV to be an absolute necessity (95%CI: 65-88%). Pain during anal cytology and DRE were considered similar to cervical cytology and graded with a median of 1/10. HRA was considered more painful by 83% (49/59) and graded with a median of 6/10. Yearly cervical cytology (current practice in WLHIV) was described as very acceptable by 85% (50/59). Anal cytology was considered very acceptable yearly by 77% (44/59), and every 2-5 years by 93% (54/59). DRE was considered very acceptable yearly by 80% (45/59) and every 2 years by 93% (53/59). HRA was described as very acceptable every 2 years by 75% (43/59), every 5 years by 90% (52/59) and every 10 years by 92% (54/59). Pain was the main reason for low acceptability. Only one participant (2%) was opposed to screening. Embarrassment, sexual assault connotations, inconvenience, and perceived non-necessity were mentioned in comments.
Conclusions: AIN is highly prevalent in WLHIV, and the vast majority of participants considered screening necessary and very acceptable. Pain management can be improved and potential adverse psychological effects of screening should be explored.

HIV-associated neurocognitive disorder (HAND)

WEPEB322

HIV-1 central nervous system infectivity models based on clinical CSF samples

B. Mora Peris, C. Herrera, A. Winston, R. Shattock
Imperial College London, Department of Medicine, London, United Kingdom
Presenting author email: b.mora-peris@imperial.ac.uk

Background: Antiretroviral drug (ARV) concentration in cerebrospinal fluid (CSF) is widely utilised as a surrogate for central nervous system (CNS) drug exposure. However, this is a pharmacokinetic measurement with no assessment of pharmacodynamic effects. We have developed a novel CNS pharmacodynamic end-point measurement whereby we assess the antiretroviral efficacy of CSF collected from subjects on antiretroviral therapy.
Methods: CSF samples were obtained from patients in a 'Rilpivirine CSF study' (n=10) and a 'Maraviroc CNS study' (n=12). All patients were receiving tenofovir and emtricitabine (245/200 mg once daily) as a backbone. In addition, patients received either rilpivirine (25mg once daily) or boosted lopinavir/maraviroc (400/150mg twice daily). CSF HIV-1 RNA load was undetectable in all cases. CSF samples from HIV-1 uninfected individuals without co-morbidities were used as controls (n=3). Anti-viral activity of ARV-containing CSF was assessed in PBMCs and neurologically derived cell-lines (373 and U87). Cell cultures were exposed to CSF in serial dilutions (1:2) prior to challenge with a brain-derived HIV strain (YU.2). Infectivity model half maximal inhibitory concentrations ($IMIC_{50}$) were calculated from sigmoid curve fits with 95% confidence intervals, and expressed as $-Log_2IMIC_{50}$. These results were correlated with the concentration of ARVs in the CSF.
Results: CSF from both studies demonstrated *in vitro* antiviral activity in all models when compared to controls. CSF anti-viral activity from patients on the 'Maraviroc CNS study' was significantly greater than CSF from patients on the 'Rilpivirine CSF study'.

$-Log_2IMIC50$ (95%CI)	Cellular Model		
	U87	373	PBMCs
The LOP/MVC CNS study (n=12)	3.06 (2.98 - 3.15)	6.00 (6.11 - 5.88)	4.82 (4.74 - 4.89)
The RPV CSF study (n=10)	2.56 (2.46 - 2.65)	4.90 (5.09 - 4.72)	3.43 (3.33 - 3.54)
Controls (n=3)	NA	NA	NA
No anti-viral activity (NA), peripheral blood mononuclear cells (PBMCs), central nervous system (CNS), Lopinavir (LPV), maraviroc (MVC) and rilpivirine (RPV)			

[Table 1. $IMIC_{50}$ of CSF from patients on different ARV combination by study]

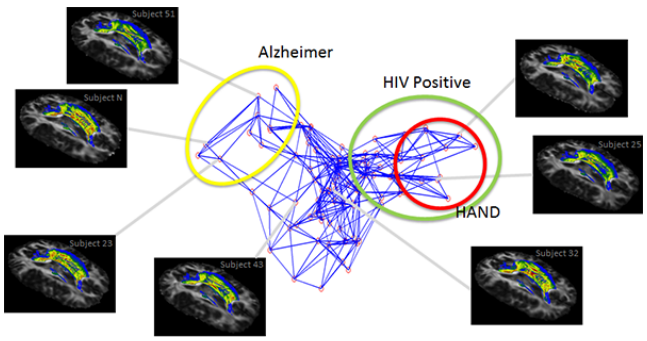
No significant correlations between individual CSF anti-viral activity and maraviroc CSF concentrations were observed. However, significant positive correlations were observed for individual CSF anti-viral activity with lopinavir CSF concentrations in 373 and U87 (p=0.04 and p=0.02, respectively) and with rilpivirine CSF concentrations in 373 and PBMCs (p=0.04 and p=0.04, respectively).
Conclusions: Anti-viral activity of CSF from patients participating in two controlled clinical studies was successfully calculated. Statistically significant differences between anti-viral activities of CSF from patients taking differing regimens were observed. Positive correlations between CSF anti-viral activity and ARV concentration of the third drugs rilpivirine and lopinavir indicate that these ARVs may drive anti-viral activity of these ARV combinations in the CSF.

WEPEB323

iMap: creating maps from longitudinal MR brain images of aging HIV population to drive HAND characterization

K.M. Pohl[1,2], N. Nichols[1,2], W. Chu[1], P. Esmaeili-Firidouni[3], H. Javitz[1], V. Valcour[3]
[1]SRI International, Center for Health Sciences, Menlo Park, United States, [2]Stanford University, Department of Psychiatry & Behavioral Sciences, Palo Alto, United States, [3]University of California - San Francisco, Department of Neurology, San Francisco, United States

Background: HIV-Associated Neurocognitive Disorders (HAND) are common in chronic HIV-infected (HIV+) patients over the age of 60. HAND can present in older patients similar to age-related neurodegenerative conditions, such as Alzheimer's Disease (AD). This results in an emerging clinical dilemma. Brain imaging is a promising approach, since HAND likely has unique regional tissue atrophy patterns enabling differential diagnosis from other neurodegenerative disorders.
Most brain imaging studies are limited by the assumption that selected clinical and demographic attributes are sufficient to define patient groups with homogeneous morphometry. Instead, we propose a data-driven approach, called iMap, that searches for identifying markers specific to HAND across two independently collected datasets by first grouping subjects according to structural attributes (e.g., gray matter heterogeneity) rather than presumed clinical markers.
Methods: We propose to apply iMap to a dataset (called $HIV^{+/-}$) consisting of 50 longitudinal brain MRIs from the UCSF Valcour Lab (called HIV^{+}), and 296 MRIs from *the Alzheimer's Disease Neuroimaging Initiative* (called HIV^{-}), which are matched with respect to age, gender, time between scans. iMap acknowledges the anatomical heterogeneity of $HIV^{+/-}$ by grouping MRIs according to common image patterns such as shown by the map shown below.



[iMap across brain MRIs of HIV+ and HIV- subjects]

These maps can represent the gradual transition of morphometric patterns associated with different diagnostic groups, such as HIV+ patients with normal cognition (HNC) and HAND. We will use these maps to separate $HIV^{+/-}$ into cohorts with distinct morphometric patterns, homogenous within each cohort, and analyze the diagnostic power of these patterns.
Results: Applied to 119 MRIs, iMap's accuracy is 88% in separating healthy controls from AD of the HIV^{-} dataset. Simulating a modified hypergeometric distribution based on these results, we would have 99% power to reject the null hypothesis of not distinguishing HAND from

HNC at 80% accuracy and 80% power to reject the null hypothesis at 71% accuracy. To achieve the same power in separating HIV- from HIV+ cases, even lower accuracy of iMap are sufficient.
Conclusions: The proposed sample size should be more than sufficient for iMap to identify markers important for meeting the emerging clinical need to distinguish cognitive impairment effects of HIV from age-related neurodegenerative conditions.

WEPEB324

Eliciting cognitive difficulties experienced by people living with HIV

M.-J. Brouillette[1], S. Askari[2], L. Fellows[3], M. Durancinsky[4], N. Mayo[2]
[1]McGill University Health Centre, Psychiatry, Montreal, Canada, [2]McGill University Health Centre, Clinical Epidemiology, Montreal, Canada, [3]Montreal Neurological Hospital and Institute, Neurology, Montreal, Canada, [4]Université Paris-Diderot, Sorbonne, EA REMES, PRO unit, Paris-Cité, France
Presenting author email: marie-josee.brouillette@mcgill.ca

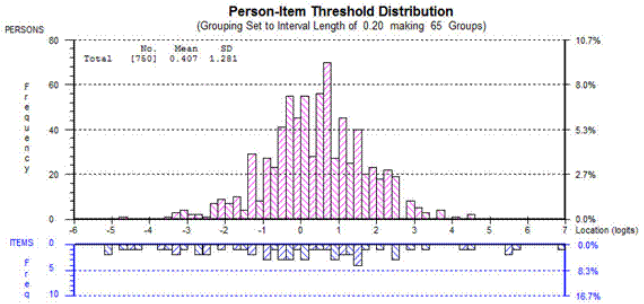
Background: People living with HIV often report deteriorating cognition even with excellent systemic viral control. Clinicians lack the tools to systematically elicit and document cognitive concerns. Instruments used in the research setting are often too long for clinical use, while briefer questionnaires developed in other health conditions may not probe into areas that are problematic for people living with HIV. The overall aim of this study is to create a bank of items reflecting the cognitive concerns expressed by people living with HIV.
Methods: We followed the steps outlined by the FDA for developing a patient-reported outcome. Semi-qualitative interviews on an international sample of 234 HIV+ individuals were carried out in 3 independent waves using an anonymous web-based survey (Canada) and face-to-face interviews (9 countries). The reported cognitive concerns were mapped to standard neurocognitive domains to identify content coverage, and compared with the domains in existing cognitive questionnaires. All items reflecting distinct concerns were compiled to create a bilingual questionnaire that was then posted on HIV community web sites across Canada to obtain estimates of prevalence and importance. Rasch analysis was used to calibrate the items and validate short forms to fit different purposes (screening, prevalence, and change over time).
Results: 136 distinct cognitive concerns were organized in the conceptual model of 15 neurocognitive domains plus emotional concerns and change. None of the generic or HIV specific questionnaires of cognitive difficulties came close to this extent of content coverage. Memory concerns were the most common (40 items) and covered prospective, episodic, semantic, immediate and procedural memory; 15 items related to attention; 12 items were identified for each of language and executive function; 4 and 3 items related to visuospatial domain and calculation.
Conclusions: This study has identified several areas of cognitive concerns in persons living in HIV, many of which were not captured by any of the existing questionnaires. This process of due diligence has contributed unique information that will serve as the basis of the development of an HIV-specific instrument. Once finalized, comparative values will be obtained from people without HIV in order to inform clinical interpretation.

WEPEB325

A novel method of measuring change in cognitive ability developed from CHARTER data could support international collaborations

M.-J. Brouillette[1], L. Fellows[2], S. Scott[3], N. Mayo[3], for the CHARTER Group
[1]McGill University Health Centre, Psychiatry, Montreal, Canada, [2]Montreal Neurological Hospital and Institute, Neurology, Montreal, Canada, [3]McGill University Health Centre, Clinical Epidemiology, Montreal, Canada
Presenting author email: marie-josee.brouillette@mcgill.ca

Background: Measuring change in cognition, a key aspect of neuroHIV research, requires summarizing results from several neuropsychological (NP) tests into a single score and calculating the difference between two test times. Raw scores are normalized using population norms, then averaged. The first step requires suitable norms which are often not available; the second step, averaging, assumes that each test contributes equally to the measure of the global construct, which may not be true.
We propose a method of measuring cognitive ability that produces a summary value with mathematical properties suitable for measuring change and that does not require norms. The specific aim of this study is to estimate the extent to which raw scores from multiple NP tests can be combined on a single calibrated measurement scale.
Methods: As part of the CHARTER study, HIV+ individuals were administered a battery of 15 NP tests every 6 months. Raw scores from all tests and all time points were combined, and Rasch analysis was applied to create calibrations for each test along a common metric.
Results: 701 patients were evaluated semi-annually for 38.5 ± 30.9 months. Data from 5254 testing sessions were available for analysis. The number of discriminatory thresholds varied across tests. All 15 tests could be combined into a single measure that fit the unidimensional and hierarchical Rasch model, creating a summary score with strong measurement properties that covered a broad range of cognitive abilities (equivalent to +3 to -6 SD units, see Figure 1). The same hierarchy was observed regardless of age, gender, education, and testing session.



[Figure 1: Person-Item Distribution]

Conclusions: The present study represents the first application of Rasch analysis, a modern psychometric method, to develop a measure of cognition that summarizes performance on 15 NP tests without applying population norms. The method produces valid measures of change across a range of ability, suitable for cross-population comparisons. The calibrated units also permit reanalysis of existing data even if only a sub-set of these tests was administered. Finally, this shows a way of using fewer, better targeted tests to measure cognition without sacrificing accuracy.

WEPEB326

Asymptomatic neurocognitive impairment (ANI) is associated with progression to symptomatic HIV-associated neurocognitive disorders (HAND) in people with HIV: results from The Ontario HIV Treatment Network (OHTN) cohort study

S.B. Rourke[1,2,3], J. Gill[4,5], A. Rachlis[3,6], C. Kovacs[7], G. Arbess[2], J. Brunetta[7], A. Carvalhal[2,3], C. Power[5], R. Rosenes[1], M. Atkinson[1], L. Cysique[8,9], T. Marcotte[10,11], A. Burchell[1,3], T. Bekele[1]
[1]The Ontario HIV Treatment Network, Toronto, Canada, [2]St. Michael's Hospital, Toronto, Canada, [3]University of Toronto, Toronto, Canada, [4]Alberta Health Services, Calgary, Canada, [5]University of Alberta, Calgary, Canada, [6]Sunnybrook Hospital, Toronto, Canada, [7]Maple Leaf Medical Clinic, Toronto, Canada, [8]Neuroscience Research Australia, Sydney, Australia, [9]University of New South Wales, Sydney, Australia, [10]HIV Neurobehavioral Research Centre, San Diego, United States, [11]University of California, San Diego, United States
Presenting author email: sean.rourke@utoronto.ca

Background: HIV-associated neurocognitive disorders (HAND) remain prevalent in people living with HIV. A recent study from the US CHARTER Cohort (Grant et al, 2014) has shown that Asymptomatic Neurocognitive Impairment (ANI) is associated with a 2- to 6-fold increased risk for the development of symptomatic HAND, i.e., mild neurocognitive impairment (MND) or HIV-associated dementia (HAD). The objective of this study is to replicate and extend these results in a Canadian sample.
Methods: Study sample included 679 adults living with HIV (81% men, 62% Caucasian, 83% on cART, 72% with undetectable HIV viral load) in Toronto, Canada and who were either normal on neuropsychological (NP) testing (NP-Normal; n=357) or had ANI (n=322) at baseline. Annual NP testing was done with brief NP battery that included measures of processing speed, attention/working memory, and learning/memory (i.e., WAIS-R Digit Symbol, Grooved Pegboard, WMS-III Spatial Span, and Hopkins Verbal Learning Test- Revised) . Cognitive complaints were assessed with four-item Medical Outcomes Study Cognitive Functioning scale. HAND status was assigned according to established criteria (Antinori et al., 2007). Cox proportional hazards regression model was used to estimate risk ratios for progression to symptomatic HAND.
Results: Over the follow-up period (median: 34 months), 150 individuals (59 NP-Normal and 91 with ANI at baseline) showed progression to symptomatic HAND. Participants with ANI had shorter time of progression than those who were NP-Normal at baseline, after adjusting for baseline and time-varying covariates: adjusted hazards ratio of 1.74 (95% confidence interval: 1.23-2.45; p< 0.001). Among covariates examined, depression (HR=1.84, p< 0.001), current cigarette smoking (HR=1.57, p=0.008), and non-Caucasian ethnicity (HR=1.62, p=0.006) were significantly associated with elevated risk of progression; whereas undetectable plasma HIV viral load was marginally associated (HR=0.68, p=0.058) with decreased risk of progression to symptomatic HAND.
Conclusions: Asymptomatic Neurocognitive Impairment is associated with almost a two-fold increased risk of progression to symptomatic HAND in our sample. Early treatment with combined antiretroviral therapy (cART) and addressing medical and mental health comorbidities may delay or lower the risk for the development and progression of symptomatic HAND.

WEPEB327

International neuropsychological normative study: neurocognitive comparison data in diverse resource-limited settings ACTG A5271

K. Robertson[1], J. Jiang[2], S. Evans[2], C. Marra[3], B. Berzins[4], J. Hakim[5], N. Sacktor[6], M.T. Silva[7], T. Campbell[8], A. Nair[9], J. Schouten[10], AIDS Clinical Trials Group
[1]UNC-Chapel Hill, Neurology, Chapel Hill, United States, [2]Harvard, SDAC, Boston, United States, [3]University of Washington, Neurology, Seattle, United States, [4]Northwestern University, Infectious Disease, Chicago, United States, [5]University of Zimbabwe, Infectious Disease, Harare, Zimbabwe, [6]Johns Hopkins, Neurology, Baltmore, United States, [7]Fiocruz, Neurology, Rio de Janeiro, Brazil, [8]University of Colorado, Infectious Disease, Denver, United States, [9]Frontier Science, Buffalo, United States, [10]Univeristy of Washington, HANC, Seattle, United States
Presenting author email: kevinr@neurology.unc.edu

Background: Neurocognitive impairment with ART remains prevalent despite substantial reductions in HIV Associated Dementia. There is a lack of infrastructure for conducting neurological research in resource limited settings (RLS), including training in neurological and neuropsychological (NP) assessment, and the lack of normative data needed for clinical interpretation. A5271 provided neurological training of clinical site personnel, and collected normative comparison data.
Methods: In seven RLS countries, we provided training for site personnel on the conduct of neurological and neurocognitive assessments. We collected normative comparison data on high risk HIV negatives from 10 sites in seven countries. Participants from Brazil (n=240), India (n=480), Malawi (n=481), Peru (n=239), South Africa (480), Thailand (n=240) and Zimbabwe (n=240) were enrolled at voluntary counseling and testing (VCT) sites aligned with the ACTG PEARLS (A5175) and International Neurological Study (A5199). Standardized NP exams were administered at baseline and at a six-month follow up in a subset. Participants presenting for HIV testing within 30 days at a VCT site were required to have a negative HIV test before participation at baseline and follow up. Strata were defined for country, gender, education (< 10 years and ≥ 10 years), and age (< 35 years and ≥35 years).
Results: Of the 2576 participants screened, 2400 were enrolled, and 770 completed the six-month follow up. The overall neurocognitive test means and SD's at baseline are presented in Table 1. Considerable between-country differences in the neurocognitive test scores were found as expected. For example, delayed recall differed across the sites (mean (SD)) of Johannesburg (8.64 (2.30)), Durban (8.62 (2.30)), Lima (7,56 (2.32)), Chiang Mai (7.95 (2.32)), Pune (7.53 (2.22)), Chennai (8,88 (2.40)), Lilongwe (6.94 (2.17)), Blantyre (7.96 (1.97)), Rio de Janeiro (7.47 (2.40)), and Zimbabwe (9.94 (2.26)) compared to the total sample (7.88 (2.35)). There was also variation between the age, gender and education strata.
Conclusions: Cultural, socioeconomic and likely many other factors underlie the country variations observed. This study provides infrastructure for future neurological and neurocognitive studies in diverse RLS and the normative data provided are a much needed resource for clinicians and researchers conducting neurological and neuropsychological assessment.

Depression and other psychiatric manifestations

WEPEB328

Sleep disturbances among persons living with HIV: a nationwide population-based study in Taiwan, 2000-2010

Y.-C. Chen[1], C.-W. Li[2], N.-Y. Ko[3,4]
[1]International Cheng Kung University, Institute of Allied Health Sciences, Tainan, Taiwan, Province of China, [2]National Cheng Kung Hospital, Tainan, Taiwan, Province of China, [3]National Cheng Kung University, Institute of Allied Health Sciences, Tainan, Taiwan, Province of China, [4]National Cheng Kung University, Department of Nursing, Tainan, Taiwan, Province of China
Presenting author email: yenchin2427@gmail.com

Background: Sleep disturbances (SDs) are among the most common symptoms reported by HIV-infected people, but the prevalence of SDs among a nationwide database is limited. This study aims to determine the prevalence and associated factors of SDs among persons living with HIV in Taiwan.
Methods: We conducted a secondary data analysis from National Health Insurance Research Database (NHIRD) identified 15,077 patients with HIV infection aged 15 and over from 2000 to 2010. SD was defined as ≥2 diagnosed by specialist and at least 1 month apart. Cox proportional hazard regression models were fitted to control the effect of confounding.
Results: One of fourth (25.5%) patients with HIV infection were diagnosed with SDs. SDs were diagnosis by different divisions of specialist: Infectious Diseases and General Medicine (46.7%), Psychiatry (32.7%), Family Medicine (8.2%) and Traditional Chinese Medicine (6.4%). The median time between the HIV diagnosis and first time diagnosis of SDs was 1.3 years. Patients with SDs were independently associated with older age (adjusted hazard ratio [aHR]: 1.00; 95% CI: 1.00-1.01), female (aHR: 1.13; 95% confidence interval [CI]: 1.03-1.26), blue collar (aHR: 1.23; 95% CI: 1.07-1.42), history of SDs (aHR: 2.66; 95% CI: 2.48-2.86), substance dependence (aHR: 1.50; 95% CI: 1.38-1.63), alcohol abusers (aHR: 1.52; 95% CI: 1.27-1.83), cardiovascular disorders (aHR: 1.37; 95% CI: 1.22-1.54), delirium (aHR: 4.06; 95% CI: 1.31-12.65), depression (aHR: 2.52; 95% CI: 2.35-2.71), and received HAART therapy (aHR: 1.26; 95% CI: 1.17-1.36).
Conclusions: Sleep disturbances are prevalent diagnoses among HIV-infected people. Further studies are needed to explore the impacts of sleep disturbances on HIV treatment and diseases related outcomes.

WEPEB329

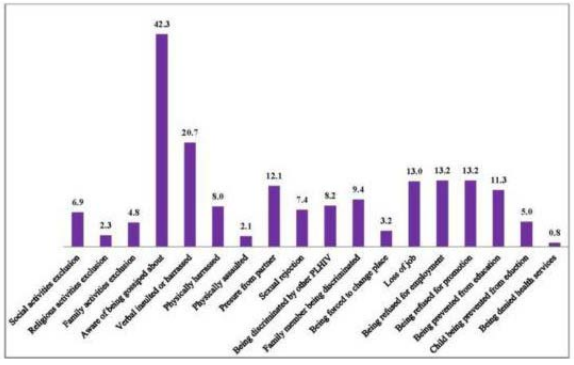
AIDS-related stigma and discrimination in relationship with mental disorders among people living with HIV: a cross-sectional study in Cambodia

S. Yi[1], P. Chhoun[1], S. Suong[1], K. Thin[1], C. Brody[2], S. Tuot[1]
[1]KHANA, Center for Population Health, Phnom Penh, Cambodia, [2]Touro University California, Global Health, Vallejo, United States
Presenting author email: siyan@doctor.com

Background: AIDS-related stigma and mental disorders have great negative impacts on the health and quality of life of people living with HIV (PLHIV). The linkage between these two common conditions has not been well addressed in many developing countries. We therefore conducted this study to examine the association of AIDS-related stigma and discrimination with mental disorders among PLHIV in Cambodia.
Methods: A two-stage cluster sampling method was used to select 1,005 adult PLHIV from six city and provinces. The People Living with HIV Stigma Index was used to measure stigma and discrimination, and a short version of general health questionnaire (GHQ-12) was used to measure mental disorders. Multivariate logistic regression analyses were conducted.
Results: The reported experiences of stigma and discrimination experienced from communities in the past 12 months ranged from 0.8% for reports of being denied health services to 42.3% for being aware of being gossiped about. Internal stigma was also common ranging from 2.8% for avoiding going to a local clinic and/or hospital to 59.6% for deciding not to have (more) children. The proportions of PLHIV who reported fear of stigma and discrimination ranged from 13.9% for fear of being physically assaulted to 34.5% for fear of being gossiped about. After adjustment, higher levels of mental disorders
(GHQ-12≥ 4) remained significantly associated with higher levels of experiences of stigma and discrimination
(AOR= 1.9, 95% CI= 1.4-2.6), higher levels of internal stigma (AOR= 1.7, 95% CI= 1.2-2.3), and higher levels of fear of stigma and discrimination (AOR= 1.5, 95% CI= 1.1-2.2).

	Total score of GHQ-12 (≤ 3)	Total score of GHQ-12 (≥ 4)	OR (95% CI)	AOR (95% CI)†
Total score of stigma and discrimination experience				
≤ 2	468 (75.2)	210 (56.1)	Ref	Ref
≥ 3	154 (24.8)	164 (43.9)	2.4 (1.8-3.1)***	1.9 (1.4-2.6)***
Total score of internal stigma				
≤ 4	434 (70.1)	196 (52.1)	Ref	Ref
≥ 5	185 (29.9)	180 (47.9)	2.2 (1.7-2.8)***	1.7 (1.2-2.3)**
Total score of fear of stigma and discrimination				
≤ 1	492 (79.1)	237 (63.4)	Ref	Ref
≥ 2	130 (20.9)	137 (36.6)	2.2 (1.6-2.9)***	1.5 (1.1-2.2)*

[Results of logistic regression analyses]



[Figure 1. Prevalence of stigma and discrimination experienced in family and communities in the past 12 months]

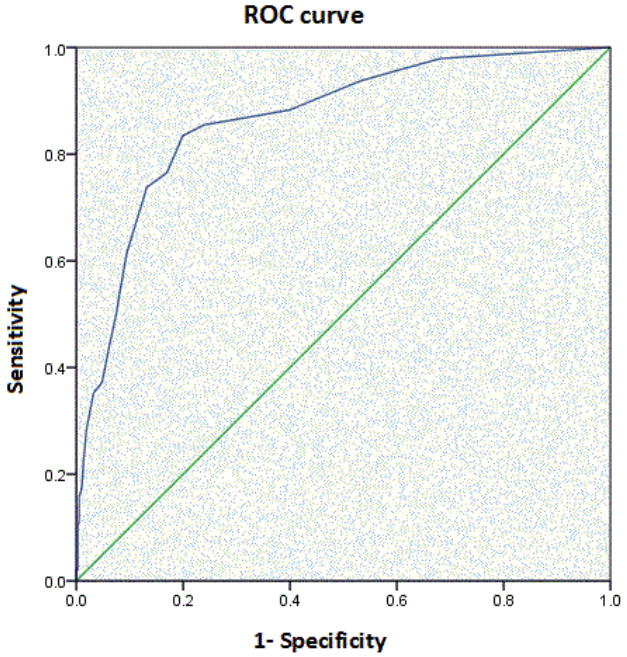
Conclusions: AIDS-related stigma and discrimination among PLHIV in Cambodia are common and may have potential impacts on their mental health conditions. These findings indicate a need for community-based interventions to reduce the stigma and discrimination in the general public and to help PLHIV to cope with this situation.

WEPEB330

The utility of Beck Depression Inventory HIV-adapted: cut-off scores for depressive symptoms screening in a specialized clinic in Mexico City. A two years' experience

V. Rodriguez[1,2], H. Vega[3], J. Cruz[4], H. Hirata[4], D. Ferreyra[5], C. Rocabert[5]
[1]Condesa Specialized Clinic, Mental Health Program, Mexico City, Mexico, [2]Autonomous National University of Mexico (UNAM), Master and Doctorate Program in Psychology, Psychology School, Mexico City, Mexico, [3]Condesa Specialized Clinic, Mental Health Program Coordinator, Mexico City, Mexico, [4]Condesa Specialized Clinic, Psychiatrist, Mental Health Program, Mexico City, Mexico, [5]Condesa Specialized Clinic, Psychologist, Mental Health Program, Mexico City, Mexico
Presenting author email: victor.psicologoacademico@gmail.com

Background: In recent decades, the Beck Depression Inventory (BDI-IA) has shown adequate psychometric properties in the general and various clinical populations in Mexico. Based on a previous study with Mexican HIV patients, we obtained an abbreviated version of the questionnaire to facilitate and shorten the application (BDI-hiv, Cronbach alpha = 0.91). Therefore the aim of this study was to obtain discriminant validity (sensitivity and specificity) of BDI-hiv against clinical diagnoses: depressive episode (F32), adjustment disorder (F43.2) and without symptoms of mental disorder (F999).
Methods: Archival data from 1781 patients assessed for mental health first time between 2013 and 2014, was analyzed. 1113 participants were selected who had an interview with ICD-10 diagnosis and also completed the BDI-hiv. ROC curves method was used for discriminant validity & Student *t* test to analyze differences between viral load (VL) ≤ & > to 1000. The statistical analysis was performed using SPSS v.20. A p ≤0.001 was considered to be significant.
Results: Findings show that 89% were men, age of 31.9 ± 9.3 years, 12.0 ± 3.6 education years, 4.5 ± 4.5 years of diagnosis, VL average 250,858 (± 896,777), CD4 of 327 ± 238 and 44% treatment ART. 33% of the sample had no symptoms (F999), 31.5% had F43.2 and 13% with F32. The ROC curve analysis showed that cutoff of 5 IDB-hiv discriminate between F999 and F32, with adequate sensitivity and specificity (85.5% and 76%, respectively) with the area under the curve (AUC) = 0.865 , 95% CI [0.83, 0.90], p ≤0.001. A cutoff 11 BDI-hiv discriminate between F43.2 and F32 with a sensitivity of 78% and specificity of 61% (AUC = 0.778, 95% CI [0.73, 0.82], p ≤0.001. We found statistically significant differences according to the VL, but this did not explain the score of BDI-hiv.



[Roc Curve BDI-hiv scores in depressive episode]

Conclusions: Our data support the clinical usefulness of this version for screening adjustment or depressives symptoms in this clinical population. The BDI-hiv has practical advantages of faster application and reduced burden on patients. We recommend a cutoff of 5 to discriminate between depressive/non-depressive symptoms, and an 11 to discriminate between adjustment/depressive symptoms.

WEPEB331

Maternal depression and maternal infant health outcomes among HIV-infected women in Kenya

B.M.O. Odeny[1], C. Mcgrath[1,2], J. Unger[1], J. Kinuthia[3], B. Singa[4], A. Langat[5], J. Pintye[1], A. Katana[5], L. Nganga[5], G. John-Stewart[1]
[1]University of Washington, Seattle, United States, [2]University of Texas Medical Branch, Galveston, United States, [3]Kenyatta National Hospital, Nairobi, Kenya, [4]Kenya Medical Research Institute, Nairobi, Kenya, [5]United States Centers for Disease Control and Prevention (CDC), Nairobi, Kenya

Background: Depression in HIV infected women may influence maternal and infant health outcomes.
Methods: A cross-sectional survey of mother-infant pairs attending week-6 and month-9 immunization visits in 140 maternal child health (MCH) clinics throughout Kenya was conducted between July and December 2013. Clinics were selected using probability proportionate to size sampling. Depression was assessed using the PHQ-9 screening instrument. Depression was defined as a PHQ-9 score ≥5, indicating at least mild depression. Data on maternal and infant health in the preceding month were obtained. Multivariable logistic regression models were used to determine prevalence, correlates, and association of maternal depression with maternal and infant health outcomes. Regression models were adjusted for clustering effects at clinic level, maternal and infant characteristics.
Results: Among 498 HIV infected women attending MCH, 116 (23%) had at least mild depression as measured by PHQ-9 criteria. Depression prevalence was comparable among the 9-month postpartum (21%) and 6-week postpartum visit cohorts (26%). Older mothers [aOR=1.28 per year (1.06-1.59), p=0.008], and those who reported intimate partner violence [aOR=2.28 (1.47-3.54), p<0.001] were significantly more likely to meet criteria for depression. Maternal depression was associated with infant symptoms including coughing [aOR=1.73 (1.09-2.75), p=0.020], difficulty feeding [aOR=2.80 (1.15-6.80), p=0.023], and vomiting [aOR=2.21 (1.12-4.34), p=0.021].
Depression was also associated with increased infant stunting (length-for-age z-score < -2) however, this was not statistically significant [aOR=1.51 (0.93-2.45), p=0.098]. Mothers with depression were less likely to exclusively breastfeed for at least 6 months [aOR=0.21 (0.09-0.48), p< 0.001]. Among women attending 9-month postpartum visit, prevalence of depression was significantly higher among those with HIV-infected infants (67% versus 19% for those with infected vs. uninfected infants, p=0.015).
Conclusions: Prevalence of depression among HIV infected mothers was high and was extremely high among women with HIV-infected infants. Maternal depression was associated with lower rates of exclusive breastfeeding and with higher rates of infant symptoms. Interventions to address maternal depression in HIV-infected women may be useful to improve both maternal and infant outcomes.

WEPEB332

Determinants of quality of life in a cohort of people living with HIV in Nigeria

B. Oladeji[1], B. Taiwo[2], K. Robertson[3], S. Fayemiwo[4], I. Adewole[5]
[1]University of Ibadan, Department of Psychiatry, Ibadan, Nigeria, [2]Northwestern University, Infectious Disease, Chicago, United States, [3]University of North Carolina, Neurology, Chapel Hill, United States, [4]University of Ibadan, Medical Microbiology, Ibadan, Nigeria, [5]University of Ibadan, Obstetrics and Gynecology, Ibadan, Nigeria
Presenting author email: bibideji@yahoo.com

Background: An increasing number of persons are living with HIV in this era of effective antiretroviral treatment (ART). Quality of life (QOL) is an important measure of medical outcome and well-being in this population. Few studies have reported on the factors that determine QOL of HIV infected persons in Nigeria, a country with the second largest population of people with HIV in the world.
Methods: Eight hundred and twenty-eight HIV patients randomly selected from the ART clinic of the University College Hospital, Ibadan, Nigeria were interviewed using the WHO Quality of Life instrument (WHOQOL-HIV BREF) and the Composite International Diagnostic Interview version 10.0 (CIDI-10) to ascertain the presence of depression or anxiety disorders. The associations of demographic and health related factors with overall and domain scores on the six domains of WHOQOL-HIV were explored using linear regression models.
Results: The mean age of the sample was 41.3 years (SD-10) and 71.1% were female; 57.4% were married, 25% single, 17.6% widowed and 41.3% had 6 years or less of education. The median CD4 count was 385 cells/mm^3 and 90% were on antiretroviral medication. A total of 66 (8.0%) met DSM-IV diagnostic criteria for major depression and/or generalized anxiety disorders; 55 (6.6%) had depression only, 9 (1.1%) had anxiety alone and 2 (0.2%) had comorbid depression and anxiety. Lower overall QOL was associated with female gender (p=0.002), being a widow (p=0.003), having fewer years of education (p<0.001) and having depression and/or generalized anxiety disorder (p<0.001). The presence of depression and/or anxiety disorder (related to 5 of the 6 domains of the WHOQOL-HIV instrument (coefficients ranging from 0.72-1.35 and p<0.001)), lower education and gender were the most consistent factors predicting domains of QOL. Receiving antiretroviral medication emerged as a significant predictor of better health related QOL (B=0.591; p=0.031).

Conclusions: These findings in a Nigerian cohort of people living with HIV emphasize the impact of mental health problems on the QOL. Clinicians need to pay special attention to subsets of the HIV population that may be more prone to decreased QOL, including women and those with anxiety and/or depressive symptoms, less education, and the widowed.

WEPEB333

Depression and anxiety amongst HIV-infected individuals enrolled in a public sector antiretroviral programme in Thailand

W. Prasithsirikul[1], S. Chongthawonsatid[2], S. Keadpudsa[3], P. Rerksirikul[3], V. Sapsirisavat[4], W. Klinbuayaem[5], S.J. Kerr[3], A. Avihingsanon[3,6], The PROGRESS Study Team
[1]Bamrasnaradura Infectious Disease Institute, Department of Disease Control, Ministry of Public Health, Nonthaburi, Thailand, [2]Mahidol University, Faculty of Social Sciences and Humanities, Nakornpathom, Thailand, [3]HIV-NAT, Thai Red Cross - AIDS Research Centre, Bangkok, Thailand, [4]HIV-NAT, Thai Red Cross AIDS Research Centre, Bangkok, Thailand, [5]Sanpatong Hospital, Chiang Mai, Thailand, [6]Division of Allergy and Immunology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand
Presenting author email: anchalee.a@hivnat.org

Background: HIV/AIDS and anxiety/depression are interlinked. HIV-infected patients suffering from depression may be more likely to have problems with adherence which may in turn result in HIV disease progression. Additionally, HIV diagnosis and/or using certain cART may trigger symptoms of anxiety/depression. We explored the prevalence and factors related to anxiety and depression in HIV-infected patients enrolled at 3 clinical sites within the Thai National HIV Treatment Program.
Methods: From January 2012 to December 2013, a cross sectional study was performed among HIV-infected out-patients aged ≥18 years attending Bamrasnaradura Infectious Institute and Thai Red Cross AIDS Research Centre, in Bangkok and Sanpatong hospital in Chiang Mai. Symptoms of anxiety and depression were measured using the Hospital Anxiety and Depression Scale (HADS). An 8+ cut-off was used to identify possible cases of anxiety and depression. Multivariate logistic regression was performed to identify associated factors.
Results: Totally 2,023 (male 57%) patients were included. The prevalence of anxiety and depression were 4.8% and 3.1%, respectively; 1.3% had both anxiety and depression. In multivariate logistic models, female gender [OR=1.6 (95%CI1.1-2.3), P=0.01], having adherence <90% [OR=2.2, (95%CI 1.5-3.4), P<0.001], fair or poor quality of life [OR=7.2, (95%CI 3.6-14.2), P<0.001] and efavirenz exposure [OR=1.6 (95%CI 1.1-2.3), P=0.01] were associated with having anxiety or depression.
Conclusions: In this cross sectional study, female gender, poor adherence, poor/fair quality of life and efavirenz use was associated with symptoms of anxiety and depression. A brief screening test to evaluate anxiety and depression symptoms prior and during cART can help to identify those most at risk so that interventions can be implemented early. Particular attention should be given to female patients and those using efavirenz.

Malignancies (including Kaposi sarcoma, lymphoma, and non-AIDS malignancies)

WEPEB334

Treatment tolerability for squamous cell carcinoma of the anus (SCCA) among HIV+ patients on ART

R. Pitts, K. Sigel, S. Goldstone, M. Gaisa, C. Sigel, A. Burnett, J. Wisnivesky
Mount Sinai Medical Center, New York, United States
Presenting author email: robertanwarpitts@gmail.com

Background: Concurrent chemoradiotherapy remains the standard treatment for invasive squamous cell carcinoma of the Anus (SCCA). There are limited data regarding antiretroviral era survival and treatment tolerability among HIV+ patients with SCCA. Previous data have demonstrated increased acute toxicity and poorer clinical outcomes among HIV+ patients undergoing treatment compared to HIV- patients.
Methods: We used data from the Surveillance, Epidemiology, and End Results (SEER) registry linked to Medicare claims to assess treatment adverse reactions among a cohort of male HIV+ and HIV- patients diagnosed with SCCA from 1997 to 2009. Outcomes included all-cause and anal cancer-specific mortality and treatment-associated toxicities. We used Kaplan-Meier methods to compare overall survival and anal-cancer specific survival among treated patients by complication status as well as by HIV status.
Results: 1,000 male patients with incident SCCA were included in our cohort, of whom 368 were HIV+. When compared to HIV- patients, HIV+ subjects were younger and had lower comorbidity scores in both earlier and later staged SCCA (Table 1). For early stage SCCA, HIV+ subjects had lower rates of all cause and anal cancer-specific mortality. There was no difference in the rate of treatment toxicities by HIV status or SCCA stage. Furthermore, among HIV+ patients who experienced treatment toxicities, there was no decrease in either overall (p=0.69) or SCCA specific survival (0.07) compared to HIV+ patients who did not experience treatment-related toxicity. Lastly, there was no difference in survival over three designated time periods by year of diagnosis for HIV+ (p=0.17) and HIV- (p=0.74) patients.

	Stage I/II			Stage III/IV		
	HIV+ (%)	HIV- (%)	P-value	HIV+ (%)	HIV- (%)	P-value
Total Number	321	539		47	93	
Race						
Caucasian	200 (62)	469 (87)	<0.05	31 (66)	78 (83)	0.12
African American	76 (24)	36 (7)		8 (17)	8 (9)	
Hispanic	37 (12)	17 (3)		7 (15)	6 (7)	
Other	8 (2)	17 (3)		1 (2)	1 (1)	
Comorbidity score (%)						
0	208 (65)	249 (46)	<0.05	33 (70)	37 (40)	<0.05
0 - 4	86 (27)	207 (39)		9 (19)	36 (39)	
> 4	27 (8)	83 (15)		5 (11)	20 (21)	
Year of diagnosis (%)						
1997 - 2001	62 (19)	128 (24)	0.05	9 (18)	23 (25)	0.69
2002 - 2005	113 (35)	210 (39)		19 (41)	38 (41)	
2006 – 2009	146 (46)	201 (37)		19 (41)	32 (34)	
Complications	194 (61)	297 (55)	0.13	34 (72)	52 (56)	0.06
All cause death	155 (48)	306 (57)	0.02	32 (68)	66 (71)	0.73
Anal cancer specific death	30 (9)	113 (21)	<0.05	10 (21)	27 (29)	0.33
Anal cancer specific median survival (Months)	37 (11 - 57)	39 (10 – 59)	0.18	34 (10 – 56)	59 (9 – 53)	0.46

[Table 1. Demographic characteristics by HIV status and stage of SCCA (N+1,000)]

Conclusions: In our population-based cohort of patients who received treatment for SCCA, we found that two-thirds of patients experienced treatment-related complications, but that there was no difference in this rate by HIV status. Treatment-related complications also had no impact on long-term survival. HIV+ SCCA patients appear to tolerate standard SCCA treatment similar to HIV- patients.

WEPEB335

Cancer treatment in elderly individuals with HIV infection in the United States

A. Rositch[1], A. Coghill[2], G. Suneja[3], E. Engels[2]
[1]Johns Hopkins Bloomberg School of Public Health, Department of Epidemiology, Baltimore, United States, [2]National Cancer Institute, Division of Cancer Epidemiology and Genetics, Bethesda, United States, [3]University of Utah Huntsman Cancer Institute, Department of Radiation Oncology, Salt Lake City, United States
Presenting author email: arositch@jhu.edu

Background: With an increasing life expectancy due to widespread use of HAART, individuals with HIV are at increased risk for many cancers. Previous studies also suggest that they may be less likely to receive treatment for cancer. The extent to which rates or specific types of cancer treatment may differ between elderly HIV-infected and uninfected individuals is unknown.
Methods: Using Medicare data linked to the SEER cancer registries, we explored differences in cancer treatment by HIV status in Americans aged 66-99 years and diagnosed with non-Hodgkin lymphoma, and anal, bladder, breast, colorectal, kidney, liver, lung, melanoma, or prostate cancer from 1991-2009. HIV was defined as the presence of 2 or more claims for ICD9 diagnosis codes 042, 043, 044 or V08 at least 30 days apart. Cancer treatment was defined as Medicare claims for surgery, chemotherapy, radiation, hormone therapy, and/or transplant specific to each type of cancer.
Results: The HIV population (n=584 cancer patients) was significantly younger than the HIV negative individuals (n=858,303; median: 71 vs. 75 years, respectively). For all cancers combined, individuals with HIV were less likely to receive cancer-type-specific treatment compared to HIV-negative cancer patients (71% vs. 77%; unadjusted prevalence ratio (PR) 0.93 (95% confidence interval (CI) 0.88, 0.98)). Variability was seen across cancer types, for example, anal cancer was more likely (91% vs. 84%) and kidney cancer was less likely (55% vs. 74%) to be treated in individuals with HIV. After taking into account differences in age, gender, race, comorbidities, cancer type, and stage at cancer diagnosis, there was no difference overall in cancer treatment by HIV status (adjusted PR 0.99; 95% CI 0.96, 1.02).
Conclusions: Differences in cancer treatment between HIV-infected and HIV-uninfected individuals in our elderly American population may reflect difference in personal, medical, or cancer-specific characteristics, rather than independent effects of HIV infection. This is in contrast to previous studies noting large disparities in care, suggesting that there are differences in how elderly individuals, or those with Medicare, are treated for cancer. Additional work is underway to explore differences across the pre/post-HAART era, role of palliative care, and interactions among the different factors.

WEPEB336

The CD206 macrophage mannose receptor acts a localization portal for targeting tumor cells and associated macrophages in HIV associated Kaposi's sarcoma

R. Zhang[1], S. Lamers[2], F. Cope[3], R. Rose[2], D. Nolan[4], M. Salemi[4], C. Souffan[5], P. Bracci[5,6], D. Garcia[5,6], M. Mcgrath[5,6]
[1]University of California, Medicine, San Francisco, United States, [2]Bioinfoexperts, LLC, Thibodaux, United States, [3]Navidea Biopharmaceuticals, Dublin, United States, [4]University of Florida, Gainesville, United States, [5]University of California, San Francisco, United States, [6]AIDS and Cancer Specimen Resource, San Francisco, United States
Presenting author email: jane.zhang@ucsf.edu

Background: Inflammation plays a role advancing HIV-associated Kaposi's sarcoma (KS). Macrophages (MOs) within KS lesions provide tumor cell growth factors, which may result from HIV activation in the microenvironment. Emerging data show that KS tumor cells co-express various MO antigens that become resistant to anti-viral therapies. MOs driving these pathological pathways share a common element, the CD206 macrophage mannose receptor. In this study, we evaluate a KS targeting agent, Manocept, which can enter tumor cells and tumor associated macrophages (TAMs) via pinocytosis of holo-CD206.
Methods: A single-genome sequencing approach targeting HIV *env-nef* was applied to DNA and cDNA generated from multiple KS biopsies and non-tumor sites in three individuals. Phylodynamic analysis estimated the evolutionary history of HIV in their tumors. The cellular location of HIV in KS tumor microarrays was assessed using *in situ* amplification. Synthetic Manocept with a dextran backbone, 12-20 mannose moieties, and a fluorescent tracer (Cy3) was used to locate Manocept on and in MOs and KS tumor cells. Localization Cy3-Manocept was assessed through flow cytometric quantitation of Cy3-Manocept uptake using *in vitro* generation of monocyte-derived CD206+ MOs. The fresh HIV+ KS tissue culture followed by immunofluorescence staining and confocal imaging was performed to confirm Cy3-Manocept uptake in KS tumor cells and TAMs.
Results: Phylodynamic analysis demonstrated that HIV was frequently compartmentalized within tumors ($p < 0.05$) and originated years before HIV at non-tumor sites. *In situ* amplification showed HIV expressed in KS immune cells. Increasing Cy3-Manocept concentrations confirmed continuous uptake of Manocept into CD206+ MOs. HIV+ KS tissue culture studies showed both Manocept uptake and CD206 staining of TAMs and KS tumor cells (HHV8+ cells). Cy3-Manocept co-localized with CD206 in nearly all KS-associated cells expressing HHV8 and/or CD68, confirming that CD206 acts both as a target and Manocept concentrating receptor for TAMs and KS tumor cells.
Conclusions: HIV is present in KS tumors where it can compartmentalize, activate immune cells and provide growth factors for KS. Manocept can be used for imaging KS tumor cells, TAMs, and more importantly, for delivery of therapeutic/diagnostic agents capable of targeting all KS-associated cells including a potential MO reservoir for HIV.

WEPEB337

Safety and efficacy of antiretroviral therapy in HIV-infected adults undergoing autologous or allogeneic stem cell transplant for hematologic malignancies

C. Johnston[1,2], A. Woolfrey[2,3], R. Jain[4], J. Schiffer[1,2], H.-P. Kiem[1,2], R. Harrington[1]
[1]University of Washington, Medicine, Seattle, United States, [2]Fred Hutchinson Cancer Research Center, Seattle, United States, [3]University of Washington, Pediatrics, Seattle, United States, [4]University of Washington, Seattle, United States
Presenting author email: cjohnsto@u.washington.edu

Background: **NOTE**Please consider for "Towards an HIV Cure Symposium"
The ability to continue antiretroviral therapy (ART) when undergoing peripheral blood stem cell transplantation (PBSCT) for treatment of hematologic malignancies is likely a critical factor in preventing establishment of the HIV reservoir in transplanted stem cells. Thus, we have studied the feasibility of continued ART therapy in our HIV-infected patients undergoing autologous or allogeneic transplantation.
Methods: All HIV-infected adults undergoing PBSCT for hematologic malignancy at Fred Hutchinson Cancer Research Center (FHCRC) between 2006 and 2014 were included; most were enrolled in a prospective clinical study to monitor HIV reservoirs post-transplant (NCT00968630 & NCT00112593). NNRTI or integrase inhibitor based ART regimens were preferred during the PBSCT and were selected pre-transplant by Infectious Disease physicians. Plasma HIV RNA was measured every other day for the first two weeks post- transplant, then every two weeks. Doses of ART missed and reasons for changing ART regimen during peri-transplant hospitalization were documented through review of inpatient pharmacy records.
Results: Six autologous and eight allogeneic transplants were performed. In 11 (79%) transplants, no changes were made to the ART regimen post PBSCT and no doses were missed. One patient missed doses on 2 non-consecutive days due to mucositis and nausea. Two patients required changes in the ART regimen: one patient developed acute renal failure and one patient could not tolerate PO medications due to a small bowel obstruction; in these patients T-20 was added to ART regimen or used as bridging monotherapy. Plasma HIV RNA remained suppressed during the first 28 days post-transplant in 13 (93%) of 14 transplants; 1 person who had not yet achieved virologic suppression at the time of PBSCT (HIV RNA level of 150 copies/ml) became undetectable at day 28 post-transplant and virologic suppression was maintained.
Conclusions: Integrase inhibitor and NNRTI based ART is safe and effective in the peri-PBSCT period. Most patients undergoing PBSCT were able to continue ART in the peri-transplant period without missed doses or ART related side effects, and emergence of HIV viremia and resistance was not observed.

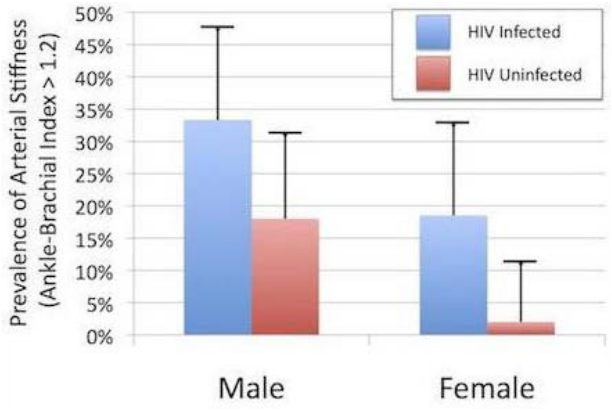
Cardiovascular disease

WEPEB338

HIV infection and vascular stiffness among older-adults taking antiretroviral therapy in rural Uganda

M. Siedner[1], J.-H. Kim[2], J. Haberer[3], J. Martin[4], A. Tsai[3], Y. Boum II[5], P. Hunt[6], D. Bangsberg[3]
[1]Massachusetts General Hospital, Medicine, Bosotn, United States, [2]Johns Hopkins School of Medicine, Baltimore, United States, [3]Massachusetts General Hospital, Boston, United States, [4]University of California, San Francisco, United States, [5]Epicentre Research Base, Mbarara, Uganda, [6]University of California, Department of Medicine, San Francisco, United States
Presenting author email: phunt@php.ucsf.edu

Background: HIV infection is associated with vascular stiffness. No studies have demonstrated this relationship among people living with HIV (PLWH) in sub-Saharan Africa, the focal point of the global epidemic.
Methods: We enrolled older-aged PLWH taking antiretroviral therapy in Mbarara, Uganda, and a community-based, age and gender-matched control group of HIV-uninfected individuals from the clinic catchment area. We collected data on demographics, smoking history, blood for CD4 count and viral load measurements, and obtained bilateral ankle-brachial index (ABI) measurements. We calculated ABI as the greater of Doppler-detected blood pressure in the left or right dorsalis pedis artery divided by the greater of Doppler-detected blood pressure in the left or right brachial artery. Our primary outcome of interest was an elevated ABI > 1.2, which is a surrogate marker of arterial stiffness that has been correlated with increased risk of all cause and cardiovascular mortality. We fit logistic regression models to estimate the associations between HIV infection and vascular stiffness after adjusting for age, gender, smoking duration, and body mass index.
Results: A total of 100 HIV uninfected and 105 PLWH were enrolled during November 2013 - October 2014. The median age was 50 years (IQR 46-53), 103 (51%) were female, with no differences by HIV status. A higher proportion of HIV-uninfected persons were current or former smokers, but the difference was not statistically significant (50% versus 36%, P=0.06). The prevalence of vascular stiffness (ABI>1.2) was 27/105 (26%) among PLWH and 10/100 (10%) in the matched control group (P=0.003, Figure 1), and only one participant had an ABI< 0.9. In univariable models, female gender (OR 0.34, 95%CI 0.16 - 0.74, P=0.01) was significantly associated with vascular stiffness and each cumulative year of smoking was marginally associated (OR 1.04, 95%CI 1.00- 1.08, P=0.09). In multivariable logistic regression models, HIV infection was associated with increased odds of vascular stiffness (AOR 3.64, 95%CI 1.57 - 8.43, P=0.003).



[Figure 1. Arterial stiffness among older-aged individuals with and without HIV infection in Rural Uganda]

Conclusions: In rural southwestern Uganda, vascular stiffness is associated with HIV infection, independent of other cardiovascular disease risk factors. Increased attention to cardiovascular disease risk and morbidity among PLWH in sub-Saharan Africa should be prioritized.

WEPEB339

Speckle tracking echocardiography-derived myocardial strain abnormalities in PLHIV

N.L. Okeke[1], F. Alenezi[2], P. Khazanie[2], G.S. Bloomfield[2,3,4], A. Dunning[4], P. Hofmann[4], M.E. Clement[1], S.H. Shah[2], S. Naggie[1,4], E.J. Velazquez[2,3,4]
[1]Duke University Medical Center, Medicine-Infectious Diseases, Durham, United States, [2]Duke University Medical Center, Medicine-Cardiology, Durham, United States, [3]Duke Global Health Institute, Durham, United States, [4]Duke Clinical Research Institute, Durham, United States
Presenting author email: lance.okeke@duke.edu

Background: While left ventricular ejection fraction is a commonly reported measure of left ventricular (LV) function, emerging data suggests that speckle tracking echocardiography (STE)-derived myocardial strain may outperform LVEF as a measure of subclinical dysfunction and in predicting adverse cardiac events.
Methods: 2D STE analyses were performed retrospectively on all transthoracic echocardiograms (TTE) performed in PLHIV at Duke University Medical Center between 2001 and 2012. Global longitudinal strain (GLS) was the average of the three apical peak longitudinal strain measurements and global circumferential strain (GCS) was the average of strain measurements for the short axis view at the level of the papillary muscle for the six wall segments. Right ventricular longitudinal strain (RVLS) was analyzed using one apical view of the chamber. Cutoffs for abnormal strain were based on reference values most cited in the literature: > -16% for LV GCS, > -21% for LV GCS and > -21% for RVLS. Demographic and CAD risk factor data were abstracted from the EMR.
Results: Among 161 PLHIV with TTEs reviewed for this analysis, patient characteristics were as follows: median age at TTE 46 yrs [IQR 38,52] ; 58% male; 79% Black, 79% with diagnosis of hypertension; 35% with diagnosis of diabetes; 23% with prior heart failure. At the time of TTE, 27% had undetectable viral load, median proximal CD4 count of 238 cells/mm^3 and median CD4+ cell count nadir of 155 cells/mm^3. Median LV GLS was -15.3% [IQR -18.0, -12.3], median LV GCS was -21.2% [IQR -26.9,-15.4], median RVLS was -16.4% [IQR -19.4, -14.0]. Overall, the prevalence of abnormalities were as follows: 56% for LV GLS, 50% for LV GCS and 84% for RVLS.
Conclusions: We observed a higher than anticipated prevalence of abnormal myocardial strain among PLHIV referred for TTE. With the rapid aging of PLHIV, STE may be a useful modality in detecting preclinical myocardial dysfunction and identifying those individuals at risk for subsequent heart failure for preventive strategies.

WEPEB340

Efavirenz leads to arterial stiffening in clinical and experimental settings

A. Caulk[1], I. Parker[2], D. Seifu[3], J. Soler[1], M. Platt[2,4], W. Amogne[5], R. Gleason Jr.[1,2,4]
[1]Georgia Institute of Technology, Mechanical Engineering, Atlanta, United States, [2]Georgia Institute of Technology, Biomedical Engineering, Atlanta, United States, [3]Addis Ababa University, Biochemistry, Addis Ababa, Ethiopia, [4]Georgia Institute of Technology, Petit Institute for Bioengineering and Bioscience, Atlanta, United States, [5]Addis Ababa University, Internal Medicine, Addis Ababa, Ethiopia
Presenting author email: acaulk@gatech.edu

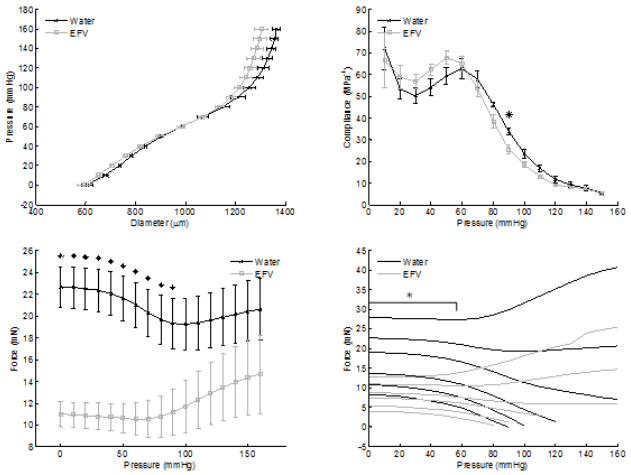
Background: Efavirenz (EFV) is the most prescribed NNRTI-class of HIV-antiretroviral drugs, yet data investigating the role of EFV in cardiovascular disease (CVD) is lacking, particularly in sub-Saharan Africa where much of the HIV burden resides. The objective of this study was to test the hypothesis that EFV treatment mediates arterial stiffening, a key first step in the progression of CVD.
Methods: To test this hypothesis, we performed a cross-sectional clinical study and a parallel mouse study. Adult HIV-negative (*n*=36), treatment naïve (*n*=51), EFV-treated (*n*=91), nevirapine (NVP)-treated (*n*=95), or ritonavir-boosted lopinavir (LPV/r)-treated (*n*=44) subjects were recruited from Black Lion Hospital in Addis Ababa, Ethiopia. Pulse wave velocity (PWV, a marker of arterial stiffness) was measured via applanation tonometry, and carotid intima-media thickness (cIMT) and brachial artery flow-mediated dilation (FMD) were measured via ultrasound. Body mass index, waist-to-hip circumference ratio, skinfold thickness, and self-reported fat redistribution were measured to quantify lipodystrophy. CD4+ cell count, viral load, fasting glucose, total-, HDL-, and LDL-cholesterol, triglycerides, hsCRP, sVCAM-1, sICAM-1, leptin and CBC were also measured. This work was approved by the IRB committees at Addis Ababa University and Georgia Institute of Technology. For the mouse studies, ApoE$^{-/-}$ mice were given EFV (75 mg/kg/day) (*n* = 4) or vehicle (*n* = 5) via oral gavage for 35 days. Arterial stiffening and IMT of abdominal aortas were quantified via ex vivo biaxial mechanical testing and histology. Atherosclerotic plaque progression was quantified for thoracic aortas. Experimental procedures were approved by the Georgia Tech IACUC.
Results: PWV, FMD, and cIMT (normalized to inner diameter) were elevated in EFV-treated subjects compared to NVP-treated subjects; normalized cIMT was elevated in the EFV-treated subjects compared to treatment-naïve subjects. PWV and cIMT were associated with current EFV use.

Endpoint	HIV-negative (n = 36)	HAART-naive (n = 51)	Efavirenz (n = 91)	Nevirapine (n = 95)	Lopinavir/r (n = 44)
Aortic SBP [mmHg]	110 (101 - 121)	103 (98 - 114)	103 (96 - 113)	109 (98 - 122)	112 (97 - 123)
Aortic DBP [mmHg]	75 (69 - 82)	71 (67 - 81)	72 (64 - 79)	73 (68 - 83)	71 (67 - 81)
Aortic PP [mmHg]	34 (30 - 42)	32 (26 - 38)	31 (28 - 36) [a]	34 (29 - 42) [b,d]	34 (31 - 47) [b,d]
Augmentation Pressure [mmHg]	8 (5 - 13)	8 (6 - 14)	8 (5 - 11)	10 (6 - 14)	10 (6 - 16)
Pulse Wave Velocity [m/s]	7.1 (6.3 - 8.4)	7.0 (6.3 - 8.2)	7.4 (6.3 - 8.4)	6.8 (6.0 - 7.5) [D]	7.4 (6.8 - 8.7) [E]
FMD [%]	6.5 (5.0 - 12.4)	10.0 (7.0 - 13.9) [a]	7.7 (4.8 - 11.2) [b]	9.2 (6.6 - 12.5) [d]	7.6 (4.5 - 12.2) [b]
cIMT-norm [%]	18.0 (16.4 - 19.8)	17.6 (16.6 - 19.3)	19.2 (17.2 - 21.7) [b]	17.5 (16.3 - 18.9) [D]	19.0 (17.4 - 21.1) [b,E]
Compliance [MPa^{-1}]	20 (12 - 24)	20 (14 - 24)	19 (15 - 23)	18 (14 - 22)	17 (14 - 20)

[A,a] = p<0.001 or p<0.05 versus HIV-negative controls, respectively; [B,b] = p<0.001 or p<0.05 versus HAART-naive, respectively; [D,d] = p<0.001 or p<0.05 versus EFV, respectively; [E,e] = p<0.001 or p<0.05 versus NVP, respectively

[Cardiovascular metrics in an Ethiopian population]

Aortic compliance and axial force were lower in EFV-treated mice compared to controls. Compliance was lower at 80-90 mmHg and axial stretches of 1.6-1.8. Aortic IMT and plaque progression were not different across groups.



[Mechanical properties of aortas at stretch of 1.7]

Conclusions: This study is the first to implicate EFV as a mediator of arterial stiffening both in mice and men and provides a novel platform for future investigations of the underlying mechanisms of EFV-induced CVD.

WEPEB341

Risk of cardiovascular events in efavirenz-containing vs. efavirenz-free antiretroviral therapy

L. Rosenblatt[1], A. Farr[2], S. Johnston[2], E. Nkhoma[3]
[1]Bristol-Myers Squibb, Plainsboro, United States, [2]Truven Health Analytics, Bethesda, United States, [3]Bristol-Myers Squibb, Wallingford, United States
Presenting author email: lisa.rosenblatt@bms.com

Background: Efavirenz (EFV) can elevate lipids; however, its impact on cardiovascular (CV) outcomes is unclear. This study compared the incidence rate and hazards of CV events between patients initiating EFV-containing vs. EFV-free antiretroviral (ARV) regimens.
Methods: This was a retrospective cohort study using commercial and multiple-state Medicaid insurance claims data spanning 2006-2013. We identified ARV-naïve patients who were age ≥18 years and initiated an EFV-containing or EFV-free regimen with ≥6 months of continuous enrollment prior to ARV initiation. Myocardial infarction (MI), stroke, and a composite CV outcome (MI, stroke, percutaneous coronary intervention, and/or coronary artery bypass graft) were ascertained using previously-validated algorithms. Outcomes were identified during an intent-to-treat (ITT) period beginning at ARV initiation and censoring at disenrollment from insurance or end of data. Outcomes were compared using propensity score weighted Cox regression adjusting for concomitant abacavir use and patient baseline demographics and CV risk factors. A subanalysis stratified by presence of abacavir at or following ARV initiation was conducted for commercial patients on the basis of a Breslow-Day test indicating effect modification.

Results: In the commercial database, there were 22,212 study patients; 83% male, mean age 40 years. In the Medicaid database, there were 7,400 patients; 51% male, mean age 41 years. Study results are displayed in the Table. In both databases, the outcomes occurred infrequently. In the commercial database, patients initiating EFV-containing regimens had significantly lower hazards of the composite CV outcome than patients initiating EFV-free regimens; differences were nonsignificant for MI and stroke. In the Medicaid database, differences were nonsignificant for the composite CV outcome, MI, and stroke. Sensitivity analyses using an as-treated follow-up with censoring at end of exposure to the initiated regimen showed no significant differences between EFV-containing and EFV-free regimens (data not shown). In subanalysis, among patients without abacavir, those initiating EFV-containing regimens had significantly lower hazards of MI and the composite CV endpoint. Among patients with abacavir, there were no significant differences (data not shown).

	Commercial: EFV-containing N=11,978	Commercial: EFV-free N=10,234	Medicaid: EFV-containing N=2,943	Medicaid: EFV-free N=4,457
Myocardial infarction: Number of events; mean (median) days of person-time to event or censoring	29; 703 days (542)	30; 583 days (424)	16; 708 days (539)	24; 594 days (391)
Myocardial infarction: Crude incidence rate [IR] (95% confidence interval [CI]) per 100,000 person-years (PYs)	125.7 (84.2-180.5)	183.4 (123.8-261.9)	280.2 (160.2-455.1)	330.9 (212.0-492.4)
Myocardial infarction: Adjusted hazard ratio [HR] (95% CI) vs. EFV-free	0.60 (0.36-1.01)		0.69 (0.36-1.31)	
Stroke: Number of events; mean (median) days of person-time to event or censoring	31; 703 days (543)	24; 585 days (425)	32; 706 days (538)	39; 593 days (389)
Stroke: Crude IR (95% CI) per 100,000 PYs	134.3 (91.2-190.6)	146.4 (93.8-217.9)	562.3 (384.6-793.8)	538.7 (383.1-736.4)
Stroke: Adjusted HR (95% CI) vs. EFV-free	0.93 (0.54-1.60)		0.94 (0.58-1.52)	
Composite cardiovascular (CV) endpoint: Number of events; mean (median) days of person-time to event or censoring	79; 701 days (541)	77; 581 days (421)	54; 701 days (534)	71; 589 days (386)
Composite CV endpoint: Crude IR (95% CI) per 100,000 PYs	343.3 (271.8-427.9)	473.0 (373.3-591.2)	954.9 (717.3-1,245.9)	987.6 (771.3-1,245.7)
Composite CV endpoint: Adjusted HR (95% CI) vs. EFV-free	0.68 (0.49-0.93)		0.83 (0.58-1.19)	

[Incidence rate/hazards of MI, stroke, and CV event]

Conclusions: In this analysis of two large real world databases, we found no evidence of increased CV risk of patients initiating EFV-containing ARV regimens.

Bone disease (including issues related to vitamin D)

WEPEB342

Prevalence and risk factor for low bone mineral density among HIV-infected patients in Thailand

T. Apornpong[1], V. Sapsirisavat[1], O. Putcharoen[2], W. Thiansanguangkul[1], O. Butterworth[1], T. Mengthaisong[1], L. Wattanachanya[3], S.J. Kerr[1], K. Ruxrungtham[1,4], A. Avihingsanon[1,4]
[1]HIV-NAT, Thai Red Cross - AIDS Research Centre, Bangkok, Thailand, [2]Faculty of Medicine, Chulalongkorn University, Department of Infectious Diseases, Bangkok, Thailand, [3]Faculty of Medicine, Chulalongkorn University, Department of Endocrinology, Bangkok, Thailand, [4]Faculty of Medicine, Chulalongkorn University, Division of Allergy and Immunology, Bangkok, Thailand
Presenting author email: anchalee.a@hivnat.org

Background: Low bone mineral density (BMD) is an emerging threat in HIV-infected patients on combination antiretroviral therapy (cART). It has been commonly documented in HIV-infected patients from many Western countries, however, there are scant published data regarding BMD in resource-limited settings, especially in Asia.
Methods: From January 2009 to December 2014, a cross sectional study was performed among HIV-infected patients aged ≥18 years attending routine clinic visits at HIV-NAT, Bangkok, Thailand. BMD of spine and hip were measured with the use of dual-energy X-ray absorptiometry. Logistic regression analyses were performed to identify factors associated with osteopenia and osteoporosis, defined as BMD T-scores between -1.0 and -2.5, and ≤ -2.5, respectively.
Results: Totally 440 (male 68%) patients with a median age of 40 years and body mass index (BMI) of 22.0 kg/m^2 were included. 19% of female were menopausal. 85.9% of patients were on cART with a median duration of 7.3 years; 85% and 53.4 % were taking tenofovir and protease inhibitors (PI), respectively. Osteopenia and osteoporosis were diagnosed in 41.8 % and 3.2%, respectively. Although, female was older than male (median 41.1 years vs 39.3 years, p= 0.03); osteopenia was significantly more prevalent in males versus females (75% versus 25%, p=0.004). In multivariate analysis, age >48 years [OR= 2.8 (95%CI 1.6-4.9), p=0.001], male gender [OR =1.9: (95%CI 1.1-3.1), p=0.01), BMI < 18 kg/m^2[OR= 3.1 (95% CI 1.7-5.6), p< 0.001] and PI exposure >5 years [OR= 2.5 (95%CI 1.5-4.1),
p< 0.01] were significantly associated with reduced BMD. Fractures of the femur and ankle only occurred in two males aged 46 and 48, after a fall.
Conclusions: Low BMD was prevalent among HIV-infected Thai adults on cART. Increased age, male gender, lower BMI and exposure to PI were significantly associated with osteopenia/osteoporosis. Our findings highlight the need for screening guideline to identify those most at risk so that effective interventions can be implemented early. Given high prevalent of low BMD in male population, secondary cause of osteopenia/osteoporosis should be further explored.

WEPEB343

Higher 25-hydroxyvitamin D is associated with higher levels of plasma soluble biomarkers in older HIV-infected patients on stable antiretroviral therapy

L.M. Gangcuangco[1,2], D. Chow[2,3], S. Keating[4], P. Norris[4,5], L. Nagamine[2], L. Ndhlovu[2], K. Kallianpur[2], C. Shikuma[2]
[1]Bridgeport Hospital-Yale New Haven Health, Dept. of Internal Medicine, Bridgeport, United States, [2]Hawaii Center for AIDS, Honolulu, United States, [3]Queen's Medical Center, Honolulu, United States, [4]Blood Systems Research Institute, San Francisco, United States, [5]University of California San Francisco, San Francisco, United States
Presenting author email: louiemarmd@gmail.com

Background: Vitamin D is an immunomodulator that stimulates or suppresses the production of proteins such as cytokines. We investigated the association of 25-hydroxyvitamin D (25(OH)D) with markers of inflammation among HIV-infected subjects on stable antiretroviral therapy (ART). We further analyzed whether seasonal differences in plasma biomarkers exist in a locality with minimal year-round variations in solar radiations (Hawaii, latitude 21^0 North) and whether these differences are associated with 25(OH)D levels.
Methods: Subjects ≥ 40 years old on stable ART for >6 months were recruited. Chemiluminescent immunoassay (DiaSorin) was used to determine plasma 25(OH)D levels. Plasma soluble biomarkers were measured by Luminex technology. Multiple linear regression analysis was used to assess the association between 25(OH)D and various soluble biomarkers. Linear regression models were adjusted for age, gender, Caucasian ethnicity, body mass index (BMI), CD4%, undetectable HIV RNA, hepatitis C co-infection, winter visit (being enrolled between October and April), and current smoking status.
Results: Of 158 patients, median age was 51 [46, 57] years and 25(OH)D was 32.3 [24, 41] ng/ml. The majority were males (88%) and had undetectable HIV RNA (84.8%); 10.1% were Hepatitis C co-infected and 24.7% were current smokers. Median CD4 count was 498.5 [341, 661] cells/µl and CD4% was 29 [21,36]%. Non-Caucasians (42.41%), subjects taking zidovudine (7.6%), and subjects enrolled in winter (56%) had significantly lower 25(OH)D levels (p< 0.05). Log-25(OH)D was independently associated with IL-10 (regression coefficient(β)=0.93, p=0.009), MPO (β=0.51, p=0.002), SAA (β=1.10, p=0.008), SAP (β=0.49, p=0.02), and TNF-α (β=0.40, p=0.04). Hepatitis C co-infection was associated with sVCAM (β=0.09, p=0.03) and sICAM (β=0.23, p< 0.001). Winter visit (October to April) was associated with higher CRP (β=0.26, p=0.046), SAP (β=0.20, p=0.008), and lower IL-10 (β=-0.29, p=0.02) independent of 25(OH)D levels.
Conclusions: In our population of older HIV-infected patients with relatively high CD4 count and good virologic control, 25(OH)D was associated with higher (not lower) levels of pro-inflammatory markers, which may be an immune response to suppress chronic HIV infection despite potent ART. The pro-inflammatory milieu is counter-balanced by a concomitant increase in IL-10. Winter visit was associated with higher pro-inflammatory biomarkers in Hawaii but was independent of 25(OH)D levels.

WEPEB344

Bone mineral density and fat distribution in adults randomized to maraviroc (MVC) once daily with darunavir/ritonavir (DRV/r) vs. tenofovir/emtricitabine (TDF/FTC) with DRV/r: week-48 results from MODERN

A. Carr[1], A. Fang[2], M. Saag[3], C. Fichtenbaum[4], S. Swindells[5], J. Brunetta[6], G. Mukwaya[2], S.R. Valluri[2], A. Clark[7], J. Heera[8]
[1]St Vincent's Hospital, Centre for Applied Medical Research, Sydney, Australia, [2]Pfizer, New York, United States, [3]University of Alabama, Birmingham, United States, [4]University of Cincinnati Medical Center, Cincinnati, United States, [5]University of Nebraska Medical Center, Omaha, United States, [6]Maple Leaf Medical Clinic, Toronto, Canada, [7]ViiV Healthcare, London, United Kingdom, [8]Pfizer, Groton, United States
Presenting author email: andrew.carr@svha.org.au

Background: Reduced bone mineral density (BMD) is common in HIV-infected adults taking TDF. TDF-sparing antiretroviral therapy (ART) may decrease bone loss. Maraviroc, a CCR5 receptor antagonist, has shown durable antiviral response with a favorable safety profile.
Methods: In this multicenter, double-blind, Phase III study (MODERN), HIV-1 infected ART-naïve adults underwent 1:1 randomization to receive MVC 150 mg QD or TDF/FTC 200/300 mg QD each with DRV/r 800/100 mg QD for up to 96 weeks. At selected sites, a sub-study was conducted to measure BMD at hip, femoral neck and lumbar spine by dual-energy x-ray absorptiometry (DXA), bone turnover markers (BTM; osteocalcin and C-terminal telopeptide [CTx]), and body fat distribution (limb fat, trunk to limb fat ratio by DXA). Sub-study endpoints were analyzed at Week 48. The study was terminated early, in Oct 2013, due to maraviroc arm inferior efficacy.
Results: The DXA analysis included 143 participants (MVC, n=66; TDF/FTC, n=77): median age 34.0 years, 10.6% female, 23.9% non-white, mean body mass index (BMI) 25.4 kg/m^2. At Week 48, changes from baseline after adjusting for baseline covariates such as age, race, gender and screening BMI are shown in table below. No significant correlations between changes in BMD and changes in osteocalcin or CTx levels were observed. Lower baseline CD4 (<200 cells/mm^3) was the only observed predictor for larger decrease in hip BMD after adjusting for the covariates (estimate: -2.14%, p=0.0055).

DXA / Bone Parameter	Maraviroc Mean (±SD) changes from baseline	TDF/FTC Mean (±SD) changes from baseline	P value
Hip (%)	-1.4 ± 2.2	-2.6 ± 2.3	0.0052
Femoral neck (%)	-2.2 ± 3.8	-3.2 ± 3.1	0.1640
Lumbar spine (%)	-2.5 ± 3.9	-3.0 ± 3.2	0.5441
Peripheral fat mass (g)	402 ± 1693	349 ± 1910	0.8379
Trunk to limb fat ratio (%)	3.2 ± 19.6	1.1 ± 12.6	0.3376
Osteocalcin (ng/mL)	5.6 ± 8.0	6.7 ± 8.3	0.1769
CTx (pg/mL)	121 ± 243	222 ± 288	0.0075

[Table 1]

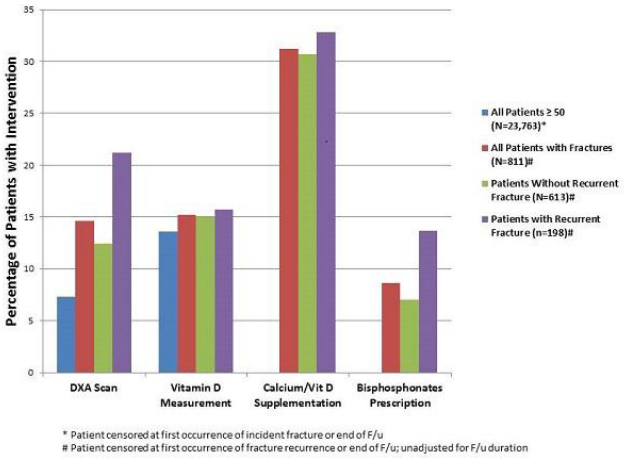
Conclusions: TDF/FTC was associated with greater hip BMD decrease and more bone turnover than MVC over 48 weeks. Lower baseline CD4 predicted greater BMD loss. No adverse effect of TDF/FTC or MVC on peripheral fat distribution was observed.

WEPEB345

Evaluation and management of fracture risk in HIV patients in the VA system

J. Cutrell[1,2], S. Zhang[3], H. Drechsler[1,2], P. Tebas[4], N.M. Maalouf[5,6], R. Bedimo[1,2]
[1]VA North Texas Healthcare System, Medical Service, Infectious Diseases Section, Dallas, United States, [2]UT Southwestern Medical Center, Medicine, Division of Infectious Diseases, Dallas, United States, [3]UT Southwestern Medical Center, Clinical Sciences, Dallas, United States, [4]University of Pennsylvania School of Medicine, Medicine, Division of Infectious Diseases, Philadelphia, United States, [5]VA North Texas Healthcare System, Medical Service, Endocrine and Mineral Metabolism Section, Dallas, United States, [6]UT Southwestern Medical Center, Medicine, Division of Endocrinology and Mineral Metabolism, Dallas, United States
Presenting author email: james.cutrell@va.gov

Background: HIV infection is associated with significant increased risk of osteoporotic fractures (OF). The 2010 IDSA guidelines recommend evaluating fracture risk in HIV patients ≥50 years. We assessed the adequacy and efficacy of primary and secondary prevention of OF among HIV-infected Veterans prior to these guidelines.
Methods: Among HIV-infected patients ≥50 years old in care at the US Veterans Affairs network from 1996 to 2010 who experienced OF (wrist, hip, or vertebra), we determined the proportions receiving assessment of bone mineral density (by DXA scan) and vitamin D levels, calcium/vitamin D and bisphosphonate prescription prior to and after incident fracture, and calculated the rate and predictors of OF recurrence.
Results: A total of 23,763 HIV-infected patients 50 or above were identified: 98% were male; 35% Black; and 39% HCV co-infected. Prior to incident fracture, 1735 (7.3%) had a DXA scan done, and 3242 (13.6%) had vitamin D levels measured.
An incident OF occurred in 811 patients during total follow-up time of 277,392 patient-years; rate: 2.92/1000 patient-years. Among these, 198 (24.4%) had a recurrent OF during 2828 patient-years of post-fracture follow-up; recurrence rate: 70.0/1000 patient-years. Following the incident OF, DXA scan was performed only in 139 (17.1%) of patients, and 238 (29.4%) had a vitamin D measurement. Calcium or vitamin D supplementation was prescribed in 295 (36.4%) and bisphosphonates in 89 (11%) patients. Figure 1 compares use of primary and secondary prevention measures between groups.



[Figure 1. Primary and secondary fracture prevention measures]

In patients with an incident OF, those with post-fracture DXA scan and vitamin D measurement had a hazard ratio (HR) for fracture recurrence of 2.80 and 2.65, respectively, and those receiving calcium/vitamin D and bisphosphonates post-fracture had a HR of 1.87 and 2.99.
Conclusions: Prior to issuance of the IDSA guidelines, only a very small proportion of HIV-infected Veterans ≥ 50 years received primary or secondary fracture prevention. Fracture recurrence rates were high. Secondary prevention assessments (DXA scan and vitamin D assessment) and interventions (calcium/vitamin D supplementation and bisphosphonates) appear to have targeted those more likely to experience recurrence. Future studies should evaluate the guidelines' impact on increasing utilization of prevention measures and on fracture recurrence.

WEPEB346

Decreased bone strength on hip structural analysis in HIV+ adults with versus without fractures

D. Tan[1], J. Raboud[2], L. Szadkowski[3], E. Szabo[4], H. Hu[4], Q. Wong[4], A. Cheung[3], S. Walmsley[5]
[1]St. Michael's Hospital, Toronto, Canada, [2]Dalla Lana School of Public Health, University of Toronto, Toronto, Canada, [3]Toronto General Research Institute, Toronto, Canada, [4]Centre for Excellence in Skeletal Health Assessment, University of Toronto, Toronto, Canada, [5]University Health Network, Toronto, Canada
Presenting author email: darrell.tan@gmail.com

Background: Bone mineral density (BMD) as assessed by dual-energy x-ray absorptiometry (DXA) is often used to assess fracture risk, but is limited by the lack of a clear fracture threshold and of validation in younger people or patients with HIV. We conducted a pilot case-control study to determine whether bone geometric parameters and estimated strength as assessed by hip structural analysis (HSA) correlate with fractures in this population.
Methods: Adults with a history of low-trauma fracture after HIV diagnosis (cases) were matched 1:1 with HIV-infected adults without prior fractures (controls) based on age, sex, race and smoking history. Participants underwent DXA at the hip and lumbar spine, and image files underwent HSA by trained study personnel. The buckling ratio (a measure of cortical stability under compressive loads, i.e. axial strength), section modulus (a measure of bending strength), cross-sectional area and average cortical thickness were compared between cases and controls using Wilcoxon signed rank sum tests, with differences expressed as percentages of control group values.
Results: 23 matched pairs were included, with median (IQR) age 50 (46,56) years, 78% male, 78% white and 57% smokers. Median (IQR) duration of HIV was 19 (11,23) years for cases and 10 (7,18) years for controls. On DXA, cases had significantly lower BMD at the total hip (median difference =-4.3%, p=0.04), but not the lumbar spine (-3.47%, p=0.33). Statistically significant differences on HSA were observed at the intertrochanteric area, where the buckling ratio was 15.1% greater (p=0.01), section modulus was 12.0% lower (p=0.03), cross-sectional area was 13.1% lower (p=0.05) and average cortical thickness was 15.3% lower (p=0.02) among cases than controls (see Table). At the femoral shaft, buckling ratio was significantly greater by 8.46% (p=0.05) and average cortical thickness was significantly lower by 11.1% (p=0.04). Differences at the narrow neck did not reach statistical significance.

	Narrow neck			Intertrochanteric area			Femoral shaft		
	Difference from control (95%CI)	% difference from control (95%CI)	p	Difference from control (95%CI)	% difference from control (95%CI)	p	Difference from control (95%CI)	% difference from control (95%CI)	p
Buckling ratio	-0.02 (-2.47, 1.68)	-0.23 (-17.8, 17.7)	0.85	0.97 (-0.05, 2.35)	15.1 (-0.61, 32.2)	0.01	0.28 (0.08, 0.46)	8.46 (2.77, 19.8)	0.05
Section modulus (cm3)	-0.18 (-0.33, 0.08)	-10.9 (-15.8, 5.89)	0.28	-0.59 (-1.95, -0.03)	-12.0 (-35.9, -0.49)	0.03	-0.10 (-0.46, 0.39)	-4.36 (-21.8, 12.8)	0.56
Cross-sectional area (cm2)	-0.12 (-0.20, 0.09)	-4.20 (-17.7, 6.37)	0.37	-0.69 (-1.89, 0.57)	-13.1 (-28.0, 9.85)	0.05	-0.27 (-1.17, 0.36)	-7.30 (-20.0, 7.18)	0.12
Average cortical thickness (cm)	-0.006 (-0.03, 0.02)	-2.71 (-17.1, 13.2)	0.53	-0.05 (-0.13, 0.01)	-15.3 (-24.1, 4.26)	0.02	-0.07 (-0.13, 0.006)	-11.1 (-15.2, 0.92)	0.04

[Differences in HSA parameters, fracture vs control]

Conclusions: A history of fracture was associated with decreased composite measures of estimated bone strength on hip structural analysis among HIV-infected adults, particularly at the intertrochanteric area. Further work is needed to characterize the role of HSA in assessing fracture risk in HIV patients.

Renal disease

WEPEB347

SNPs of the genes encoding transporter proteins of renal tubular cells do not associate with tenofovir-related renal dysfunction: a pharmacogenetic study

T. Nishijima[1,2], T. Hayashida[1], T. Kurosawa[3], N. Tanaka[4], K. Tsuchiya[1], S. Oka[1,2], H. Gatanaga[1,2]
[1]National Center for Global Health and Medicine, AIDS Clinical Center, Tokyo, Japan, [2]Kumamoto University, Center for AIDS Research, Kumamoto, Japan, [3]Tokyo University of Science, Department of Mathematical Science for Information Sciences, Tokyo, Japan, [4]National Center for Global Health and Medicine, Biostatistics Section, Department of Clinical Research and Informatics, Clinical Science Center, Tokyo, Japan
Presenting author email: tnishiji@acc.ncgm.go.jp

Background: Tenofovir disoproxil fumarate **(**TDF) causes mitochondria toxicity in the proximal renal tubular cells, which can lead to tubulopathy and then decrement in renal function. To date, among single nucleotide polymorphisms (SNP) in the genes encoding transporter proteins at kidney tubular cells, only SNPs in *ABCC2* gene have been identified to associate with TDF-related tubulopathy. However, the effect of these SNPs on actual decrement in renal function of the patients who initiated TDF remains unknown.
Methods: The association between TDF-related renal function decrement and SNPs in the *ABCC2* gene (-24 and 1249) were investigated in 661 Japanese patients who initiated TDF-containing antiretroviral therapy at our clinic. Three renal endpoints were examined by the logistic regression model; decrement in estimated glomerular filtration rate (eGFR) of >10 ml/min/1.73m^2 relative to the baseline, >25% decrement in eGFR, and eGFR < 60 ml/min/1.73m^2 ≥3 months apart.

-24 of ABCC2	Adjusted OR	95%CI	P value	1249 of ABCC2	Adjusted OR	95%CI	P value
Genotype C/C versus T/T	0.8	0.30-1.99	0.85	Genotype A/A versus G/G	2.0	0.41-9.30	0.29
Genotype C/T versus T/T	0.7	0.26-1.74	0.33	Genotype A/G versus G/G	0.7	0.48-1.09	0.13
CD4 count per 1/µl increment	1.0	1.00-1.00	0.0038	CD4 count per 1/µl increment	1.0	1.00-1.00	0.0049
Baseline eGFR per 1ml/min/1.73m2 increment	1.0	0.99-1.02	0.44	Baseline eGFR per 1 ml/min/1.73m2 increment	1.0	0.99-1.02	0.48
Weight per 1kg increment	1.0	0.97-1.01	0.17	Weight per 1kg increment	1.0	0.97-1.00	0.16
Nephrotoxic drug use	0.8	0.49-1.31	0.38	Nephrotoxic drug use	0.8	0.50-1.35	0.44
Ritonavir-boosted protease inhibitor use	1.0	0.68-1.51	0.95	Ritonavir-boosted protease inhibitor use	1.1	0.71-1.58	0.79
Hypertension	0.7	0.42-1.04	0.073	Hypertension	0.7	0.41-1.03	0.069
Dyslipidemia	1.0	0.69-1.38	0.88	Dyslipidemia	1.0	0.67-1.35	0.79

[The effect of SNPs of ABCC2 on renal dysfunction]

Results: 66% of the study patients were treatment-naïve [median CD4 246 /µl, median baseline eGFR 94.4 ml/min/1.73m^2 (IQR 88.3-100.6), median exposure to TDF 3.69 years (IQR 1.93-5.58)]. Decrement in eGFR of >10 ml/min/1.73m^2 occurred to 284 (70%) of 406, 155 (68%) of 227, and 22 (79%) of 28 patients with genotype C/C, C/T, and T/T at -24, respectively, and to 9 (82%) of 11, 88 (64%) of 137, and 364 (79%) of 513 patients with genotype A/A, A/G, and G/G at 1249, respectively. Decrement in eGFR of >10 ml/min/1.73m^2 was not associated with genotypes either at -24 or 1249 of *ABCC2* (-24, p=0.57; genotype C/C versus T/T, OR 0.8, 95%CI 0.30-1.99; genotype C/T versus T/T, OR 0.7, 95%CI 0.26-1.74) (1249, p=0.24; genotype A/A versus G/G, OR 2.0, 95%CI 0.41-9.30; genotype A/G versus G/G, OR 0.7, 95%CI 0.48-1.09) in the multivariate analysis.
More than 25% decrement in eGFR and eGFR < 60 ml/min/1.73m^2 were not associated with genotypes at -24 or 1249 either. The results were the same when we applied the dominant, additive, and recessive models instead for statistical analyses.
Conclusions: Although SNPs at *ABCC2* have been known to associate with TDF-induced tubulopathy, these SNPs did not associate with actual renal function decrement in patients who initiated TDF-containing ART.

WEPEB348

Progressive kidney function decline and increasing incidence of tubular renal alteration in HIV-infected patients receiving a tenofovir-containing regimen

J.L. Casado[1], S. Bañón[1], C. Santiuste[2], M. Tenorio[3], F. Liaño[3], J.M. Del Rey[2], S. Moreno[1]
[1]Ramon y Cajal Hospital, Infectious Diseases, Madrid, Spain, [2]Ramon y Cajal Hospital, Biochemistry, Madrid, Spain, [3]Ramon y Cajal Hospital, Nephrology, Madrid, Spain
Presenting author email: smoreno.hrc@salud.madrid.org

Background: There are controversial data about the incidence and importance of tubular renal damage and renal function decline in patients on tenofovir (TDF).
Methods: Prospective cohort of 283 HIV-infected patients (15 no TDF, 25 naive), with sequential determinations of estimated glomerular filtration rate (eGFR; CKD-epi equation), serum cystatin C and phosphate, and measurement in urine of proteinuria (UPC), glycosuria, phosphaturia, tubular reabsorption of phosphate -TRP-, and tubular proteins beta-2-microglobulin -B2M- and cystatin C -CysC-. Tubular dysfunction was defined as ≥ 3 alterations in tubular parameters, and TDF discontinuation was recommended in case of reduced eGFR and significant tubular alterations.
Results: Mean age was 46.1 years (23-74). After 58.8 months on therapy (IQR, 33.4-81.4), 96% had HIV RNA level < 50 copies/ml, and CD4+ count was 586 cells/ml. Mean eGFR was 95.7 ml/min (51.3-151.2), -2.9 ml/min with respect to baseline (-9.9 TDF+IP, +2.23 no TDF; p< 0.01). Also, hypophosphatemia was observed in 15%, cystatin C > 1mg/dl in 28%, UPC >100 mg/dl in 40%, glycosuria in 8%, and 52% of patients had a reduced TRP (< 80%). Urinary CysC and B2M were increased on TDF, especially with PI (p< 0.05), and there was a significant correlation between urinary parameters and time on TDF. Thus, tubular dysfunction was found in 35% of TDF-treated patients. In a second evaluation, after 10.2 m (IQR, 4.4-12.8), patients on same therapy progressed in comparison with TDF-discontinued patients, both in rate of eGFR (-3.45 vs +5.04; p < 0.01), and in tubular damage (TRP, -0.2 vs +4.1%; B2M, -51214 vs +4179 mcg/g; CysC, -6095 vs -74 mcg/g). Notably, eGFR improvement was greater in patients discontinuing TDF before an established diagnosis of tubular disease (+12.8 vs +2.3 ml/min). In a third evaluation after 6.23 months (3.6-8.2) there was additional worsening in patients continuing TDF (eGFR, -2.36 ml vs +1.22 ml/min;
p< 0.01; 84% with TRP < 80). Overall, 33% of patients discontinued TDF.
Conclusions: There is a progressive incidence of tubular damage and decreasing eGFR in patients receiving a TDF-containing regimen. Following strict criteria, one third of patients discontinued therapy, although our data suggest a greater benefit in case of early switching.

Endocrine and metabolic issues (including diabetes, hyperlipidemia)

WEPEB349

Switching lopinavir/ritonavir to atazanavir/ritonavir versus adding atorvastatin in HIV-infected patients who received second-line antiretroviral therapy with hypercholesterolemia: a randomized controlled trial

P. Wangpatharawanit, S. Sungkanuparph
Faculty of Medicine Ramathibodi Hospital, Mahidol University, Department of Medicine, Bangkok, Thailand
Presenting author email: ssungkanuparph@yahoo.com

Background: Lopinavir/ritonavir (LPV/rtv)-based antiretroviral therapy (ART) has been the recommended second-line regimen in resource-limited settings. While lipid-lowering agents are still not available in the National AIDS Program (NAP) of many developing countries, atazanavir (ATV) has been available in the NAP of some countries for substitution of LPV in patients with LPV/rtv-induced hypercholesterolemia. This study aimed to compare lipid profiles between switching LPV/rtv to ATV/rtv versus adding atorvastatin in patients with LPV/r-induced hypercholesterolemia. The better strategy could be applied for the NAP in resource-limited settings.
Methods: A randomized, controlled, clinical trial was conducted in HIV-infected patients who received LPV/rtv-based regimen with hypercholesterolemia and had undetectable HIV RNA. Patients were randomized to switch from LPV/rtv to ATV/rtv (Group A) or to add atorvastatin and continue LPV/rtv-based regimen (Group B), and were followed-up for 24 weeks. Changes in lipid profiles, HIV-RNA, and CD4 were analyzed.
Results: Forty patients were enrolled, 20 in each group. Mean age was 46.8 years and 50% were males. Mean baseline CD4 cell count was 512 cells/μL. Baseline characteristics including age, sex, CD4 cell count, and duration of ART between the two groups were similar (p>0.05). Mean baseline values for total cholesterol (TC), LDL, HDL, and triglycerides (TG) were 257, 141, 48, and 293 mg/dl, respectively. There were no significant differences in lipid values at baseline between the two groups (p>0.05). At 24 weeks, mean TC, LDL, HDL, and TG between the two groups (Group A vs B) were 246 vs 195 (p=0.004), 150 vs 93 (p< 0.001), 53 vs 44 (p=0.150), and 195 vs 238 (p=0.434) mg/dl, respectively. Mean reduction of TC was significantly greater in Group B when compared to Group A (55 vs 19 mg/dl, p=0.004). Similar reduction was also observed for LDL (35 vs -7.2 mg/dl, p< 0.001). No significant changes in HDL, TG, and CD4 cell count in both groups (p>0.05). All patients had sustained virologic suppression (HIV-RNA < 50 copies/ml).
Conclusions: Adding atorvastatin to unchanged LPV/rtv-based regimen results in more significant reduction in TC and LDL than switching LPV/rtv to ATV/rtv, without increased risk of virologic failure. Atorvastatin should be accessible for NAP in resource-limited settings.

WEPEB350

HIV and cardiometabolic disease in rural and urban Malawi: a population-based study

A.C. Crampin[1], A. Amberbir[1], C. Musicha[2], N. Kayuni[2], O. Koole[1], A. Price[1], B. Mwagomba[3], J.R. Glynn[4], T. Tafatatha[5], S. Jaffar[4], M. Nyirenda[1]
[1]London School of Hygiene and Tropical Medicine, Karonga Prevention Study, Chilumba, Malawi, [2]Karonga Prevention Study, Chilumba, Malawi, [3]Malawi Ministry of Health, Non-Communicable Disease, Lilongwe, Malawi, [4]London School of Hygiene and Tropical Medicine, London, United Kingdom, [5]Karonga Prevention Study, Karonga, Malawi
Presenting author email: mia.crampin@lshtm.ac.uk

Background: Sub-Saharan Africa faces a substantial dual burden of HIV and non-communicable diseases. In rural and urban Malawi we are conducting a large population-based study in Africa of hypertension, diabetes, dyslipidaemia and HIV.
Methods: The study is in a well-established demographic surveillance site in rural Malawi (Karonga) and an enumerated high-density area of the capital city (Lilongwe). All adult residents are consented for a lifestyle and medical history interview, examination and body measurements, fasting venepuncture (for glucose and lipids) and HIV testing. Individuals are sought on three occasions (including weekends). Resting blood pressure measurements are repeated three times.
Results: 10,785 urban and 11,322 rural participants are enrolled. Approximately 20% refused HIV testing but reported a prior test result. Crude HIV prevalence was 11.3% urban and 10.0% rural. The urban population was younger. Overall HIV positive people were more likely than HIV negative people to have hypertension, diabetes and dyslipidaemia (Table).

	HIV negative N=15,200	HIV positive and not known to be on ART N=600	HIV positive on ART N=1,209	HIV status unknown N=5,098
Hypertension (diastolic >=90 mmHg and/or systolic>=140mmHg and/or on treatment for hypertension)				
Prevalence	11.5%	11.4%	14.7%	18.3%
Odds ratio	ref	0.99 (0.77-1.27)	1.16 (0.98-1.39	1.72 (1.58-1.88)
Adjusted odds ratio*	ref	0.84 (0.65-1.10)	0.76 (0.63-0.92)	1.23 (1.12-1.36)
Diabetes (previous diagnosis or fasting blood glucose >7mmol/l)				
Prevalence	2.2%	2.5%	2.9%	2.6%
Odds ratio	ref	1.11 (0.64-1.92)	1.34 (0.92-1.95)	1.18 (0.93-1.48)
Adjusted odds ratio*	ref	0.84 (0.48-1.46)	0.83 (0.57-1.22)	0.79 (0.62-1.01)
Dyslipidaemia (triglygerides >=1.7 mmol/l or HDL-C <0.9mmol/l (male) and <1.0 (female))				
Prevalence	32.0%	55.5%	40.0%	32.1%
Odds ratio	ref	2.66 (2.24-3.15	1.41 (1.24-1.61)	1.00 (0.93-1.09)
Adjusted odds ratio*	ref	2.64 (2.22-3.13)	1.37 (1.20 -1.56)	1.00 (0.92-1.08)
***adjusted for age, sex, urban/rural residence**				

[Association : HIV and cardiometabolic disorders]

The association with hypertension and diabetes disappeared on adjustment. Similar results were seen in the rural and urban areas, with more stringent outcome definitions, after excluding those who only had reported HIV status and after adjusting for body mass index (BMI). Those with unknown HIV status (mainly young and elderly men) had significantly higher adjusted odds of hypertension. When adjusted for age, sex and residence, HIV positive individuals not on ART were significantly more likely to be current smokers and alcohol consumers, but no difference was observed between those on ART and HIV negative people. HIV positive people (particularly those on ART) had significantly lower BMI. BMI, age and urban residence were the major risk factors for hypertension and diabetes.
Conclusions: Dyslipidemia levels were very high, and higher in HIV positive individuals, especially prior to ART. This group also has the highest prevalence of smoking and alcohol consumption. Crude prevalence of diabetes and hypertension were also higher in HIV positive people. This has implications for both the diagnosis and management of those with multiple chronic conditions in overburdened health services, particularly as they may have worse outcomes. Higher levels of hypertension in HIV test refusers may reflect general attitudes towards healthy lifestyles.

WEPEB351

Dysfunctional HDL among HIV-infected adults in Nairobi: a pilot study

A. Njoroge[1,2], C.Y. Han[3], A. Chait[3], C. Farquhar[2]
[1]Kenyatta National Hospital, Research & Programs, Nairobi, Kenya, [2]University of Washington, Global Health, Seattle, United States, [3]University of Washington, Division of Metabolism, Endocrinology & Nutrition, Department of Medicine, Seattle, United States

Background: High-density lipoprotein cholesterol (HDL) function may be a more accurate predictor for risk of developing atherosclerosis than absolute levels. This is important among HIV-infected individuals as antiretroviral therapy (ART) is associated with increased HDL levels. This pilot study assessed the anti-inflammatory effect of HDL on palmitate-induced inflammation of adipocytes in HIV-infected individuals with normal levels (> 40mg/dl) of plasma HDL.
Methods: HDL was isolated from plasma samples by ultracentrifugation. 3T3-L1 murine pre-adipocytes were propagated and differentiated according to standard procedures. The adipocytes were pre-exposed to HDL (50μg/ml) from HIV-infected individuals or control HDL from HIV-uninfected for 6h then incubated with 250 μmol/L palmitate for 24h. The HDL isolated from each sample was tested for its ability to inhibit palmitate-induced serum amyloid A3 (SAA3) gene expression in the adipocyte cultures. Total mRNAs were isolated and analyzed by reverse transcription PCR. Each sample was analyzed in triplicate and normalized using glyceraldehyde 3-phosphate dehydrogenase (GAPDH)as control. The higher the level of SAA3 expression in the adipocytes, the less the anti-inflammatory effect of the HDL.
Results: Of the 11 ART-naive subjects, 7 were female. Median age was 30 years [Interquartile range (IQR): 27-33 years] and median CD4 count was 516.5cell/ml (IQR: 422-794. Nine subjects had viral loads >1000 copies/ml. Median BMI was 26.9 (IQR: 23.8-31.6). The mean SAA3/GAPDH ratio was higher in the HIV-infected compared to the control (p=0.001). High viral load was significantly associated with increased SAA3 mRNA (Spearman Correlation r=0.72 p=0.01). hs-CRP was inversely associated with the SAA3/GAPDH ratio (r= -0.88,p=0.001). Age, gender, CD4 count and BMI were not associated with HDL anti-inflammatory activity.
Conclusions: These preliminary findings suggest that the anti-inflammatory properties of HDL are impaired in HIV-infected persons despite normal HDL levels. Reasons why viral load significantly correlated with the adipocyte inflammation independent of hs-CRP require further investigation. Other lipoprotein levels may be important to consider when screening for atherosclerosis risk factors among HIV-infected individuals.

Ageing in persons with HIV (including frailty)

WEPEB352

Analysis of risk factors of telomere length shortening and its association with leukoaraiosis

R. Minami, S. Takahama, Y. Kaku, M. Komatsu, M. Yamamoto
National Hospital Organization,Kyushu Medical Cent, Clinical Research Institute, Fukuoka, Japan
Presenting author email: rrhh@qmed.hosp.go.jp

Background: HIV infection is associated with short telomere length (TL), which is linked to old age and cardiovascular disease risk in the general population. In this study, we measured TL in HIV-infected and uninfected individuals, and examined which biological and environmental variables determined TL. We also investigated the influence of TL on leukoaraiosis, which is an indicator of cerebral small vessel disease, in HIV-infected individuals.
Methods: Three hundred and twenty-four HIV-infected individuals on stable combination antiretroviral therapy (cART) for >1 year who achieved a viral load < 40 copies/ml, and 112 HIV-uninfected individuals were enrolled. Relative TL in leukocytes was estimated by quantitative real-time polymerase chain reaction. Leukoaraiosis was assessed in 184 HIV-infected individuals by fluid-attenuated inversion recovery magnetic resonance imaging. We analyzed several variables such as some markers related to HIV infection, antiretroviral therapy, and social/environmental factors. Variables found to be important in univariate analysis were multivariate model candidates.
Results: In HIV-infected individuals, TL was significantly shorter, and the rate of decline by age was greater than in uninfected individuals. Simple linear regression analysis in HIV-infected individuals showed that old age, cART without integrase-stand transfer inhibitors (INSTI), non-achievement of HIV RNA < 40 copies/ml within 1 year of initiating cART, and present and/or previous substance use were significantly correlated with shorter TL, even after adjustment for age. Other HIV disease or environmental parameters such as smoking were unrelated. Single logistic regression analysis indicated a risk of leukoaraiosis with old age, shorter TL, hypertension, and carotid artery plaque. Multivariate regression analysis indicated that old age and shorter TL were significant risk factors for leukoaraiosis, with an odds ratio of 1.167 and 1.23 (95% confidence interval, 1.04-1.31 and 1.03-1.45).
Conclusions: TL shortening is independently associated with leukoaraiosis, and is associated with age, virological response to cART, use of INSTI, and substance use, which masks the influence of other HIV disease or environmental parameters. Good virological control with cART can help improve outcomes among HIV-infected individuals.

WEPEB353

Aging & HIV in the ANRS CO3 Aquitaine Cohort. Cross-sectional results of the Skin, Muscle & Bone Aging Determinants (SIMBAD) study

P. Mercié[1], L. Richert[2], F. Le Marec[3], P. Duffau[4], S. Lawson-Ayayi[5], B. Milpied[6], N. Barthe[7], E. Lazaro[8], F. Bonnet[9], I. Pellegrin[10], H. Amiéva[3], P. Dehail[11], S. Reigadas[12], C. Cazanave[13], M. Dupon[13], D. Neau[13], F. Dabis[5], SIMBAD Study Group (Supported by ANRS, Paris, France)
[1]CHU de Bordeaux, Service de Médecine Interne et Immunologie Clinique and INSERM U 897, Bordeaux, France, [2]Université de Bordeaux, Pôle de Santé Publique and INSERM U 897, Bordeaux, France, [3]Université de Bordeaux, INSERM U 897, Bordeaux, France, [4]CHU de Bordeaux, Service de Médecine Interne et Immunologie Clinique, Bordeaux, France, [5]Université de Bordeaux, INSERM U 897, COREVIH and GECSA, Bordeaux, France, [6]CHU de Bordeaux, Service de Dermatologie, Bordeaux, France, [7]CHU de Bordeaux, Service de Médecine Nucléaire, Bordeaux, France, [8]CHU de Bordeaux, Service de Médecine Interne et Maladies Infectieuses, Bordeaux, France, [9]CHU de Bordeaux, Service de Médecine Interne et Maladies Infectieuses and INSERM U 897, Bordeaux, France, [10]CHU de Bordeaux, Laboratoire d'Immunologie, Bordeaux, France, [11]CHU de Bordeaux, Service de Médecine Physique et Réadaptation, Bordeaux, France, [12]CHU de Bordeaux, Laboratoire de Virologie, Bordeaux, France, [13]CHU de Bordeaux, Service des Maladies Infectieuses et Tropicales, Bordeaux, France
Presenting author email: patrickmercie33@gmail.com

Background: With increasing life expectancy comorbidities have become a concern for ART-treated people living with HIV (PLHIV). These comorbidities are more frequent at a given age than in the general population without clear explanations, except for ART- or hepatitis co-infection related complications.
We prospectively investigated age-related comorbidities and functional limitations and their clinical and biological determinants in PLHIV in care.
Methods: The SIMBAD study enrolled consenting adult PLHIV from the ANRS CO3 Aquitaine Cohort with a previous bone DXA measurement. Participants underwent standardized neurocognitive and locomotor functional tests, a repeat DXA, measurement of plasma 25-OH vitamin D, T-cell immune activation (CD4+/CD8+DR+) and immunosenescence (CD4+/CD8+CD57+CD28-) markers. Functional test results were compared to age-specific norms of the general population when available. Correlations between different tests were described in a principal component analysis (PCA), and determinants per test assessed by multivariable linear regression.
Results: 109 patients were assessed: mean age 54 years (SD: 9), 80% male, 64% homobisexuals, 61% CDC stage A, and 93% with undetectable plasma HIV-1 RNA. Mean CD4+ level was 588/mm^3 (SD: 217) and nadir 279/mm^3 (SD: 163).
Test results differed significantly from population norms for spine and femoral neck bone mineral density (BMD), the timed-up-and-go and neurocognitive tests (p< 0.05); mean differences were modest and seemed to attenuate with increasing age. Marked alterations (locomotor Z-score > | 2 | , 2 neurocognitive Z-scores > | 1 | , osteoporosis) were found in < 25% per domain. Tests of different domains correlated weakly (r< | 0.4 |).
Multivariable linear regression models of femoral neck BMD, lower limb muscle performance, verbal fluency and psychomotor speed showed that increasing age was the only consistently significant determinant of poorer test results (Table). Other determinants (lean mass index, lipoatrophy, CD4 nadir, type of ART) varied between tests. No associations were found with vitamin D levels or T-cell immune activation/senescence markers in any of the regression models.

	Femoral neck BMD		Five times sit-to-stand test		Psycho-motor speed (Wechsler codes)		Verbal fluency test	
Explanatory variables	Beta	p-value	Beta	p-value	Beta	p-value	Beta	p-value
Age (years)	-0.012	0.2570	-0.037	0.0010	-0.038	0.0003	-0.024	0.0284
Lean mass index (kg/m2)	0.345	0.0254	0.354	0.0281	.	.	.	.
Lipoatrophy (yes vs. no)	-0.546	0.0089	.	.	.	.	0.443	0.0409
Type of ART		0.0249						
ARV no-cART vs. cART	-0.473		.	.	.	.	.	.
naive vs. cART	0.971		.	.	.	.	.	.
Nadir (/mm3)	.	.	.	.	0.002	0.0267	.	.
Viral load indectectability (yes vs; no)	.	.	.	.	.		0.766	0.0444

[Table]

Conclusions: In this cross-sectional analysis of the SIMBAD study, bone, muscular and neurocognitive alterations appear to be of low severity and not related to biologic markers in PLHIV care. Longitudinal analyses will allow for further assessment of the relationships with aging.

Strategies promoting long term health: screening for non-communicable comorbidity

WEPEB354

High levels of pain and undertreated pain among HIV-positive people who use illicit drugs in Vancouver, Canada

P. Voon[1], T. Kerr[1,2], H. Dong[1], J. Montaner[1,2], E. Wood[1,2], M.-J. Milloy[1,2]
[1]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada, [2]University of British Columbia, Department of Medicine, Vancouver, Canada
Presenting author email: pvoon@cfenet.ubc.ca

Background: Although the advent of highly-active antiretroviral therapy has contributed to dramatic prognostic improvements for people living with HIV/AIDS (PLWHA), there remain several barriers to achieving optimal treatment outcomes among PLWHA. Given that chronic pain is a common comorbidity among illicit drug users and PLWHA, this study investigated perceived undertreated pain, pain intensity and functional interference among a cohort of HIV-positive people who use illicit drugs in Vancouver, Canada.
Methods: Bivariable and multivariable logistic regression was used to evaluate factors associated with perceived undertreated pain among participants reporting major persistent pain in the ACCESS study, an ongoing longitudinal cohort of HIV-positive illicit drug users. Perceived undertreated pain was defined as participants believing that they required a stronger dose or type of medication for the purpose of analgesia than what they were currently prescribed. Pain intensity and functional interference were examined using the Brief Pain Inventory.
Results: Between June 1, 2014 to November 30, 2014, 215 participants were eligible for this analysis, of which 75 (34.0%) were female, and 183 (85.1%) had major pain that had persisted longer than six months. In total, 91 (42.3%) participants reported undertreated pain, which was positively and independently associated with self-managing pain (Adjusted Odds Ratio [AOR]: 2.11, 95% Confidence Interval [CI]: 1.11-4.00) and having a physical disability (AOR: 2.10, 95%CI: 1.12-3.93). Participants reporting undertreated pain had significantly higher average pain intensity (OR: 1.89, 95%CI: 1.09-3.33) and functional interference (OR: 1.92, 95%CI: 1.11-3.33) than those who did not report undertreated pain.

Characteristic	Unadjusted		Adjusted	
	Odds Ratio (95% CI)	*p* - value	Odds Ratio (95% CI)	*p* - value
Age (per year older)	1.04 (1.00, 1.08)	0.047	1.04 (1.00, 1.08)	0.077
Gender (male vs. female)	1.08 (0.61, 1.91)	0.805		
Ethnicity (Caucasian vs. other)	0.81 (0.47, 1.39)	0.438		
Highest level of education completed (≥ high school diploma vs. < high school diploma)	1.34 (0.77, 2.33)	0.303		
Hepatitis C status (Positive vs. Negative)	0.94 (0.41, 2.19)	0.890		
Homelessness* (yes vs. no)	0.90 (0.35, 2.30)	0.825		
Sex work* (yes vs. no)	0.66 (0.24, 1.83)	0.423		
Enrolled in methadone maintenance treatment*	0.82 (0.47, 1.41)	0.467		
Physical disability* (yes vs. no)	2.40 (1.30, 4.43)	0.005	2.10 (1.12, 3.93)	0.021
Mental illness diagnosis* (male vs. female)	0.67 (0.12, 3.76)	0.653		
CD4 cell count△ (per 100 cells/mL)	1.06 (0.93, 1.21)	0.391		
Plasma viral load△ (per log10 increase)	0.90 (0.74, 1.09)	0.274		
Illicit drug use*				
(any illicit drug use vs. none)	1.11 (0.52, 2.34)	0.793		
(any injection drug use vs. none)	1.50 (0.60, 3.71)	0.384		
Incarceration* (yes vs. no)	0.38 (0.08, 1.87)	0.234		
Overdose* (yes vs. no)	2.19 (0.75, 6.38)	0.153		
Denied pain medication* (yes vs. no)	0.86 (0.38, 1.93)	0.710		
Self-managed pain* (yes vs. no)	2.31 (1.24, 4.31)	0.008	2.11 (1.11, 4.00)	0.022

* Denotes activities/events within in the six months prior to participant's interview
△ Denotes activities/events at baseline

[Table 1. Bivariable and multivariable logistic regression analysis of factors associated with perceived undertreated pain among HIV-positive people who use illicit drugs reporting major persistent pain in Vancouver, Canada (n=215)]

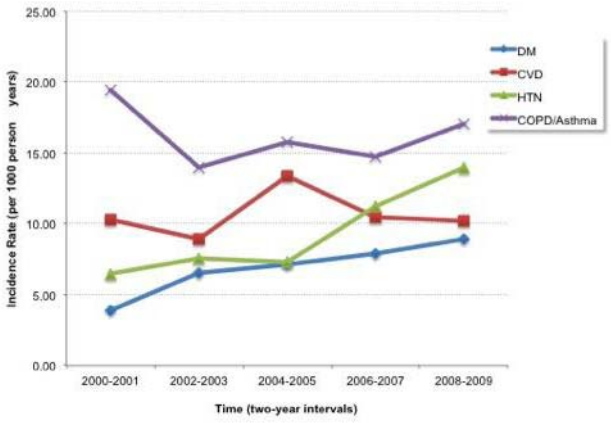
Conclusions: The high prevalence of perceived undertreated pain highlights the need for increased attention to pain management among PLWHA who use illicit drugs, given its major potential role in engaging and retaining this population in clinical care. It is troubling that individuals reporting undertreated pain were more likely to report self-managing their pain, as this may be contributing to highly elevated risk of overdose, morbidity, mortality, and HIV transmission if self-management activities involve ongoing illicit drug use.
These findings indicate areas for clinical intervention and patient education in order to minimize risk behaviors associated with undertreated pain, and to improve quality of life among PLWHA who use illicit drugs.

WEPEB355

Trends of non-HIV chronic comorbidities among HIV-positive individuals on highly active antiretroviral therapy in British Columbia from 2000-2009

B. Gali[1,2], W. Chau[1], W. Zhang[1], O. Eyawo[1], H. Samji[1], V. Lima[1], K. McGrail[2], R. Hogg[1], D. Moore[1]
[1]BC - Centre for Excellence in HIV/AIDS, Vancouver, Canada, [2]University of British Columbia - School of Population and Public Health, Vancouver, Canada
Presenting author email: bgali@alumni.ubc.ca

Background: Highly active antiretroviral therapy (HAART) has transformed HIV from a uniformly fatal condition into a largely treatable chronic disease. Reduced HIV-related morbidity and mortality has allowed other chronic diseases to assume greater importance among HIV-positive individuals. We designed a study to characterize how HAART expansion in British Columbia (BC), Canada has affected the incidence of chronic non-HIV related comorbidities.
Methods: Our analysis was performed using an administrative population-based dataset of HIV-positive individuals (≥19 years) in BC. Using ICD-9/ICD-10 codes for case identification, we assessed the following chronic diseases among HIV-positive individuals who had accessed HAART during the study period from 2000 to 2009: cardiovascular disease (CVD), diabetes mellitus (DM), hypertension (HTN) and asthma/chronic obstructive pulmonary disease (COPD). Prevalent cases of these diseases were identified pre-baseline (4-year washout period) and excluded from the analyses. Disease incidence was determined by the number of new cases per two-year intervals over a ten-year period. We used Poisson's log-linear regression analysis to measure trends in incidence rates.
Results: The study sample (n=8620) was predominantly white (70%, based on known ethnicity) male (83%) with a median CD4 count of 240 cells/μL and viral load of 80,000 copies/ml at HAART initiation. Between 2000-2009, incidence rates per 1000 person-years (95% confidence interval) of DM and HTN significantly increased each year after adjusting for age, sex, baseline CD4 and viral load (p =0.004 and p< 0.001 respectively). Incidence rates were more than doubled from 2000-2001 compared to 2008-2009 for DM (3.89 (95% CI: 2.37, 6.40) to 8.90 (95% CI: 6.95, 11.40)) and HTN (6.48 (95% CI: 4.42, 9.49) to 13.95 (95% CI: 11.32, 17.19)) respectively. Incidence rate patterns for CVD and COPD/asthma did not change over the study period (Figure 1).



[Figure 1. Two-year interval incidence rates of four chronic diseases among HIV-positive individuals on HAART over a ten year period (DM = Diabetes Mellitus; COPD = Chronic Obstructive Pulmonary Disease; HTN = Hypertension; CVD = Cardiovascular Disease)]

Conclusions: We observed marked population-level increases in incidence rates for both DM and HTN, but not for CVD and COPD/asthma among HIV-positive individuals on HAART over a ten-year period. Understanding how these chronic conditions affects future disability and death among the aging HIV-positive population is an important area of further research.

WEPEB356

Rates and predictors of injury among HIV-positive individuals in British Columbia, Canada

H. Samji, D. Shopin, W. Zhang, O. Eyawo, G. Colley, M. Hull, J. Montaner, R. Hogg
BC Centre for Excellence in HIV/AIDS, Epidemiology and Population Health, Vancouver, Canada
Presenting author email: hasinasamji@gmail.com

Background: Injuries are responsible for significant morbidity and mortality, constituting the third leading cause of death globally and the leading cause of death for those between the ages of 1 and 44 years. The epidemiology of injury among HIV+ individuals has not been well-elucidated. This study seeks to characterize rates and predictors of injury among HIV+ individuals compared to the general population in British Columbia (BC), Canada, from 1996 to 2010.
Methods: An administrative dataset of HIV+ individuals and a comparison group consisting of a 1% sample of the general BC population was created to assess the health service use and outcomes among HIV+ individuals compared to the general population. In this analysis, rates of intentional (self-harm and assault), unintentional (falls, motor vehicle collisions, poisoning, suffocation, fire/burns, natural/environmental, other land transportation and cut/pierce injuries) and all-cause injury, classified using International Classification of Diseases 9 and 10 codes and based on the external cause of the injury, were assessed. Generalized estimating equation (GEE) Poisson regression models were fit to estimate the effect of HIV status on rates of injury after adjusting for age, sex and region. A second model examined factors associated with all-cause injury among HIV+ individuals, adjusting additionally for a history of injecting drug use, Aboriginal ethnicity, CD4 count and viral load at initiation, and adherence < 95% during the first year of treatment.
Results: 106,493 individuals contributed a total of 1,058,129 person-years. HIV+ individuals were more likely to report unintentional injury (incidence rate ratio (IRR): 2.73, 95% confidence interval: 2.55-2.93) and intentional injury (IRR: 5.98 (5.36-6.68)). Predictors of all-cause injury among HIV+ individuals were younger age (IRR: 1.10 (1.02-1.19), per decade); Aboriginal descent (IRR: 1.39 (1.16-1.67)); living on Vancouver Island (IRR: 1.46 (1.20-1.77)) and in the North (IRR: 1.89 (1.46-2.44)) versus in the Coastal region; injecting drug use (IDU) (IRR: 3.65 (3.03-4.41)); and poor adherence (IRR: 1.39 (1.20-1.61)).
Conclusions: HIV+ individuals were more likely to report both intentional and unintentional injuries compared to the general population. Targeted efforts are needed to decrease rates of injury among this population, particularly among IDU and those of Aboriginal descent.

WEPEB357

Prevalence of risk factors for non-communicable diseases (NCDs) and co-morbid conditions among adult persons living with HIV (PLWH) initiating antiretroviral therapy (ART) in Kenya

M. Hawken[1], D. Chege[1], A. Zerbe[2], R. Juma[3], W. El-Sadr[2]
[1]ICAP at Columbia University, Nairobi, Kenya, [2]ICAP at Columbia University, New York, United States, [3]Kenya Medical Research Institute, Nairobi, Kenya
Presenting author email: wme1@cumc.columbia.edu

Background: With the decrease in AIDS-related morbidity and increased longevity with ART use, non-AIDS events have become more prevalent including NCDs such as cardiovascular disease (CVD), liver disease, renal disease, and non-AIDS cancers. We report on the prevalence of risk factors for NCDs and co-morbid conditions among a cohort of PLWH initiating ART.
Methods: Between March 2014 and October 2014, PLWH initiating ART were recruited from 7 clinics in western Kenya as part of a cohort study to examine inflammatory and coagulation biomarkers. Baseline assessments included demographic characteristics, medical and family history and focused clinical assessment including blood pressure and BMI.
Results: Of 685 participants, 64% were female, median age was 34 years [29-42 years] and median CD4+ count was 316 cells/μL [175-430 cells/μL]. Of all, 7.9% reported a history of tuberculosis (TB) and 5.5% current TB (of latter 92% pulmonary and 8% extrapulmonary). In addition, 3% of participants reported history of high blood pressure (HBP) and none reported history of diabetes. A family history of HBP and diabetes was reported by 9% and 8% of participants, respectively. Ten percent reported smoking history of median duration of 9 years [5-16 year] with 3.1% reporting current smoking and 10% current excessive alcohol use. Median BMI was 20.1 [18.7-22.9], with 72% normal BMI (BMI18-25), 17% underweight (BMI<18), 9% overweight (BMI>25-30) and 2% obese (BMI>30). The mean of two measured blood pressure readings after resting indicated that 59% of the cohort had a blood pressure within normal range, 34.2% with pre-hypertensive (blood pressure between 120/80 mmHg and 139/89 mmHg) and 2% with hypertensive readings (>140/90 mmHg).
Conclusions: In this cohort of PLWH initiating ART, a substantial proportion had modifiable risk factors for CVD which were easily detected by simple screening methods. High blood pressure was common and should be prioritized for appropriate management. Simple screening for risk factors for NCDs and at minimum for HBP should be included in HIV primary care in resource-limited settings.

WEPEB358

Impact of binge alcohol on mortality among people who inject drugs

C. Johnson[1], H. Dong[2], K. Ahamad[3], K. Hayashi[4], M. Milloy[4], T. Kerr[4], E. Wood[5]
[1]British Columbia Centre for Excellence in HIV/AIDS, University of British Columbia, Vancouver, Canada, [2]British Columbia Centre for Excellence in HIV/AIDS, Vancouver, Canada, [3]British Columbia Centre for Excellence in HIV/AIDS, University of British Columbia, Family Practice, Vancouver, Canada, [4]BC Centre for Excellence HIV/AIDS-Urban Health Research Initiative, Department of Medicine, University of British Columbia, Vancouver, Canada, [5]British Columbia Centre for Excellence, University of British Columbia, Medicine, Vancouver, Canada
Presenting author email: hdong@cfenet.ubc.ca

Background: While the impacts of illicit drug use on mortality have been well described, the impact of poly-substance use with alcohol has received less attention. We examined the impact of binge alcohol use on mortality among a cohort of people who inject drugs (PWID) in a Canadian setting.
Methods: Prospective cohort study of PWID in Vancouver, Canada recruited between May 1996 and November 2013. We ascertained mortality rates and causes of death through a confidential linkage with the provincial vital statistics registry and examined the impact of various patterns of alcohol use. The primary outcome of interest was all-cause mortality and we used Cox proportional hazard regression to determine factors associated with mortality, including socio-demographics, drug use behaviours and other risk behaviours.
Results: During the study period, 2550 individuals were followed (844 of which were HIV positive) for a median of 75.4 months (interquartile range 37.9 - 113.2) among whom 795 (31%) participants reported binge alcohol use at any time during the study period. In multivariate analyses, binge alcohol use remained independently associated with all cause-mortality (adjusted hazard ratio=1.41; 95% confidence interval: 1.06-1.88) whereas other patterns of alcohol use were not associated with mortality
Conclusions: Binge alcohol use was associated with all cause mortality among PWID in this setting. Since alcohol use is often overlooked as a risk factor for mortality among this population, these findings highlight the continued need to incorporate addiction treatment and public health interventions that address binge alcohol use to reduce alcohol related harms.

Linkage to care

WEPEB359

Prevalence of HIV infection, access to HIV care, and response to antiretroviral therapy among partners of HIV-infected individuals in Thailand

S. Kiertiburanakul[1], P. Wongprasit[2], A. Phuphuakrat[1], D. Chotiprasitsakul[1], S. Sungkanuparph[1]
[1]Faculty of Medicine Ramathibodi Hospital, Department of Medicine, Bangkok, Thailand, [2]Buriram Hospital, Department of Medicine, Buriram, Thailand
Presenting author email: sasisopin.kie@mahidol.ac.th

Background: Healthcare providers usually focus on HIV-infected index patients and they seldom retrieve information of patients' partners. Clinical studies regarding characteristics of HIV-infected patients' partners are limited.
Methods: During January 2011-December 2013, a cross-sectional study was conducted in 2 hospital settings: a university hospital in Bangkok and a provincial hospital in northeastern part of Thailand. Factors associated with anti-HIV positive results in partners were determined by multiple logistic regression.
Results: Of 294 partners, median [interquartile range (IQR)] duration of living with HIV-infected index patients was 9.0 (4.3-15.3) years. Median (IQR) age was 39.8 (33.8-45.7) years and 56.5% were males. Of these, 78.9% had health insurance, 96.9% had heterosexual practice, 22.8% had other underlying diseases, 5.8% had positive HBsAg, 1.4% had positive anti-HCV, and 62.2% used condom. A total of 176 (59.9%) partners had anti-HIV positive results, 77.3% had been receiving antiretroviral therapy, 87.3% had undetectable HIV RNA, and median current CD4 count was 232 (96-428) cells/mm^3. Partners with anti-HIV positive results were older (age 40.8 years vs. 36.8 years, p=0.010), had longer duration of living with HIV-infected index patients (10.4 years vs. 6.3 years, p < 0.001), more likely to be followed at the university hospital in Bangkok (72.1% vs. 53.2%, p=0.002), have health insurance (88.1% vs. 65.2%, p < 0.001), have HBsAg positive (8.0% vs. 2.5%, p < 0.001), and have anti-HCV positive (1.7% vs. 0.8%, p < 0.001). Partners with anti-HIV positive results had a higher proportion of having HIV-infected index patients with detectable HIV RNA (7.6% vs. 2.3%, p=0.082). The proportion of condom usage were comparable (60.8% vs. 64.4%, p=0.636). By multivariate logistic regression, duration of living with HIV-infected index patients [odds ratio (OR) 1.05 per year; 95% confidence interval (CI) 1.01-1.08, p=0.014), had health insurance (OR 3.40; 95% CI 1.72-6.70, p < 0.001), and followed at the university hospital in Bangkok (OR 2.37; 95% CI 1.20-4.69, p=0.014) were associated with anti-HIV positive results in partners.
Conclusions: Prevalence of HIV infection among partners of HIV-infected Thai individuals is not low. Interventions for decreasing HIV transmission from HIV-infected patients to their partners should be promoted, e.g. early antiretroviral therapy and condom usage.

WEPEB360

Linkage from HIV testing to care: predictors of enrollment failure and associated factors among VCT clients newly diagnosed with HIV infection, Ho Chi Minh City, Vietnam

M.H. Vo Thi[1], L.V. Le[2], T.P. Le[1], T.N. Nguyen Thi[1], D. Baughman[3], M. Ackers[2], M. Mc Connell[4], T.V. Tieu Thi[1]
[1]Ho Chi Minh City AIDS Committee, Ho Chi Minh, Vietnam, [2]U.S. Centers for Disease Control and Prevention, Vietnam, Ho Chi Minh, Vietnam, [3]U.S. Centers for Disease Control and Prevention, USA, Atlanta, United States, [4]U.S. Centers for Disease Control and Prevention, Vietnam, Ha noi, Vietnam
Presenting author email: monghien_pac@yahoo.com

Background: Ensuring that HIV-positive individuals successfully enroll for HIV care and treatment is critical to reduce morbidity and mortality and prevent further HIV transmission. To improve linkage to care, we investigated the characteristics of individuals who tested HIV-positive at voluntary counseling and testing (VCT) sites, but who did not register for care services.
Methods: Program data from VCT clients newly diagnosed with HIV infection between 7/1/2011-6/30/2012 at 20 sites in Ho Chi Minh City were examined to determine predictors of enrollment at any of the 21 public outpatient clinics (OPC) in HCMC. We abstracted VCT testing dates and OPC registration dates from logbooks and matched records using a citywide database containing both VCT and OPC identification numbers. We calculated the duration of time between HIV diagnosis and OPC registration during the study, and defined failure to enroll as not having enrolled in an OPC within 17 months after testing. We used a log-binomial model to estimate adjusted prevalence ratios (APR) and 95% confidence intervals (CI) for failure to enroll.
Results: Among 3271 HIV-positive clients, 72% registered at one of 21 OPCs. Mean and median duration from HIV diagnosis to OPC registration were 35 and 19 days, respectively. In multiple regression analysis (see table), clients were less likely to enroll in care if they were aged < 25 years, were from provinces other than HCMC, had no formal education, and had recently or ever injected drugs. Clients referred for testing by healthcare providers were more likely to enroll in care.

Conclusions: Over one quarter of VCT clients newly identified with HIV infection failed to enroll in HIV care and treatment services within 17 months after testing. Intensive counseling should be provided for clients with high risks for failure to enroll. Integrating VCT and care services may also reduce the time between diagnosis and care enrollment and increase the proportion of patients linked to care.

Characteristic	Total N=1996	failed to register at OPC n (%)	Adjusted PR* (95% CI)	Characteristic	Total N=1996	failed to register at OPC n (%)	Adjusted PR* (95% CI)
Age group, years 15 - 19	28	14 (50.0)	2.35 (1.56-3.54)	Residence Urban HCMC district	1632	396 (24.3)	1.00 (Ref)
Age group, years 20-24	189	62 (32.8)	1.48 (1.12-1.96)	Residence Rural HCMC district	121	17 (14.0)	0.57 (0.35-0.93)
Age group, years 25-29	577	130 (22.5)	0.97 (0.8-1.18)	Residence Other province	243	69 (28.4)	1.20 (0.93-1.56)
Age group, years ≥ 30	1202	276 (23.0)	1.00 (Ref)				
Education -None	80	28 (35.0)	1.55 (1.07-2.25)	Injection drug use-in past 7 days	140	47 (33.6)	1.48 (1.14-1.93)
Education -1-5	437	126 (28.8)	1.24 (0.91-1.70)	Injection drug use-ever	656	172 (26.2)	1.22 (1.03-1.44)
Education -6-9	804	186 (23.1)	1.01 (0.77-1.32)	Injection drug use-never	1200	263 (21.9)	1.00 (Ref)
Education -10-12	511	105 (20.5)	0.89 (0.68-1.18)	Referred for testing by healthcare provider	843	159 (18.9)	0.71 (0.53-0.97)
Education -≥13	161	36 (22.4)	1.00 (Ref)	Not referred for testing by healthcare provider	1153	323 (28.0)	1.00 (Ref)

[Table: Association between selected characteristics and failure to register at an outpatient clinic]*

*Adjusted for HIV testing site and all variables in the table.

WEPEB361

Facilitators and barriers to linkage to HIV care among female sex workers receiving HIV testing services at a community-based organization in Peri-urban Uganda

S. Nakanwagi[1,2], B. Nsangi[3], F. Kaharuza[4], J. Matovu[5], D. Nabukalu[6], R. Wanyenze[5]
[1]Makerere University School of Public Health, College of Health Sciences, Kampala, Uganda, [2]Reach Out Mbuya Parish HIV/AIDS Initiative, Kampala, Uganda, [3]Reach Out Mbuya HIV/AIDS Initiative, Kampala, Uganda, [4]Makerere University School of Public Health, Kampala, Uganda, [5]Makerere University, College of Health Sciences, Kampala, Uganda, [6]Rakai Health Sciences Research Project, Data Management, Kampala, Uganda
Presenting author email: sharonshaloam@gmail.com

Background: Although nearly 40% of female sex workers (FSWs) in sub Saharan Africa are HIV positive, less than half are enrolled in HIV care. We explored the facilitators, barriers and time to linkage to HIV care among FSWs receiving HIV testing services at a community-based organization in peri-urban Uganda.
Methods: We conducted a mixed-method cross-sectional study among 301 FSWs who tested HIV positive at Reach Out Mbuya HIV/AIDS Initiative in Uganda from May 2012 to December 2013 according to the HCT registers. Structured interviews were conducted with 144 HIV-positive FSWs. In-depth interviews were conducted with 29 positive FSW (15 in care and 14 not in care) and five staff and eleven peer educators as key informants. Data were collected on time taken to register in care, age, marital status, distance to facility and facilitators and barriers to linkage to HIV care. Univariate and multivariable logistic regression analysis was conducted to identify socio-demographic and behavioral factors associated with linkage to care using STATA v.13 while qualitative data were manually analyzed following a thematic framework approach.
Results: Out of the 301 positives, 144 (48%) were reached and of these 125 (86.8%) had registered into HIV care with 112 (78%) registering within one month of diagnosis. Participants mean age was 31 years and 14% were married. Older FSWs (>31 years) were 2.6 times more likely to register early compared to the younger FSW (95% CI: 1.01-7.04). Unmarried FSW were less likely than married FSW to be registered within one month (Adj. OR =0.11, 95% CI: 0.01-0.96). Linkage facilitators included caring health workers, follow up by peer educators, membership to a saving group and a perceived need to be healthy. Barriers included perceived stigma, fear to be seen at the HIV clinics, fear and myths related to ART, lack of time to attend clinic, unaware of treatment center location, and financial constraints.
Conclusions: Providing friendly health care services and strengthening peer support mechanisms may enhance timely linkage into care for FSWs.

Retention in care

WEPEB362

Retention of patients on antiretroviral therapy in The AIDS Support Organization among patients initiating treatment from 2004-2009

L. Ssali[1], A. Eggessa[1], S. Okoboi[2], J. Wangisi[2], C. Bakanda[1], D. Moore[3,4]
[1]The AIDS Support Organisation (TASO), Programme Management, Kampala, Uganda, [2]The AIDS Support Organisation (TASO), Advocacy and Research, Kampala, Uganda, [3]BC Centre for Excellence in HIV/AIDS, Research Department, Vancouver, Canada, [4]University of British Columbia, Faculty of Medicine, Vancouver, Canada
Presenting author email: stonessali@yahoo.com

Background: We conducted a retrospective cohort analysis of clients who initiated ART in the first five years of a large ART treatment program encompassing 11 clinical care centres across Uganda to determine the proportion of those retained in care in 2013.
Methods: We used data from TASO Health Information System to identify and characterize patients who initiated ART between Jan2004 and July 2009. We then examined which of these patients had at least one visit record in the database January to June 2013. For all patients we established their current status as being a known death, transferred out, lost to follow up (LTFU) or retained in care. We conducted bivariate analyses to compare baseline characteristics associated with each clinical state. We used Cox regression analysis to determine factors associated with the combined outcome of time to death or LTFU
Results: A total number of 17,827 participants initiated ART during the study period, of whom 12,803 (72%) were, female- and 5024 (28 %.) were male. In 2013, after a median of 6 years on ART (IQR 5 - 7 years), 15,469(87%) were retained in care 121(1%) had transferred out, 1390 (8%) were known to have died and 847(5%) were LTFU. The proportion retained in care varied across the TASO centres with a range of 66% to 87%. (p< 0.001). Of those initiating ART in 2004-05, 82% were retained compared with 79% in 2006-2007 and 77% in 2008-09 (p< 0.001). Mortality/LTFU was associated with male, WHO stage 4 illnesses, CD4 cell counts ≤200 cells/ µL at ART initiation TASO center, lower education levels and having no occupation.

Data Elements	Central Uganda	Northern Uganda	Western Uganda	Eastern Uganda	Overall
No. of Clients initiated on ART	4452	1777	5450	6148	17827
Active on ART	3901	1479	4780	5309	15469
Dead	264	115	447	564	1390
Lost to followup	265	167	163	252	847
Transfered	26	16	60	23	127
Percent Retained on ART	87.6	83.2	87.7	86.4	87.0

[Retention of clients in Care in Regions]

Conclusions: After a median of over 6 years on ART, patient retention was close to 86% in TASO programs. However, retention was lower among individuals initiating treatment in more recent years and there were large variations across the TASO sites. These suggest that additional measures could be implemented to better retain clients within TASO.

WEPEB363

Temporal improvements in clinical outcomes among HIV-positive individuals initiating combination antiretroviral therapy in Canada

M. Irick[1], A. Cescon[1,2], S. Patterson[1,3], H. Samji[1], E. Ding[1], J. Raboud[4,5], H. Wong[1], G. Colley[1], T. Antoniou[6], A. Bayoumi[5,6], A.N. Burchell[5,7], C. Cooper[8], M.B. Klein[9], M. Loutfy[5,10], N. Machouf[11], J.S.G. Montaner[1,12], A. Rachlis[13], S.B. Rourke[7], C. Tsoukas[9], R.S. Hogg[1,3], CANOC Collaboration
[1]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada, [2]Northern Ontario School of Medicine, Sudbury, Canada, [3]Simon Fraser University, Burnaby, Canada, [4]University Health Network, Toronto, Canada, [5]University of Toronto, Toronto, Canada, [6]St. Michael's Hospital, Toronto, Canada, [7]Ontario HIV Treatment Network, Toronto, Canada, [8]University of Ottawa, Ottawa, Canada, [9]McGill University, Montreal, Canada, [10]Women's College Hospital, Toronto, Canada, [11]Clinique Médicale l'Actuel, Montreal, Canada, [12]University of British Columbia, Vancouver, Canada, [13]Sunnybrook Health Sciences Centre, Toronto, Canada
Presenting author email: acescon@nosm.ca

Background: We aim to describe temporal changes in the demographic and clinical profile of HIV-positive individuals initiating combination antiretroviral therapy (ART) in Canada from 2000-2011.
Methods: Participants of the Canadian Observational Cohort (CANOC) collaboration, a multisite cohort of HIV-positive individuals aged ≥ 18 years and initiating ART naively after 2000 in British Columbia (BC), Ontario, and Quebec, were included. Participants with < 12 months of follow-up were excluded. Participants were grouped by era of ART initiation (2000-2002, 2003-2005, 2006-2008, 2009-2011). Demographic and clinical characteristics were compared

by era using Pearson's χ^2 and Wilcoxon rank-sum tests. Cox proportional hazards models were used to estimate the effect of calendar period of ART initiation on virologic responses to ART, including time to viral load suppression (2 measures <50 copies/mL at least 30 days apart) and rebound (2 measures >200 copies/mL at least 30 days apart, after suppression).

Results: Of 8006 participants, 1453 (18%) were female, 46% lived in BC, 33% in Ontario, and 19% in Quebec. The median baseline age at treatment initiation was 38 (IQR=33-45) in 2000-2002, compared to 40 (IQR=32-47) in 2009-2011 (p<0.001). The proportion of participants with IDU history decreased from 26% in 2000-2002 to 19% in 2009-2011 (p<0.001). After adjustments for age, sex, province, transmission risk category, Aboriginal ancestry, baseline CD4 count, baseline viral load, baseline third ARV class, and viral load testing rate, participants initiating ART in 2003-2005, 2006-2008, and 2009-2011 were more likely to achieve viral suppression than those in 2000-2002 (aHR=1.16 [95% CI=1.07-1.25], aHR=1.22 [95% CI=1.10-1.34], aHR=1.14 [95% CI=1.01-1.26], respectively). After adjusting for the same confounders, participants initiating ART in the later eras were significantly less likely to experience viral rebound than in 2000-2002 (aHR=0.68 [95% CI=0.59-0.79], aHR= 0.54 [95% CI=0.43-0.67], aHR=0.31 [95% CI=0.23-0.42], respectively).

Conclusions: Notable temporal changes in the demographic profile and improvements in virologic response to ART are evident among CANOC participants. Characterizing the demographic and clinical profile of affected populations supports the optimal delivery of clinical care for the evolving Canadian HIV epidemic.

WEPEB364

Optimizing retention of PLHIVs in rural HIV clinics in North Central Nigeria: experience and challenges

E. Nwabueze[1,2], N. Ndulue[1], M. Makumbi[1], G. Egesimba[1], A. Etsetowaghan[1], N. Onuaguluchi[1]
[1]MSH, ProACT, Abuja, Nigeria, [2]UOA, CLSM, Aberdeen, United Kingdom
Presenting author email: enwabueze@msh.org

Background: Poor retention in care is a major driver of poor program performance, poor adherence and increases resistance to ARVs and transmission of resistant HIV virus causing morbidity and mortality. Long waiting times, non-decentralized HIV clinic days and poor client tracking and counselling services contribute significantly to poor outcomes and quality of services provision. HIV care and services are managed vertically/standalone in most hospital settings in Nigeria (separate laboratory, pharmacy and clinic days). These provide avenue for patient's stigmatization and attrition. Very few hospitals have currently fully integrated all their HIV care and services.

Methods: We evaluated retention rates in care for clients on ARV per state among 5 of integrated health facilities versus 5 of non-integrated ones, to determine the current status and major causes of poor retention. We designed and deployed an innovative retention calendar across them. This tool tracks individual patient receiving services rather than existing aggregated tracking and provides real time flagging of clients who miss appointments for immediate tracking. We also analyzed the Management Science for Health MSH's FY14 and FY15 first quarter cohort retention data using the retention calendar.

Results: The analysis showed highest retention across facilities with fully integrated HIV services. 90% of these integrated facilities had client retention above 75%. Facilities with the least integration had as low as 45% retention rates. 76% out of the 90% of tracked clients using the deployed retention calendar across these 10 facilities continued with their care. The newly introduced M&E tool showcased early ART defaulters and enabled easier/better services. Complaints from Health Care Workers HCWs include too many M&E tools handled manually, poor training, short staffing, and consistent staff rotation from the health ministry. Clients' complaints were poor health care services and strict appointment.

Conclusions: Integration of ART services and the innovative retention calendar are true positives to retention in care. They provide freer access to health care for PLHIV and reduction of work for HCWs. If ART services are fully integrated across all facilities, surely there will be an increase ART retention.

WEPEB365

Impacts of the spatial 'risk environment' on ART interruptions among sex workers living with HIV/AIDS: implications for ART programmes and policy reforms

S. Goldenberg[1,2], K. Deering[1,2], O. Amram[1,3], P. Nguyen[1], J. Chettiar[1], S. Guillemi[2,4], J. Montaner[2,5], K. Shannon[1,2]
[1]Gender and Sexual Health Initiative, BC Centre for Excellence in HIV/AIDS, Vancouver, Canada, [2]University of British Columbia, Department of Medicine, Vancouver, Canada, [3]Simon Fraser University, Department of Geography, Vancouver, Canada, [4]Clinical Education and Training Program, BC Centre for Excellence in HIV/AIDS, Vancouver, Canada, [5]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada
Presenting author email: sgoldenberg@cfenet.ubc.ca

Background: Despite the high HIV burden faced by women in sex work (SWs), data on SWs' access and retention in antiretroviral therapy (ART) are limited, with most studies focused on clinical/behavioural determinants. Using an innovative spatial approach, we aimed to explore the independent effect of spatial 'threats' (e.g., client violence, policing, legal restrictions) on ≥2 day ART interruptions among female SWs living with HIV in Metropolitan Vancouver, BC, over a 3.5 year period.

Methods: Baseline and semi-annual questionnaire data were drawn from a prospective cohort (AESHA, 2010-2013), and linked administrative data on ART dispensation. Using geographic information systems mapping and logistic regression with generalized estimating equations (GEE), we examined the effects of density of spatial 'threats' within a buffer of SWs' place of residence on ART interruption (no ART dispensed for ≥2 consecutive days in a 6-month period) among women living with HIV who had previously used ART.

Spatial 'threats' included client-perpetrated violence, police harassment, community harassment/threats, physical dislocation due to policing, and "red zone"/legal restrictions on working locations, and were measured as the density of reported events within a 250-meter buffer of a participants' residential location.

Results: Among 66 SWs included in the analysis, there were 83 ART interruption events over a 3.5-year period. In a series of multivariate GEE models adjusted for key confounders (age, homelessness, injection drug use, duration of known HIV positivity), increased density of displacement due to policing within a 250-meter buffer of one's residential location independently correlated with ART interruptions (AOR: 1.02, 95%CI: 1.00-1.04); "red zone" restrictions (AOR: 1.03, p=0.08) and combined spatial 'threats' (AOR: 1.00, p=0.07) were also marginally correlated.

Conclusions: Spatial 'threats' related to policing, legal restrictions, and other structural risks within SWs' neighborhood environments may undermine sustained use and retention in ART. These findings contribute to a body of global evidence highlighting the ways in which laws and policies that criminalize aspects of sex work and their enforcement undermine SWs' access to health and human rights, including retention in ART. Programmes facilitating access to safer living and working spaces for women living with HIV/AIDS should be explored as potential intervention strategies, alongside critically-needed policy reforms.

WEPEB366

Retention in care of HIV-infected pregnant and lactating women starting Option B+ ART in rural Mozambique

J. Llenas-García[1], P. Wikman-Jorgensen[1], M. Hobbins[2], J. Ehmer[2], F. Mbofana[3], M.A. Mussa[4], G. Wandeler[5,6]
[1]SolidarMed, Ancuabe, Mozambique, [2]SolidarMed, Luzern, Switzerland, [3]National Health Institute, Maputo, Mozambique, [4]Health Provincial Directorate. Operational Research Nucleus of Pemba, Pemba, Mozambique, [5]Institute of Social and Preventive Medicine, University of Bern, Bern, Switzerland, [6]University Hospital Bern, Department of Infectious Diseases, Bern, Switzerland
Presenting author email: gilles.wandeler@ispm.unibe.ch

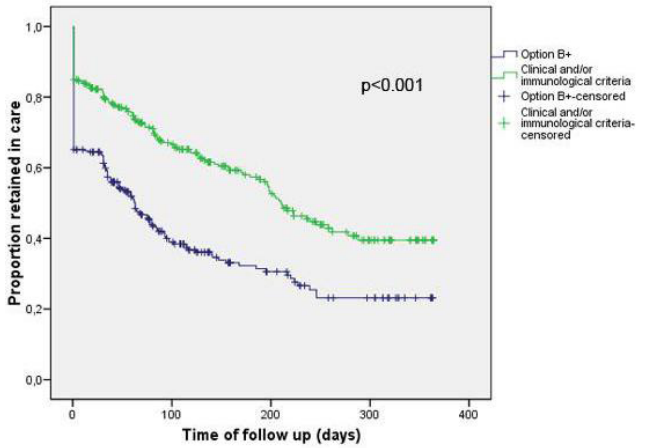
Background: In 2013, Mozambique adopted WHO-option B+ as the national strategy for PMTCT of HIV. We aimed to analyze retention in care of pregnant and lactating women (PLW) starting antiretroviral treatment (ART) under option B+ in Ancuabe, a rural district in Northern Mozambique with a decentralized ART provision system.

Methods: We compared outcomes of PLW starting ART under option B+ with those of childbearing age women starting ART following clinical and/or immunological criteria between July 2013 and June 2014. We also compared outcomes of B+ PLW with those of pregnant women on ART for their own health under option A between January 2011 and June 2013. LTFU was defined as not coming back to the clinic for >60 days after last visit. Categorical variables were compared using the Chi-squared test. Kaplan-Meier analyses were used to assess retention in care and multivariable Cox regression to analyze attrition.

Models were adjusted for type of facility, age, baseline CD4, WHO stage and time from HIV diagnosis to ART.

Results: 606 women started ART between July 2013 and June 2014; 301 under option B+ (236 pregnant, 65 breastfeeding) and 305 following clinical and/or immunological criteria. They were followed up for 160.6 person-years. Option B+ women were more likely to be

LTFU(61.8%vs. 39.3%; p<0.001) and to not return after the first visit (34.9%vs. 15.1%; p<0.001) but were less likely to die (0.7%vs. 5.2%; p=0.001). Retention in care was poorer in option B+ women (figure 1).



[Figure 1]

In adjusted analysis, option B+ (HR:2.24; $CI_{95\%}$.1.60-3.15; p< 0.001) and baseline CD4< 350 (HR:1.66; CI95%:1.18-2.33; p=0.003) were associated with attrition.
When comparing pregnant women starting ART under option B+(n=236) and under option A (n=72), LTFU (65.3%vs. 61.4%) and death (1.4%vs. 0.4%) rates were similar but option B+ women were more likely not to return after their first visit (36.4%vs. 13.9%; p< 0.001). In adjusted analyses, factors associated with higher attrition were option B+ (HR:3.32; $CI_{95\%}$.1.84-5.99; p<0.001) and WHO-stage I/II (HR:2.05; $CI_{95\%}$.1.08-3.86; p=0.03).
Conclusions: Retention among PLW starting ART under option B+ in rural Mozambique was poor, and seemed to be mainly driven by early losses to follow-up.

WEPEB367

Effect of gender and age on mortality and retention among HIV-2-infected individuals starting antiretroviral therapy in West Africa: a multicentre cohort study

B.K. Tchounga[1,2], P.J. Coffie Ahuatchi[1,3], E. Balestre[2], E. Messou[3,4], A. Sawadogo[5], M. Seydi[6], A. Minga[7], D. Hawerlander[8], S.P. Eholie[1,3], F. Dabis[2], D.K. Ekouevi[1,2,9]
[1]Programme PACCI, Site de Recherche ANRS, Abidjan, Cote D'Ivoire, [2]Université de Bordeaux, ISPED, Centre INSERM U 897- Epidémiologie-Biostatistique, Bordeaux, France, [3]Service des Maladies Infectieuses et Tropicales, CHU de Treichville, Abidjan, Cote D'Ivoire, [4]Centre de Prise en Charge de Recherche et de Formation. CePReF-Aconda, Abidjan, Cote D'Ivoire, [5]Service des Maladies Infectieuses et Tropicales, CHU Souro Sanou, Hôpital de Jour, Bobo Dioulasso, Burkina Faso, [6]Service des Maladies Infectieuses et Tropicale CHU FANN, Dakar, Senegal, [7]Centre Médical de Suivi de Donneurs de Sang/CNTS, Abidjan, Cote D'Ivoire, [8]Centre Intégré de Recherches Biocliniques d'Abidjan CIRBA, Abidjan, Cote D'Ivoire, [9]Université de Lomé, Département des Sciences Fondamentales et Santé Publique, Lome, Togo
Presenting author email: boris.tchounga@yahoo.fr

Background: HIV-2 infected individuals usually initiate ART at an advanced age compared to HIV-1 patients and this could impact retention in care and treatment outcomes. This study aimed at investigating the effect of gender and age on mortality and lost-to-follow-up (LTFU) among HIV-2 patients in care in Africa.
Methods: AnaAnalyses were conducted using the database of the IeDEA-HIV-2 West Africa collaboration including 15 West African clinics. All patients who initiated ART were eligible and LTFU was considered if >180 days since last visit. Probability of death and LTFU were estimated with Kaplan-Meier method according to gender and age (16-39; 40-49; ≥50 years). A Cox regression model was used to identify factors associated with death and/or LTFU.
Results: A total of 1,392 HIV-2 patients were included with a median age of 45 years (interquartile range [37-51]) and median CD4 count at ART initiation of 175/µL [78-248]; 832 (60%) were women, 482 (35%) were aged 16-39, 522 (38%) aged 40-49 and 388 (28%) ≥50 years.
At baseline, 176 (13%) patients were at WHO clinical stage III/IV, 290 (20%) had a BMI <18, 251 (18%) had haemoglobin >10 g/dL and 312 (22%) had CD4 <100 cell/µL.
The median follow up was 22.5 months [7.1 - 48.2] during which 150 patients died (10.8%) and 821 (59%) were LTFU.
Males were more likely to die than females (14% vs 9%; p=0.003). LTFU was more frequent in patients aged ≥50 (39%) than in those aged 16-39 (31%) and 40-49 years (31%) (p=0.001).
In multivariate analysis, male gender (hazard ratio HR=2.2; 95%CI [1.5; 3.2]; p<0.01), CD4 count <100 cell/µL (HR=7.3 [1.7; 32.3]; p<0.01), severe anaemia <7g/dL (HR=7.0 [2.6; 19.1]; p<0.01) and BMI <18 Kg/m² (HR=2.7 [1.4; 5.6]; p=0.03) were associated with higher mortality. Adjusted on other factors, age was no longer associated with LTFU.
Conclusions: The risks of death and LTFU among HIV-2 patients on ART seem comparable to those in HIV-1 patients in West Africa, despite ART initiation at an advanced age. However, the mortality and LTFU rates remain elevated in this population where preventive and corrective interventions should be explored.

WEPEB368

Risk factors for mortality and lost to follow-up before antiretroviral therapy: a multicentric retrospective cohort study of 41 Médecins Sans Frontières HIV programmes

M. Bastard[1], D. O'Brien[2], E. Casas[3], J. Greig[2], A. Telnov[4], C. Ferreyra[5], H. Bygrave[6], E. Szumilin[7], S. Balkan[7], J.-F. Etard[1,8]
[1]Epicentre, Paris, France, [2]Manson Unit, Médecins Sans Frontières, London, United Kingdom, [3]Médecins Sans Frontières, Amsterdam, Netherlands, [4]Médecins Sans Frontières, Geneva, Switzerland, [5]Médecins Sans Frontières, Barcelona, Spain, [6]Médecins Sans Frontières, Brussels, Belgium, [7]Médecins Sans Frontières, Paris, France, [8]UMI 233 TransVIHMI, Institut de Recherche pour le Développement, Université Montpellier 1, Montpellier, France
Presenting author email: mathieu.bastard@geneva.msf.org

Background: In the past decade, access to antiretroviral treatment (ART) has greatly increased in resource-limited settings. Few studies explore the period before the start of ART (pre-ART), and gaining understanding of pre-ART is needed to improve strategies of care and maximize long-term patient outcomes. This study describes rates of mortality and lost to follow-up (LTFU) and associated risk factors during the pre-ART period.
Methods: We conducted a multicentric retrospective cohort study among HIV-infected adult patients followed but not yet started on ART in 41 Médecins Sans Frontières HIV programmes. Patient follow-up started at programme enrollment and ended at the earliest of: death, transfer-out, ART initiation or last pre-ART clinic visit. Risk factors for mortality and LTFU were investigated using Cox and competing-risks regression models.
Results: A total of 137,545 patients (61.2% women) were included in the study with a median [IQR] age of 33 [27-40], median CD4 count of 221 cells/µL [94-404] and 50.2% of them were in WHO clinical stage 3/4. Overall mortality reached 3.9% (95%CI 3.8-4.1%), 5.2% (95%CI 5.0-5.3%) and 6.2% (95%CI 6.0-6.4%) at 3, 6 and 12 months, respectively. Patients with low CD4 counts (< 50 vs. ≥500, aHR=6.62, 95%CI 5.74-7.64), aged >30 years (aHR=1.23, 95%CI 1.15-1.31), treated in urban area (aHR=1.18, 95%CI 1.11-1.25) and men (aHR=1.29, 95%CI 1.22-1.37) were at higher risk of pre-ART death. LTFU reached 19.3% (95%CI 19.1-19.6%), 24.4% (95%CI 24.1-24.7%) and 31.5% (95%CI 31.2-31.8%) at 3, 6 and 12 months, respectively. A higher CD4 count at enrollment (≥500 vs. < 50, aSHR=1.62, 95%CI 1.54-1.71), younger patients (< 30 vs. >50 years, aSHR=1.32, 95%CI 1.26-1.38) and men (aSHR=1.23, 95%CI 1.20-1.25) were associated with pre-ART LTFU.
Conclusions: Our study, conducted among one of the largest pre-ART cohorts, shows higher pre-ART deaths among patients with advanced stage of HIV disease, and those who are younger, male and treated in urban areas. LTFU rate is high and appears increased among patients with high CD4 counts at enrolment, male gender and younger age. There is an urgent need for programmes to develop targeted strategies to address associated factors to reduce rates of death and LTFU prior to ART.

Indicators of quality of care

WEPEB369

Findings from a cross-sectional study of health care provider attitudes toward PLHIV at Nelson Mandela Academic Hospital in Mthatha, South Africa

B. Longo-Mbenza[1], C. Moyana[1], O.V. Adeniyi[2], I. Malema[3], N. Dlatu[2], D.T. Goon[4], A.I. Ajayi[2], C.R. Carty[5,6]
[1]Walter Sisulu University, Health Sciences, Mthatha, South Africa, [2]University of Fort Hare, School of Humanities and Social Science, East London, South Africa, [3]University of Pretoria, Pretoria, South Africa, [4]University of Fort Hare, School of Health Sciences, East London, South Africa, [5]The Relevance Network, Research and Implementation Science, Johannesburg, South Africa, [6]Mater Misericordiae University Hospital, Dublin, Ireland
Presenting author email: ccarty@therelevancenetwork.com

Background: HIV constitutes an occupational risk to healthcare professionals worldwide. This hazard is compounded in settings where supply chain inefficiencies limit compliance to universal precaution guidelines. Healthcare providers' perceived risks of occupational exposure to HIV infection is largely understudied. This investigation measured the association between sociodemographic characteristics and knowledge of modes of HIV transmission through a lens of stigmatising attitudes and practices. Participants comprised healthcare providers at the Nel-

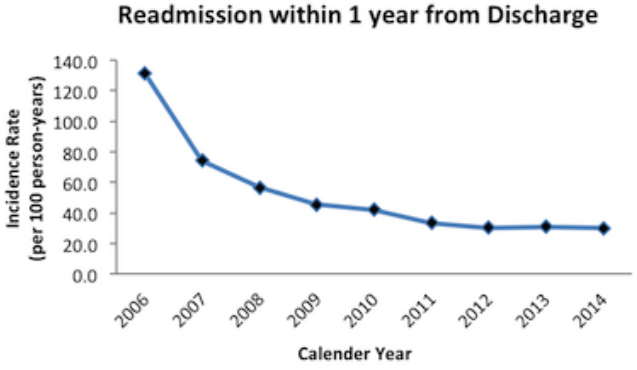
son Mandela Academic Hospital in Mthatha, Eastern Cape Province, South Africa.
Methods: A cross-sectional study was conducted using a structured, piloted and validated questionnaire. A 10% stratified random sample (n = 137/1370) of healthcare staff were engaged. Relevant self-reported data consisted of sociodemographic characteristics, HIV knowledge, perceived risk of HIV exposure, and fear and anxiety associated with caring for PLHIV. Univariate and multivariate (logistic regression models) analyses were conducted to identify predictors for discriminatory clinical practices. A p-value of ≤0.05 was considered statistically significant.
Results: 94.9% of the sample reported that HIV is transmitted by saliva. 69.3% were not comfortable sharing a bathroom with an HIV+ individual. The majority (>92%) expressed fears about performing invasive procedures (inserting IV drips, vaccination, phlebotomy, wound dressing and surgery) on patients known to be seropositive. 18.2% reported generalized fear about caring for patients with HIV. Female providers were more sympathetic than their male counterparts. Lack of latex surgical gloves was the most significant independent determinant (OR = 9.1 95%CI 1.7 - 49.5; p<0.001) related to occupational distress. Beliefs that shame would fall upon a family with an HIV+ member (OR = 4.8 95%CI 1.3 - 18; p = 0.021) and perceived acceptable social and cultural norms among colleagues (OR = 20.4 95% CI 3.6 - 115; p<0.001) were also significant factors.
Conclusions: Evidence from one large health centre situated in a municipality with high HIV prevalence revealed that attitudes and beliefs expressed by health care providers results in significant stigma-perpetuating behaviours and practices. Lack of basic knowledge about HIV coupled with structural barriers to risk-reduction supplies impacts negatively on the clinical care of people living with HIV. This research urges immediate corrective measures through targeted education and capacity building programmes.

WEPEB370

Readmissions to the HIV Ward at St. Paul's Hospital, Vancouver, British Columbia, Canada from 2005-2014

J.H. Kremer[1], M. Hull[1,2], P. Phillips[1,2], D. Jaworsky[2], Z. Cui[1], N. Oliveira[1], R.S. Hogg[1,3], J. Montaner[1,2]
[1]British Columbia Centre for Excellence in HIV/AIDS, Vancouver, Canada, [2]University of British Columbia, Vancouver, Canada, [3]Simon Fraser University, Burnaby, Canada
Presenting author email: hkremer@cfenet.ubc.ca

Background: Although hospital admissions for AIDS-defining illness have declined with the advent of effective antiretroviral therapy (ART), addictions and aging-related comorbidities may now have a greater impact on hospitalizations in HIV-infected individuals. We evaluated hospital readmissions to the HIV ward at St. Paul's Hospital (SPH) in Vancouver, British Columbia, Canada as a potential marker for comorbid health status.
Methods: We conducted a retrospective analysis of data collected for patients discharged from the SPH HIV ward between July 1, 2005 and Dec 31, 2014. Readmission was defined as having more than one admission to the SPH HIV/Addictions ward during pre-defined time-periods (7 days, 30 days, and 1 year). Viral load, ART usage, and CD4 cell counts at the time of admission or readmission were obtained through linkage with the provincial Drug Treatment Program database. Rates of readmissions over time were determined and factors associated with readmission within 1 year were evaluated using multivariate generalized estimating equations.
Results: Of 3915 visits, 343 (8.8%) readmissions occurred within 7 days, 722 (18.4%) within 30 days, and 1740 (44.4%) within 1 year of discharge. The incidence rate of readmissions within 1 year of discharge date declined from 131.1 per 100 person-years in 2006 to 75.4 per 100 person-years in 2014 (Adjusted Relative Risk [ARR] 0.939, 95% Confidence Interval [CI] 0.911 - 0.969) (Figure 1). Factors positively associated with readmission within 1 year included AMA discharge on previous admission (ARR 1.452, 95% CI 1.142 - 1.697), current or past IDU history (ARR 1.699, 95% CI 1.379 - 2.094), and Veterans Aging Cohort Study (VACS) index score (ARR 1.012, 95% CI 1.008 - 1.017). Use of marijuana was negatively associated with readmission within 1 year (ARR 0.841, 95% CI 0.710 - 0.996).



[Figure 1]

Conclusions: Readmission rates to the HIV ward within one year of initial admission have declined over time, but represent a significant proportion of admissions. Previous discharge AMA, underlying IDU, and a higher VACS index score as a surrogate for medical comorbidity were associated with readmission. This highlights the need to enhance community continuity of care, including addictions services, and involve primary care providers in discharge planning.

WEPEB371

What is the cost of antiretroviral drug durability?

J.R. Campbell[1], S. Essajee[2], N. Kumarasamy[3], J. Harwell[4], P. Domanico[5]
[1]Clinton Health Access Initiative, Applied Analytics, Boston, United States, [2]Clinton Health Access Initiative, Clinical Services, New York, United States, [3]Clinton Health Access Initiative, Research and Development, Chennai, India, [4]Clinton Health Access Initiative, Hong Kong, Hong Kong, [5]Clinton Health Access Initiative, Research and Development, New York, United States
Presenting author email: jcampbell@clintonhealthaccess.org

Background: There are an increasing number of antiretroviral drug (ARV) options that may be combined to produce highly active treatment regimens. ARV quality has improved and costs have reduced. However, the need for more expensive second-line treatment is expected to increase with greater access to viral load testing and growing resistance to non-nucleoside reverse transcriptase inhibitors drugs. This reinforces the importance of optimizing the durability of first-line regimens to keep patients on effective first-line treatment as long as possible. As new drugs become available and different drug are being discussed for first-line treatment, it is important to understand the cost implications of more effective but expensive options.
Methods: We looked at durability as the time on first-line treatment, using an Excel closed cohort model to compare costs of current first-line and second-line regimens to hypothetical more expensive and more durable regimens. The costs of ARVs, toxicities and switching were included in the 20 year forecast. We used a cohort of one-million patients and the current Clinton Health Access Initiative costs of the preferred first-line and second-line regimens of TDF/3TC/EFV (TLE) and AZT/3TC/LPV/r and TDF/3TC/LPV/r. We first assumed a conservative 10% migration rate to second-line and 10% toxicity rate.
Results: If the new regimen cost increased to $200 per patient year(ppy) (compared to TLE currently at $130 ppy) and the migration and toxicity rates were halved, this results in a $20 lower cost ppy over 20 years and over $400million savings. The increased durability yields 50% of the forecasted patient years that would be spent on second-line as opposed to 75% using the TLE. If the cost of the new regimen is increased to $250 ppy, and TLE migration reduced to 5%, the new regimen would need to have a migration rate <1% to neutralize costs.
Conclusions: As patients are spending more time on treatment due to earlier initiation and living longer, the longevity of the first-line treatment becomes increasingly important. Greater durability means less time on more expensive second-line treatment and this exercise demonstrates the impact on total costs regardless of higher regimen prices.

Cascade and retention: from HIV testing to care and treatment

WEPEB372

Cascade of care before antiretroviral treatment: a multicentric retrospective cohort study of 41 Médecins Sans Frontières HIV programmes

M. Bastard[1], D. O'Brien[2], E. Casas[3], J. Greig[2], A. Telnov[4], C. Ferreyra[5], H. Bygrave[6], E. Szumilin[7], S. Balkan[7], J.-F. Etard[1,8]
[1]Epicentre, Paris, France, [2]Manson Unit, Médecins Sans Frontières, London, United Kingdom, [3]Médecins Sans Frontières, Amsterdam, Netherlands, [4]Médecins Sans Frontières, Geneva, Switzerland, [5]Médecins Sans Frontières, Barcelona, Spain, [6]Médecins Sans Frontières, Brussels, Belgium, [7]Médecins Sans Frontières, Paris, France, [8]UMI 233 TransVIHMI, Institut de Recherche pour le Développement, Université Montpellier 1, Montpellier, France
Presenting author email: mathieu.bastard@geneva.msf.org

Background: Access to antiretroviral treatment (ART) has considerably increased in resource-limited settings. Understanding of the period before the start of ART (pre-ART) is needed to improve strategies of care and maximize long-term patient retention. However, few studies have focused on this period. This study describes the cascade of pre-ART care in a large cohort of HIV-infected patients.
Methods: We conducted a multicentric retrospective cohort study among HIV-infected adult patients not yet started on ART in 41 Médecins Sans Frontières programmes. Patients with at least one clinic visit and enrolled at least one year before the administrative censoring date were included in the study. Characteristics at enrollment were described and initial and acquired eligibility and delays in ART start were retrospectively assessed using WHO guidelines.

Results: A total of 137,545 patients (61.2% women) were included, median [IQR] age was 33 [27-40], median CD4 count was 221 cells/µL [94-404] and 50.2% were in clinical stage 3/4. At enrollment, 88,306 (64.2%) patients were eligible for ART: 72.0% of them started ART in a median time of 1.15 months [0.7-2.6], 4.9% died and 19.8% were LTFU pre-ART. Among the 22.8% (31,377) not ART eligible patients: 47.9% became eligible in a median time of 5.0 months [IQR 0.2-12.3] and started ART in a median time of 6.9 months [IQR 1.9-15.2], 1.2% died, 30.9% were LTFU pre-ART and 20.0% were still in pre-ART care. Finally, eligibility at enrollment could not be determined for 13.0% (17,862) of patients and among them: 39.3% became eligible in a median time of 6.4 months [IQR 1.8-17.6] and started ART in a median time of 4.1 months [IQR 1.3-14.6], 2.9% died, 46.5% were LTFU pre-ART and 11.3% were still in pre-ART care.

Conclusions: Our study, conducted among one of the largest pre-ART cohorts, shows an important proportion of patients eligible at enrollment who receive ART. However, there are increased rates of LTFU in patients not ART eligible at baseline. Broadening the ART eligibility criteria and reducing delays in determining ART eligibility are important to maximize patient retention in HIV programmes. These results provide a strong support in favor of the Test-and-Treat strategy.

WEPEB373

Advanced HIV disease at first presentation to HIV care: cross-sectional analysis of baseline data from the WelTel Retain study in Nairobi, Kenya

M.L. van der Kop[1,2], R. Gichuki[3], K. Kinagwi[3], S. Muhula[3], B. Abduneh[3,4], J. Kimani[4], R.T. Lester[2], A.M. Ekström[5]
[1]Karolinska Institutet, Public Health Sciences, Stockholm, Sweden, [2]University of British Columbia, Vancouver, Canada, [3]Amref Health Africa, Nairobi, Kenya, [4]Kenya AIDS Control Programme, Nairobi, Kenya, [5]Karolinska Institutet, Stockholm, Sweden
Presenting author email: miavanderkop@gmail.com

Background: Individuals who present to care with advanced HIV disease (CD4< 200 cells/mm^3 or presentation with an AIDS-defining event) have reduced life expectancy and an increased risk of onward transmission. Many HIV-positive persons in sub-Saharan Africa first present to care with advanced disease; however, little is known about whether this is because of late diagnosis or delayed entry to care after diagnosis. We conducted a cross-sectional analysis of baseline study data in Nairobi, Kenya to determine the proportion of patients presenting with advanced HIV disease and whether this was due to delayed diagnosis or a delay in seeking care after diagnosis.

Methods: Between April 2013 and October 2014, participants were recruited into a randomized trial and supplementary cohort study at the Kibera and Babadogo comprehensive care clinics in Nairobi. Patients were eligible to participate if they were over 18 years old, HIV-positive, and had not previously enrolled in HIV care. Pregnant women were excluded. Baseline data were collected by interviewer-administered questionnaires and from clinical records. Descriptive statistics were used to quantify the proportion of individuals who presented to care with advanced HIV disease (CD4< 200 cells/mm^3 or WHO Clinical Stage 4).

Results: Of 667 patients screened for the study, 492 eligible patients consented to participate. CD4 and WHO clinical stage data were available for 98% (482/492) and 85% (416/492) of participants respectively. Of 154 (154/482; 32%) participants who presented to care with advanced HIV disease, 82 (53%) were women and 56 (36%) were diagnosed with HIV for the first time. Among those with advanced HIV disease who had been previously diagnosed (n=98), the median time to presentation to care after initial diagnosis was 18 days (interquartile range: 5.5-72.5); 76 participants presented to care within three months of their first diagnosis.

Conclusions: Almost two-thirds of the individuals presenting to care at two comprehensive care clinics in Nairobi with advanced HIV disease had been previously diagnosed with HIV; however, over three-quarters of these individuals presented to HIV care within three months of their first diagnosis. Our findings suggest that of those who present to care with advanced HIV disease, late diagnosis is a significant factor.

WEPEB374

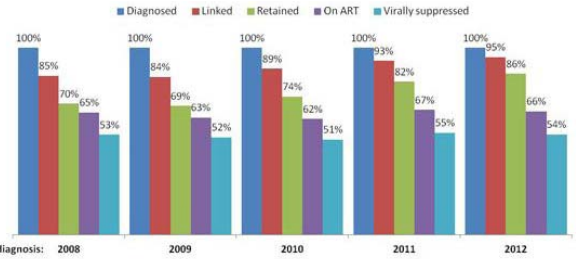
Cascade of care in the country of Georgia: how long it takes to achieve each stage?

N. Chkhartishvili[1], O. Chokoshvili[1], L. Sharvadze[1,2], A. Abutidze[1], J. Dehovitz[3], C. del Rio[4], T. Tsertsvadze[1,2]
[1]Infectious Diseases, AIDS & Clinical Immunology Research Center, Tbilisi, Georgia, [2]Ivane Javakhishvili Tbilisi State University, Faculty of Medicine, Tbilisi, Georgia, [3]SUNY Downstate Medical Center, Brooklyn, United States, [4]Emory University, Atlanta, United States
Presenting author email: nikoloch@yahoo.com

Background: Georgia is an Eastern European country that provides antiretroviral therapy (ART) to all patients in need. Treatment guidelines rapidly evolved over the last 5 years towards earlier ART initiation and the country has implemented a comprehensive package of care services. We evaluated patient engagement in the HIV care continuum and time required to achieve each stage.

Methods: The study included HIV-infected persons diagnosed in Georgia in 2008-2012, who were followed through 2013. Data was extracted from the national HIV/AIDS database. The following stages of HIV care were quantified: HIV diagnosed, linked to care, retained in care, on ART and virally suppressed. Time to achievement of stages of care was estimated from the date of HIV diagnosis.

Results: Among 1,931 patients diagnosed in 2008-2012, the median CD4 count at diagnosis was 221cell/mm^3. The proportion of patients with CD4 cell count <350 increased from 65% in 2008 to 71% in 2012 (p=0.005). 368 patients died over the follow-up: 64 (17%) before linkage to care, 92 (25%) after linkage but before ART initiation and 212 (58%) after ART initiation. Among the remaining 1,563 patients, 1407 (90%) were linked to care, 1,209 (77%) were retained in care, 1,010 (65%) started ART and 828 (53%) achieved viral suppression. The median time to linkage was 1 month with 1,229 (79%) linked within 3 months. The proportion of patients who linked within 3 months after diagnosis increased from 71% in 2008 to 89% in 2012 (p<0.0001). The median time to ART initiation after diagnosis was 3 months. Time to ART initiation decreased from 10 months among those diagnosed in 2008 to 2 months among those diagnosed in 2012 (p< 0.0001). Time to viral suppression after HIV diagnosis also decreased over time from 23 months among those diagnosed in 2008 to 8 months among those diagnosed in 2012 (p< 0.0001).



Year of HIV diagnosis:	2008	2009	2010	2011	2012
Total # of diagnosed:	234	257	328	330	414
Linked within 3 months:	166 (71%)	177 (69%)	243 (74%)	273 (83%)	370 (89%)
Median time to (months):					
- linkage to care	1	0.9	1	0.8	0.8
- ART initiation	9.8	7.6	4.3	2.3	1.8
- viral suppression	22.7	17.6	15.4	11.8	8.2

[Cascade of Care by Year of Diagnosis]

Conclusions: Patient engagement in the HIV care continuum in Georgia has been improving over time. However, only 53% of all diagnosed patients were virally suppressed. More efforts are needed to further increase patient retention in care as well as adherence to ART.

WEPEB375

From home-based HIV testing to initiation of treatment: The AIDS Support Organization (TASO) experience with Home-Based HIV Counselling and Testing (HBHCT) among adolescents in Uganda, 2005-2011

S. Okoboi[1], L. Ssali[2], A. Egessa[1], C. Bakanda[2], J. Lyavala[2], S. Kalibala[3], F. Obare Onyango[4]
[1]The AIDS Support Organization, Research Department, Kampala, Uganda, [2]The AIDS Support Organization, Monitoring and Evalution, Kampala, Uganda, [3]HIVCore/Population Council, Quality Improvement, Washington, United States, [4]Population Council, Quality Improvement, Nairobi, Kenya
Presenting author email: stephenokoboi@yahoo.co.uk

Background: We examined the cascade of HIV testing, support and treatment services in Uganda under the TASO HBHCT program and compares the patterns among adolescents aged 10-19 years with those of adults aged 20 years and above.

Methods: Data included individuals who were counselled and tested for HIV at their homes through the TASO HBHCT program. Analysis entailed simple frequencies to determine the proportions of adolescents and adults that:
(i) tested positive among those who received HBHCT from 2005 to 2011;
(ii) were enrolled in care and support programs at TASO centres among those who tested positive during HBHCT;
(iii) were determined to be eligible for ART among those who were enrolled in care and support programs at TASO centres; and
(iv) were initiated on ART among those who were determined to be eligible.

Results: Between 2005 and 2011, TASO tested a total of 55,228 clients aged 10 years and above through the HBHCT program;40% were adolescents aged 10-19 years. The proportion of adolescents who tested positive under the program was consistently lower than that of adults across the years (between 2% to 5% compared to between 10% and 14% among adults). The proportion of HIV-positive adolescents that were enrolled in TASO centres more than tripled from 9% in 2005 to 32% in 2006 and steadily increased to 41% in 2008. By contrast, the proportion of HIV-positive adults that were enrolled in TASO centres increased from 21% in 2005 to 31% in 2006 before levelling off at 33% in 2007.The proportion of adolescents who were found to be eligible for ART more than doubled from 15% in 2006 to 40% in 2011 while the propor-

tion of eligible adults increased from 16% in 2006 to 36% in 2007 but fluctuated between 30% and 35% thereafter. Among those who were eligible for ART between 2005 and 2011, 89% of adolescents and 93% of adults were initiated on ART at TASO.
Conclusions: The HBHCT program contributed to improved uptake of HIV services among adolescents aged 10-19 years who would otherwise not have accessed the services at all or in time.

WEPEB376

Temporal changes in CD4 counts and clinical stage at HIV diagnosis over 10 years in a large, multicentric patient cohort supported by Médecins Sans Frontières

M. Bastard[1], D. O'Brien[2], E. Casas[3], J. Greig[2], A. Telnov[4], C. Ferreyra[5], H. Bygrave[6], E. Szumilin[7], S. Balkan[7], J.-F. Etard[1,8]
[1]Epicentre, Paris, France, [2]Manson Unit, Médecins Sans Frontières, London, United Kingdom, [3]Médecins Sans Frontières, Amsterdam, Netherlands, [4]Médecins Sans Frontières, Geneva, Switzerland, [5]Médecins Sans Frontières, Barcelona, Spain, [6]Médecins Sans Frontières, Brussels, Belgium, [7]Médecins Sans Frontières, Paris, France, [8]UMI 233 TransVIHMI, Institut de Recherche pour le Développement, Université Montpellier 1, Montpellier, France

Background: Access to antiretroviral treatment (ART) has considerably increased in resource-limited settings. However, the success of the therapy is closely linked with the level of immunosuppression and the stage of the disease at diagnosis. This study evaluates temporal changes in CD4 counts and clinical stage at HIV diagnosis in a large cohort of 41 Médecins Sans Frontières programmes in resource-limited settings over 10 years.
Methods: We conducted a multicentric retrospective cohort study among HIV-infected adult patients. Patients with at least one clinic visit were included in the study. Baseline median (interquartile range, IQR) CD4 counts and proportion of patients in clinical stage 3 or 4 were reported per year of enrollment over the period 2002-2012. Random-intercept linear and logistic mixed models were fitted to assess temporal changes in CD4 counts and clinical stage at enrollment.
Results: From 2002 to 2012, 192,117 HIV-positive patients (61% females) were included in our programmes. Baseline median CD4 count at HIV diagnosis increased from 136 cells/µL [IQR 53-272] in 2002 to 203 cells/µL [IQR 75-382] in 2011 despite a slight decrease in 2012. The proportion of patients in clinical stage 3 or 4 at enrollment was stable at approximately 60% between 2002 and 2006, and then decreased to 47.8% in 2011, despite a slight increase in 2012. Results of the mixed model showed a significant increase of +7.4 cells/µL (95%CI 6.7-8.1) in baseline CD4 counts each year. In addition, females were enrolled at significantly higher CD4 counts than men (difference in 2008: +66.5 cells/µL (95%CI 63.8-69.2) in favour of females) and this difference increased by +6.8 cells/µL (95%CI 5.7-7.8) each year. A significant decreasing trend over years was observed in the proportion of patients enrolled in stage 3 or 4 and this decrease tended to be more pronounced among females.
Conclusions: This study, conducted among one of the largest HIV cohorts, shows that HIV-infected patients are diagnosed and enrolled at an earlier stage of disease each year. However, there is still an important proportion of patients diagnosed at advanced stage of HIV disease and more efforts are needed to diagnose patients earlier, especially targeted at males.

WEPEB377

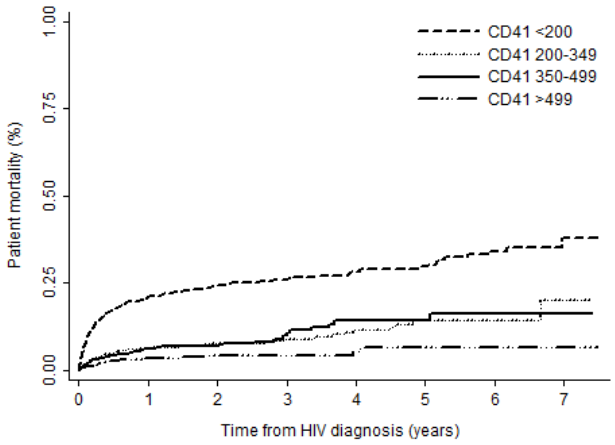
High prevalence of late presentation among HIV-infected patients in Guinea-Bissau: a cohort study from West Africa

B. Langhoff Hønge[1,2,3], S. Jespersen[1,3], J. Aunsborg[1,3], C. Medina[4], D. da Silva Té[4], Z. José da Silva[1,5], A. Lund Laursen[3], C. Erikstrup[2], C. Wejse[1,3,6], The Bissau HIV Cohort Study Group
[1]Bandim Health Project, Indept Network, Bissau, Guinea-Bissau, [2]Aarhus University Hospital, Department of Clinical Immunology, Aarhus, Denmark, [3]Aarhus University Hospital, Department of Infectious Diseases, Aarhus, Denmark, [4]Ministry of Health, National HIV programme, Bissau, Guinea-Bissau, [5]Ministry of Health, National Public Health Laboratory, Bissau, Guinea-Bissau, [6]Aarhus University, GloHAU, Center for Global Health, School of Public Heath, Aarhus, Denmark
Presenting author email: bohonge@gmail.com

Background: In sub-Saharan Africa a large proportion of HIV infected persons are late presenters (LPs) and late presenters with advanced disease (AD). Late presentation has been associated with higher mortality, higher cost of medical management, impaired CD4 cell count increment and potentially ongoing risk of HIV transmission. We describe the proportion of LP and AD at an HIV clinic in Guinea-Bissau, West Africa, to identify risk factors and to evaluate the outcome.
Methods: During June 2005 - December 2013 we included all patients >15 years diagnosed with HIV. Patients were followed until December 2014. AD, LP and non-LP was defined as patients with CD4 cell count at HIV diagnosis of < 200 cells/µL, 200-349 cells/µL and >349 cells/µl, respectively.
Results: During the study period 5,566 patients were diagnosed with HIV (68.3% HIV-1, 17.3% HIV-2, 10.3% HIV-1/2 and 4.1% HIV type unknown) and 3,704 (67%) had a CD4 cell count measured within the first 90 days of HIV diagnosis. The median time between HIV diagnosis and CD4 cell count among these patients was 1 day (interquartile range 1-5 days). Forty-nine percent of the patients were AD and additionally 23% were LP. CD4 cell count varied in the study period, with the lowest values measured in 2007 (median 144 cells/µl) and the highest values in 2011 (median 229 cells/µl, p< 0.01). In a multivariable analysis risk factors significantly associated with AD were HIV diagnosis in 2007 versus 2013 (adjusted odds ratio (aOR) 1.9), male gender aOR 1.5, age >30 years (aOR 1.6), HIV-1 infection (aOR 2.2), HIV-1/2 dual infection (aOR 1.7), civil status (single versus married) (aOR 1.4), Fula (aOR 1.5) and Mandinga (aOR 2.3) ethnicity,
A total of 528 (14.3%) patients were registered as dead and the AD/non-LP mortality rate ratio (MRR) was 3.79 (p< 0.01). The mortality rate was not significantly higher among LP than non-LP (MRR 1.31, p=0.13).

	Late presenters with advanced disease (AD), n(%)	Late presenters (LP), n(%)	Non-late presenters (non-LP), n(%)	Total
Female	1134 (46.0)	571 (23.2)	760 (30.8)	2465
Age ≤ 30 years	466 (44.6)	246 (23.6)	332 (31.8)	1044
2007	126 (59.4)	42 (19.8)	44 (20.8)	212
2008	272 (52.3)	120 (23.1)	128 (24.6)	520
2009	348 (50.8)	151 (22.0)	186 (27.2)	685
2010	366 (45.5)	201 (25.0)	238 (29.6)	805
2011	283 (43.5)	162 (24.9)	206 (31.6)	651
2012	224 (49.2)	102 (22.3)	131 (28.7)	457
2013	191 (51.1)	80 (21.4)	103 (27.5)	374

[Characteristics of late presenters]



[Figure 1]

Conclusions: A high proportion of HIV infected patients were AD and these patients exhibited a much higher mortality. Initiatives to enroll patients in care at an earlier point are needed and should focus on males, unmarried and other risk groups.

WEPEB378

Gaps in care among HIV-infected adults receiving care in western Kenya

B. Rachlis[1,2,3], H. Lee[4], B. Genberg[4], B. Musick[5], D. Ochieng[1], F.F. Some[1,6], M. Nyambura[1], E. Sang[1], J. Hogan[1,4], P. Braitstein[1,2,6]
[1]Academic Model Providing Access to Healthcare (AMPATH), Eldoret, Kenya, [2]University of Toronto, Dalla Lana School of Public Health, Toronto, Canada, [3]Ontario HIV Treatment Network, Toronto, Canada, [4]Brown University, School of Public Health, Providence, United States, [5]Indiana University, School of Medicine, Indianapolis, United States, [6]Moi University, College of Health Sciences, School of Medicine, Eldoret, Kenya
Presenting author email: brachlis@ohtn.on.ca

Background: While some individuals may permanently disengage from care, others may experience transient interruptions. We sought to characterize gaps in care among HIV-infected adults enrolled in the Academic Model Providing Access to Healthcare (AMPATH) program in western Kenya.
Methods: HIV-infected adults (≥18 years) enrolled in an AMPATH supported site between 01/2008 and 09/2012 with ≥1 follow-up visit were eligible for inclusion. This analysis was limited to visits scheduled ≥12 months prior to the database closure (09/2013). Based on the next expected visit date, five possible outcomes were determined: the patient was on time (returned ± 6 days from an expected visit date), had a short (7-89 days late), medium (90-364 days late), or long gap (≥365 days late), or died. Covariates included gender, age at enrolment, WHO stage

at enrolment, and ART status as a time-varying predictor. Multinomial regression was used to assess the effect of these covariates on the relative probability of each outcome as compared to being on time, accounting for the frequency of visits and underlying temporal variations in estimating covariates effects. Robust standard errors accounted for multiple visits per patient.

Results: In total, 57,508 patients (67% female; median age at enrolment: 35 years (Interquartile Range (IQR): 28.4-43.0)) with 793,723 follow-up visits were included. The median number of patient visits was 15 (IQR: 6-26). The distribution of visits across outcomes was 80% on time, 15% with a short gap, 2% with a medium gap and 3% with a long gap. Ninety-four percent of patients had ≥1 gap; 70% had ≥1 short gap, 22% had ≥1 medium gap and 40% had ≥1 long gap. Fourteen percent of patients with a long gap subsequently returned to care. By database closure, 86% of patients who were ≥1 year late had not returned. WHO stage III/IV was associated with an increased risk of all gaps whereas male gender was associated with an increased risk of medium and long gaps only. Older age and being on ART were negatively associated.

	Adjusted Relative Risk Ratio (95% Confidence Intervals)±			
	Short Gap vs. On Time	Medium Gap vs. On Time	Long Gap vs. On Time	Died vs. On Time
Male- yes vs. no	0.96 (0.94-0.98)*	1.09 (1.04-1.14)**	1.24 (1.20-1.27)**	1.79 (1.65-1.95)**
Age-25-44 vs. 18-24	0.86 (0.83-0.88)**	0.62 (0.59-0.66)**	0.57 (0.55-0.60)**	1.02 (0.87-1.18)
Age-45+ vs. 18-24	0.79 (0.77-0.82)**	0.48 (0.44-0.51)**	0.43 (0.41-0.45)**	1.16 (0.98-1.37)
On ART-yes vs. no	0.72 (0.71-0.73)**	0.34 (0.33-0.36)**	0.34 (0.33-0.35)**	0.98 (0.90-1.08)
WHO Stage III/IV vs. I/II	1.32 (1.29-1.34)**	2.17 (2.07-2.26)**	1.67 (1.62-1.72)**	4.27 (3.83-4.75)**

*p<0.05, ** p<0.001, ± Adjusted for calendar year at enrolment, expected frequency of visits

[Factors associated with gaps in care]

Conclusions: While most visits occurred on time, gaps were common with patients experiencing multiple gaps suggesting current definitions of losses to follow-up may need further consideration.

WEPEB379

Monitoring achievement of the latest UNAIDS HIV 90-90-90 Target: a need for harmonization of the HIV cascade of care

L. Lourenco[1], M. Hull[1], B. Nosyk[1,2], J. Montaner[1,3], V. Lima[1,3]
[1]British Columbia Centre for Excellence in HIV/AIDS, Vancouver, Canada, [2]Simon Fraser University, Burnaby, Canada, [3]University of British Columbia, Faculty of Medicine, Vancouver, Canada
Presenting author email: llourenco@cfenet.ubc.ca

Background: UNAIDS recently released the "90-90-90 Target" calling for 90% of HIV-infected individuals to be diagnosed by 2020, 90% of them to be started on ART, and 90% of them to achieve sustained virologic suppression. Achieving these goals will require uniform monitoring of HIV care outputs. The HIV cascade of care (cascade) provides a framework to identify step-wise attrition and has become a key programmatic monitoring tool. However, without standard cascade development guidelines, cascades cannot be compared across jurisdictions. Here, we use the example of four cascades to propose harmonization in stage definitions.

Methods: We compared definitions and outputs of four cascades from the USA, British Columbia (Canada), France and Denmark.

Results: The USA, BC, and France cascades all begin with the estimated HIV-positive population. However, the Danish cascade begins with the number of diagnosed HIV cases; this immediately increases the proportion retained along their cascade. 'Linkage' and 'retention' in care definitions also varied: France was the only cascade not to distinguish between linkage and retention, instead using a composite referred to as 'in care'. All cascades defined a stage 'on ART'. USA and Danish cascades defined 'on ART' as any ART record within the year of interest. BC and France, however, required evidence of sustained use of ART within the calendar year. When defining virologic suppression, Denmark used the most recent viral load (VL) < 500 copies/mL, the USA used VL≤200 copies/mL at the latest available test, France used a single VL < 50 copies/mL per calendar year, and BC used ≥2 VLs< 50 copies/mL over a period ≥3 months per calendar year. Consequently, the proportion suppressed amongst the estimated HIV-infected population varied substantially, at 25%, 35%, and 52% for the USA, BC, and France, respectively; and, of those HIV-diagnosed was 70% for Denmark.

Author, Country, Journal/ Conference, Year	Data Source/Data Presented	Estimated HIV-Infected population	Diagnosed	Linked	Retained	ART Indicated	On ART	ART Adherence	Virologic Suppression
Hall et al. JAMA Intern Med. 2013	National HIV Surveillance System-used to estimate infected population using back-calculation methods. Behavioural Risk Factor Surveillance System Medical Monitoring Project database for ART prescriptions and percent achieving virologic suppression./Cascade for USA in 2009.	National HIV Surveillance System used to estimate HIV infected population. 1, 148, 200 (100%) estimated HIV-infected population in 2009.	The number of HIV diagnoses was obtained from the National HIV Surveillance System. Calculated as a proportion of those infected. 82% of infected individuals were diagnosed.	Defined as having ≥1 measurement of a CD4 or viral load test result within 3 months after diagnosis. Calculated as a proportion of those diagnosed. 66% of infected individuals were linked to HIV care.	The proportion of adults with HIV who received at least one medical care visit between January and April 2009. 37% of infected individuals were retained in care.	Not included in the cascade.	Prescription of ART was defined as documentation in the medical record of any ART prescription in the past 12 months. 33% of infected individuals were on ART.	Not included in the cascade.	Medical record documentation of the most recent VL as ≤200 copies/mL. 25% of infected individuals achieved viral suppression.
Nosyk et al., British Columbia, Canada, Lancet Infectious Diseases, 2014	Linked-Population Level database/Longitudinal data from 1996-2011	HIV prevalence estimates from Public Health Agency of Canada 11, 700 (100%) estimated HIV-infected population in 2011.	Defined as the first instance of any one of: • a confirmed HIV-positive test • detectable plasma viral load† •an HIV-related MSP billing or hospital admission • a reported AIDS-defining illness • dispensation of antiretroviral therapy 71% of infected individuals were diagnosed.	Among diagnosed cases; defined as: (i) Among those with confirmed HIV test: the first instance of HIV-related service‡ following HIV diagnosis. (ii) Among those with no confirmed HIV test: the first instance of HIV-related service‡ ≥ 30 days following derived HIV diagnosis date. 67% of infected individuals were linked to care.	Among individuals linked to HIV care; defined as: (i) HIV-related physician visits OR diagnostic tests (CD4 or pVL) ≥3 months apart within the calendar year OR (ii) At least two antiretroviral drug dispensations ≥3 months apart, within the calendar year. 57% of infected individuals were retained in care.	Among individuals retained in HIV care but not currently on HAART; defined as meeting the primary or secondary IAS-USA initiation criteria within the calendar year from 1996-2011. 53% of infected individuals were ART indicated.	Among those in need of antiretroviral therapy; defined as receiving at least two antiretroviral drug dispensations ≥3 months apart, within the calendar year. 51% of infected individuals were on ART.	Among individuals on antiretroviral therapy; defined as having at least 80% adherence2in the calendar year, or from the point of antiretroviral initiation for those beginning therapy within the calendar year. 44% of infected individuals were ART adherent.	Among individuals adherent to therapy, defined as having no detectable pVL3 over a period ≥3 months in duration within the calendar year. 35% of infected individuals achieved viral suppression in 2011.
Helleberg et al. Sweden and Denmark PlosOne, 2013	Swedish-Danish HIV Cohort (a population-based nationwide cohort study of all HIV-infected individuals who have been treated at Danish HIV centres) database/ Cascade for Denmark in 2010.	Not included in the cascade.	The numbers of HIV diagnoses were obtained from the annual national HIV surveillance reports 1995-2010. 100% of diagnosed individuals in 2010.	The number of individuals enrolled in the Danish HIV Cohort Study who were diagnosed from 1995 to 2010. 95% of diagnosed individuals were linked to care.	Individual had visited an HIV care center and/or undergone measurement of VL or CD4 count within 13 months before July 1st, 2010. 88% of diagnosed individuals were retained in care.	Not included in the cascade.	Among patients retained in care, the number on HAART. 73%of diagnosed individuals were on ART.	Not included in the cascade.	Among patients retained in care, the number with viral suppression (VL <500 copies/mL at last measurement). 70% of diagnosed individuals achieved viral suppression.
Supervie et al., France, CROI, 2013	HIV-infected individuals in care: data from the French health insurance scheme . Receiving cART and viral suppression were estimated using data from the FHDH-ANRS-CO4 cohort, which is representative of HIV patients in care in France/ Cascade for France in 2010.	Estimated infected population back-calculated from HIV surveillance data. 149, 900 (100%) estimated HIV-infected population in 2010.	HIV-infected individuals in care: data from the French health insurance scheme on the number of individuals having long-term disease agreement for HIV; all HIV-infected individuals newly enrolled in care in France are eligible for long-term disease agreement for HIV. 81% of infected individuals were diagnosed.	The authors only showed "in care" and did not differentiate between linked and retained, defined as all individuals enrolled in the French health insurance scheme as having long-term disease agreement for HIV. 74% of infected individuals were "in care".		Not included in the cascade.	On cART for greater than 6 months. 60% of infected individuals were on ART.	Not included in the cascade.	Proportion of individuals "on cART" who achieved complete viral load suppression (<50 copies/mL). 52% of infected individuals achieved viral suppression.

[WEPEB379 Table: Comparison of four HIV cascades of care]

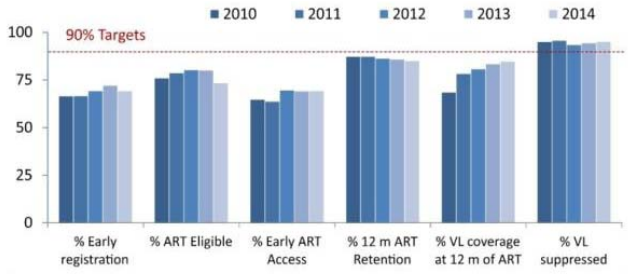
Conclusions: Differences in cascade outputs are partially explained by varying health-care systems but also by varying cascade designs. To monitor the success of the 90-90-90 target it is, thus, reasonable to postulate that cascade definition harmonization is urgently warranted. This would ensure the promotion of best individual and societal outcomes and the ability to directly compare cascades between jurisdictions.

WEPEB380

Monitoring of key performance indicators to improve management of antiretroviral treatment, upper-north region, Thailand

S. Bhakeecheep[1], A. Teeraratkul[2], K. Phokasawad[2], P. Kantipong[3], P. Pathipvanich[4], T. Roels[2,5]
[1]National Health Security Office, Region 1, Chiangmai, Thailand, [2]Thailand Ministry of Public Health-U.S. Centers for Disease Control and Prevention Collaboration, Global AIDS Program Thailand/Asia Regional Office, Nonthaburi, Thailand, [3]Chiangrai Prachukroa Regional Hospital, Ministry of Public Health, Muang, Thailand, [4]Lampang Regional Hospital, Minitry of Public Health, Muang, Thailand, [5]U.S. Centers for Disease Control and Prevention, Center for Global Health, Division of Global HIV/AIDS, Atlanta, United States
Presenting author email: a.teeraratkul@gmail.com

Background: Analyzing monitoring data regularly in order to determine the success of the early antiretroviral treatment (ART) strategy is essential, especially in areas with high burden of HIV such as Upper-North of Thailand (Region 1).
Methods: The HIV/AIDS care and treatment program performance of 115 hospitals in Thailand's Region 1 from 2010-2014 was analyzed for key performance indicators (KPIs). Patient records from the National HIV Patient Monitoring, an electronic web-based information system with real-time linkage to the National Death Registry, were used for this purpose. Selected KPIs were then graphed to represent the early ART recruitment and retention cascade.



% Early registration	% newly diagnosed patients registered and had CD4 by 3 m after diagnosis
% ART eligible	% newly registered PWHA who had CD4<350 cells/mm^3 or AIDS symptom
% Early ART Access	% newly registered PWHA had ART by 3 m after the eligibility was indicated
% 12 m ART Retention	% PWHA retained to ART at 12 month after initiation
% VL coverage	% PWHA ART who had VL at least once during 3-12 month after initiation
% VL suppressed	% PWHA whose VL at 12 m after ART was <1,000 copies/ml

[Figure 1: Annual cascade on ART recruitment and retention. National AIDS program monitoring, Region 1, Thailand, 2010-2014]

Key Performance Indicators	2010	2011	2012	2013	2014	*p value (Wilcoxon NP test for trend)*
PWHA currently receiving services	27,413	29,764	31,675	39,087	39,401	-
1) % registration by 3 month after diagnosis	66.5 (30.0-88.4)	66.6 (51.3-75.8)	69.3 (50.0-76.0)	72.1 (62.5-82.1)	69.2 (59.7-86.7)	0.162
2) % lost-to-follow up during pre-ART	28.1 (23.2-30.8)	26.8 (20.7-33.0)	27.0 (17.3-32.8)	24.1 (21.2-28.3)	30.7 (15.8-50.0)	0.841
3) % CD4 at ART initiation <200 cells/ mm3	78.6 (22.6 83.0)	72.8 (41.8-69.1)	73.9 (36.5-70.0)	60.7 (48.2-72.0)	61.7 (45.7-78.5)	<.027*
4) % Lost during 12 month after ART initiation	5.5 (2.4-11.4)	5.0 (1.9-7.1)	6.8 (3.3-10.8)	6.2 (2.6-9.4)	6.9 (4.4-8.5)	0.032*
5) % VL test at least once at 12 month after ART initiation	68.5 (53.9-83.3)	78.4 (63.3-87.5)	80.7 (62.4-89.1)	83.4 (65.5-89.4)	84.7 (73.2-95.6)	<.036*
6) % VL suppressed <1,000 copies/ml at 12 month after ART	95.1 (90.2-97.1)	95.8 (89.5-97.5)	93.5 (88.2-96.3)	94.4 (89.3-97.4)	95.2 (89.3-97.1)	0.841
7) % death during pre-ART care	9.7 (5.1-12.7)	10.1 (8.0-14.5)	10.0 (8.4-13.5)	11.8 (10.0-16.8)	11.4 (8.0-16.6)	0.110
8) % death during 12 month after ART initiation	7.7 (4.7-10.3)	8.0 (5.5-11.1)	7.4 (4.0-10.7)	8.6 (6.9-14.9)	8.7 (5.7-13.5)	0.021*

[Table 1: Trend of KPIs on HIV Care and ART]

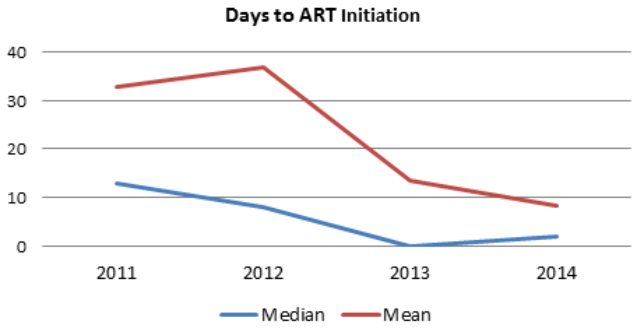
Results: Annual KPIs and trends in cascade parameters are summarized in Figure 1 and Table 1. By September 2014, 36,450 (82% of 44,437) and 2,951 (23.9% of 12,323) persons with HIV/AIDS (PWHA) were retained in ART and pre-ART services respectively. KPIs related to early recruitment did not significantly improve. In 2014, 60.9% of patients newly diagnosed and registered to care had CD4 <200 cells/mm^3 and 69.3% of PWHA eligible for ART had received ART. Median CD4 at start of therapy significantly increased from 82 in 2010 to 131 in 2014, however, 61.7% started ART at late stage (CD4 <200 cells/mm^3) in 2014. Lost-to-follow-up during pre-ART care and in the 12 months after ART initiation remained high in 2014, 30.7% and 6.9% respectively. Viral load (VL) at 12 month after ART increased from 68.5% in 2010 to 84.7% in 2014 (p<0.05) and more than 90% had VL suppression (>1,000 copies/ml). Death rate slightly increased during pre-ART care (9.7% in 2010 to 11.4% in 2014, P>0.05) and during the 12 months after ART initiation (7.7% in 2010 to 8.7% in 2014, P <0.05).
Conclusions: Effective coordination to improve early referral of PWHA to care and ART, reduce loss to follow up during pre-ART and after ART initiation, and exploring factors related to increasing death remain priorities in Thailand's Region 1. In response to these findings, appropriate clinical management training and strategies for health care providers in Region 1 need to be reinforced.

WEPEB381

ART initiation among infants enrolled in the HITSystem in Kenya from 2011-2014

C. Martin[1], A.-L. Cheng[2], B. Gautney[3], V. Okoth[4], S. Khamadi[5], J. Dougherty[3], K. Goggin[6], R. Wafula[7], I. Mukui[7], S. Finocchario-Kessler[1], HITSystem Team
[1]University of Kansas Medical Center, Department of Family Medicine, Kansas City, United States, [2]University of Missouri - Kansas City, Kansas City, United States, [3]Global Health Innovations, Kansas City, United States, [4]Kenya Medical Research Institute, Nairobi, Kenya, [5]Walter Reed Program/HJFMRI Tanzania, Mbeya, Tanzania, United Republic of, [6]Children's Mercy Hospitals, Kansas City, United States, [7]National AIDS and STI Control Program, Nairobi, Kenya
Presenting author email: cmartin8@kumc.edu

Background: The national pediatric HIV/AIDS treatment guidelines in Kenya recommend immediate initiation of antiretroviral treatment (ART) for all HIV-infected infants. However, studies indicate that only 11.5% - 60.1% of HIV-infected infants receive ART, with median time to ART initiation ranging from 14 - 40 days. The HIV Infant Tracking System (HITSystem ©) is an eHealth intervention that targets early infant diagnosis (EID) outcomes, including timely ART initiation among HIV-infected infants.
Methods: We conducted a retrospective analysis among 158 infants with a confirmed HIV-positive diagnosis at 16 health facilities in Kenya utilizing the HITSystem between June 2011 and July 2014 (staggered start dates). We assessed proportion of positive infants initiated on ART and time from notification of results to ART initiation. A regression analysis calculated the trend in days to ART initiation from 2011-2014.
Results: Of the 158 HIV-infected infants, 126 (79.7%) initiated ART. After excluding 27 (17.1%) infants who were discharged early, 131 infants were eligible for ART initiation at the facility, of which 126 (96.2%) were initiated. Reasons for early discharge included: 2 (1.3%) mothers refused treatment for their infant, 5 (3.2%) transferred facility, 4 (2.5%) moved from the catchment area, and 16 (10.1%) HIV-infected infants died. From 2011-2014, mean time from mother notification to ART initiation was 18.7 days (median=5; SD=37; range= 0-207) but varied depending on infant age at initial test: 12.5 days and 27.6 days in infants tested before and after 24-weeks postnatal, respectively (one-sided t-test, t(60.2)= -1.98, p=0.026). By year, overall mean time to ART initiation was 19.7 days (median=13; SD=25.0; range= 0-7) in 2011, 28.7 days (median=8; SD=48.1; range= 0-207) in 2012, 13.6 days (median=0; SD=33.9; range= 0-175) in 2013, and 6.3 days (median=2; SD=10.11; range= 0-35) in 2014. The linear regression slope of days to ART initiation from 2011 to 2014 was -0.02 (p=0.051).



[Days to ART Initiation: 2011-2014]

Conclusions: The rate of ART initiation among HIV-infected infants enrolled in the HITSystem was higher than rates reported in other studies, while mean time to ART initiation was shorter. Mean time to ART initiation was shorter in infants tested before 24-weeks postnatal. Speed of ART initiation improved from 2011-2014.

WEPEB382

An analysis of linkage policies within the HIV continuum of care in national HIV guidelines of President's emergency program for AIDS relief (PEPFAR)-supported countries

S. Hunter[1,2], D. Flynn[3,4], C. Johnson[3], V. Wong[1], R. Baggaley[5]
[1]United States Agency for International Development, Office of HIV AIDS, Washington DC, United States, [2]Lafayette College, Easton, United States, [3]World Health Organization, HIV Department, Geneva, Switzerland, [4]Griffith University School of Medicine, Queensland, Australia, [5]World Health Organiation, HIV Department, Geneva, Switzerland
Presenting author email: stephaniehunter613@gmail.com

Background: Linkage to care (LTC) is the process of supporting HIV-diagnosed persons to enter medical care and HIV negative persons to access prevention services. Forty-one percent of those diagnosed in Africa are not linked-to-care. Both PEPFAR's goal of an AIDS-free generation and UNAIDS' Three 90s targets necessitate high linkage rates. We reviewed and analyzed national HIV treatment and linkage policies to assess linkage integration.
Methods: We electronically searched for national HIV treatment policies and linkage strategies published from 2008-2014 using Google, government and NGO websites, WHO databases, and by contacting key experts. Policies were reviewed and data on linkage and referral systems for HIV prevention, care, and treatment were extracted. No geographic or language restrictions were placed on the search, however analysis was limited to PEPFAR-supported countries.
Results: In total, 25 policies were identified in 19 PEPFAR-supported countries, across 4 WHO regions (15/19 African Region, 1/19 Eastern-Mediterranean Region, 2/19 Western Pacific Region, 1/19 Southeast Asia Region); 12 of which are from voluntary medical male circumcision (VMMC) countries. About half (10/19) include policies on linkages to HIV prevention, care, and treatment services. Of the 12 VMMC priority country policies, only 2 include linkage and 5 mention VMMC but do not specify referral or linkage. Nearly all (18/19) countries mention a referral system to care and treatment, while only 14/19 outline referral to prevention services, most commonly prevention of mother-to-child transmission (PMTCT) services. Mention of linkage to care could be found in less than half (12/25) of total policies from 10 PEPFAR countries. The majority of VMMC policies (10/12) containing guidelines on LTC were from 2010 onward. The level of detail explaining LTC was strongest in policies dated 2013-2014.
Conclusions: Strengthening the quantity and content of policies on linkage to HIV prevention, care, and treatment services is needed. It appears more countries are including LTC policies in national treatment guidelines, however few include linkage to prevention, especially for HIV negative persons and few have linkage strategies. Country activities towards new global targets will require clear linkage strategies and clarification within prevention, care and treatment policies.

WEPEB383

Effect of point-of-care CD4 testing on time to ART-initiation and Pre-ART attrition in rural decentralized health centers in Chiradzulu District, Malawi

S. Nicholas[1], B. Schramm[2], E. Poulet[2], L. Wolters[3], A. Rakesh[3], I. Amoros[4], J.-F. Etard[2,5], L. Salumu[6], M. Gueguen[6], E. Szumilin[6]
[1]Epicentre, Research Department, Paris, France, [2]Epicentre, Paris, France, [3]Médecins sans Frontières, Chiradzulu, Malawi, [4]Médecins sans Frontières, Lilongwe, Malawi, [5]UMI 233 Institut de Recherche pour le Développement, Montpellier, France, [6]Médecins sans Frontières, Paris, France
Presenting author email: birgit.schramm@epicentre.msf.org

Background: Médecins Sans Frontières (MSF) in collaboration with the Ministry of Health has provided antiretroviral-therapy (ART) in decentralized rural health centers (HCs) with centralized CD4 testing supported by MSF in Chiradzulu District, Malawi. In June 2013, PIMA-Alere CD4 point-of-care (POC) was implemented with MSF-UNITAID co-funding. We assessed the effect of CD4-POC testing on ART initiation and Pre-ART attrition amongst those eligible by CD4.
Methods: A retrospective observational cohort analysis was conducted on HIV-positive-, ART-naïve patients ≥2 years age, enrolled into care between 1st July 2013 and 30th April 2014 in one HC with CD4-POC testing and two HCs with centralized CD4 laboratory testing. Database was censored on 31st October 2014. Eligibility by CD4 used the threshold of 350 till February 2014 and 500 afterwards, as per national protocol. Attrition was defined as died or lost-to-follow-up (LFU).
Results: Overall 377 (POC site) and 391 (non-POC-sites) patients were analyzed. Sex and age at enrolment were similar between POC- and non-POC sites (p>0.5, 62% female; median age 32 years). Nearly all patients in the POC-site had a CD4 blood-draw at enrolment (92.4% vs 56.7%, p< 0.01). The percentage eligible by CD4 was higher in the POC-site (59% (N=221) vs 47% (N=183), p< 0.01). Among patients eligible by CD4, 198 (90%) initiated ART in the POC- vs 173 (94%) in the non-POC sites (p=0.07) and median time between program-entry and ART-initiation was 14 days [IQR:6-24] (POC-site) vs 30 days [IQR:22-57] (non-POC site) (p< 0.01). CD4-eligible patients were 8-times more likely to start ART within 1 week of enrolment in the POC- than in non-POC-sites with 38.4% vs 4.6% (p< 0.01). Pre-ART attrition amongst patients eligible by CD4 was slightly higher in POC-sites (6.8% vs 3.3 %, p=0.11). In both sites, losses to care occurred within a month of enrolment and two-thirds had only 1 visit.
Conclusions: In MSF-supported rural HCs setting where many patients were ART-eligible at enrolment, Pre-ART attrition was low. While ART-initiation was already relatively quick thanks to MSF's logistical support to centralized CD4-testing, CD4-POC significantly reduced the time between enrolment and ART-start, and furthermore supports fast-track initiation within 1 week of program-entry.

WEPEB384

HIV testing and treatment cascade in rural South Africa: initial results from a representative household surveillance sample

A.B. Kharsany[1], C. Cawood[2], D. Khanyile[2], A. Grobler[1], L. Mckinnon[1], K. Govender[3], G. George[3], S. Beckett[3], L. Zembe[4], M.T. Glenshaw[4], Z. Chipeta[4]
[1]Centre for the AIDS Programme of Research in South Africa, CAPRISA, Durban, South Africa, [2]Epicentre, Durban, South Africa, [3]University of KwaZulu-Natal, Health Economics and HIV and AIDS Research Division, Durban, South Africa, [4]U.S. Centers for Disease Control and Prevention, Pretoria, South Africa

Background: South Africa has successfully scaled up a broad range of HIV-related programmes including the provision of antiretroviral therapy (ART). HIV testing and linkage to treatment substantially improves outcomes at the individual level; at the population level, effective ART plays an important role in reducing HIV transmission. We evaluated the uptake of HIV testing and linkage to treatment in a representative household sample of rural South Africans.
Methods: The HIV Incidence Provincial Surveillance System (HIPSS) is a longitudinal study to monitor HIV incidence in sub-districts of Vulindlela and the Greater Edendale in the uMgungundlovu municipality, KwaZulu-Natal, South Africa. Population based household surveys of 10 000 individuals selected randomly in the age group 15-49 years are being undertaken. Study staff administered an in-depth questionnaire including information on the uptake of HIV testing and ART. Participant responses were linked to laboratory testing for HIV-1 RNA viral load in those who reported to be HIV positive.
Results: A total of 4778/ 6401 (74.6%) of randomly selected households consented to study participation. From these households 4231/4778 (88.5%), randomly selected individuals were enrolled of whom 2745/4231 (64.9%) were females and 1486/4231 (35.1%) were males. Although two thirds 2825/4231 (66.8%) of the participants had received an HIV test, females (1967/2745, 71.7%) were much more likely to be tested than males (858/1486, 57.7%; p< 0.001). Of those reporting to be tested, 770/1967, (39.1%) were females and 206/858 (24.0%) were males (p value < 0.001). HIV positive 480/770 (62.3%) females and 124/206 (60.1%) males were on ART (p value=0.573) and of these 363/480 (75.6%) females and 79/124 (63.7%) males had viral suppression at < 20 copies/ml
(p value = 0.009).
Conclusions: These results suggest that there is a need for public health interventions to enhance HIV testing and on-going support to increase access and retention on ART. Males were less likely to have received an HIV test and despite knowledge of HIV positive status were less likely to initiate ART and achieve viral suppression. Novel interventions and strategies are needed to enhance the uptake of HIV testing and effectiveness of ART in men to optimize its therapeutic and preventative benefits.

Complications of HIV, its therapy and comorbidities in children and adolescents

WEPEB385

Prevalence of and risk factors for chronic lung disease among HIV-infected children

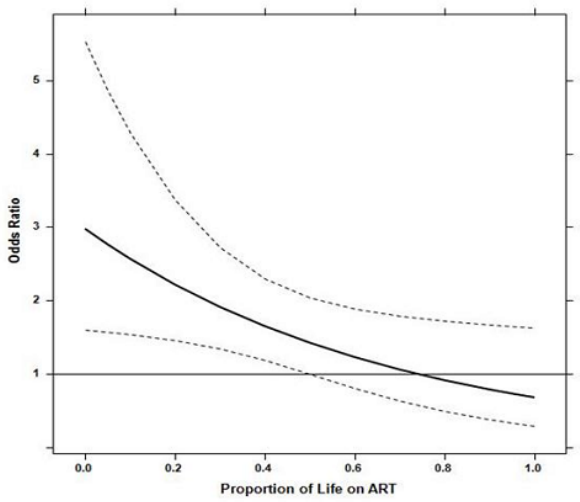
S. Lloyd[1], N.K. Taylor[1], E. Koumans[1], S. Gutreuter[1], H. Alexander[1], C. Hatcher[1], D. Singer[2], S. Gupta[2], S. Modi[1]
[1]Centers for Disease Control and Prevention, Center for Global Health/Division of Global HIV/AIDS, Atlanta, United States, [2]Centers for Disease Control and Prevention-Malawi, Center for Global Health/Divsion of Global HIV/AIDS, Lilongwe, Malawi
Presenting author email: wid6@cdc.gov

Background: HIV-infected children in resource-limited settings face serious medical complications especially as they survive into adolescence. We investigated the prevalence of and risk factors for chronic lung disease (CLD) among HIV-infected children in Malawi.
Methods: Between March 25 and April 23, 2014, we enrolled 615 HIV-infected children ages 5-14 years from seven outpatient HIV clinics in a cross-sectional investigation including in-depth caregiver interviews, physical exam, spirometry, laboratory testing for CD4, and medical

record abstraction. CLD cases were defined as children with (1) chronic cough (>4 weeks) and self-reported breathlessness or (2) one of the above symptoms and either hypoxia (resting oxygen saturation ≤92%), resting tachypnea (respiratory rate >24 per minute), or finger clubbing. CLD prevalence was calculated using cross-sectional data. We used nested case-control data in a multivariable complete-case analysis which included 461 children (65 cases and 396 non-cases) to evaluate CLD risk factors. Proportion of life on ART equaled the number of documented months a child received any ART regimen divided by the child's age in months. We used odds ratios (OR) with 95% confidence intervals (CI) to estimate risk.

Results: Among 615 participants, median age was 11 years (IQR: 9-13) and 319 (51.9%) were female. Overall CLD prevalence was 15.3% (95% CI: 12.5-18.4). CLD prevalence was 17.6% for males versus 13.2% for females (p=0.48) and 15.9% among 10-14 year olds versus 14.1% among 5-9 year olds (p=0.91). CLD was not associated with age category, sex, initial or most recent CD4, initial or most recent WHO stage, number of prior pulmonary TB or upper respiratory tract infections, or age at HIV diagnosis. The effect of each additional lower respiratory tract infection (LRTI) significantly increased CLD risk as the proportion of life on ART decreased (Figure 1).

Conclusions: The burden of CLD among HIV-infected children in Malawi is substantial. Recurrent LRTIs in HIV-infected children with delayed ART initiation (i.e., shorter proportion of life on ART) appear to be an important risk factor for CLD. These findings suggest earlier initiation of ART and preventive/treatment strategies aimed at reducing LRTI burden among HIV-infected children, regardless of age, may reduce CLD risk.



*Final model was developed by identifying potentially important covariates (p<0.25) using bivariate conditional logistic regression matching on clinic site, followed by identifying the best predictors of CLD using a multivariate model including the covariates and their two-way interactions and then sequentially removing unimportant (p>0.05) covariates based on Bayesian Information Criterion.

[Figure 1: Effect of each additional LRTI on CLD risk stratified by proportion of life on ART. Dashed lines represent 95% CIs]*

WEPEB386

Chronic respiratory ill-health in children with vertically acquired HIV: clinical features and lung function

J. Rylance[1,2], G. McHugh[3], S. Desai[4], E. Majonga[3,5], J. Metcalfe[6], S. Munyati[3], T. Bandason[3], H. Mujuru[7], K. Kranzer[5], R. Ferrand[3,5]
[1]University of Liverpool, Liverpool, United Kingdom, [2]Liverpool School of Tropical Medicine, Liverpool, United Kingdom, [3]Biomedical Research and Training Institute, Harare, Zimbabwe, [4]King's College Hospital NHS Foundation Trust, London, United Kingdom, [5]London School of Hygiene and Tropical Medicine, London, United Kingdom, [6]UCSF, San Francisco, United States, [7]University of Zimbabwe, Department of Paediatrics, Harare, Zimbabwe
Presenting author email: tbandason@brti.co.zw

Background: Limited studies suggest high rates of chronic respiratory symptoms in children with vertically acquired HIV, predominantly breathlessness and cough. We report early results of a cross-sectional study systematically examining symptom burden, lung function and radiological pattern.

Methods: HIV infected older children and adolescents (age 6-16) on antiretroviral therapy for at least 6 months were recruited from Harare Hospital, Zimbabwe. Assessment included clinical questionnaire, laboratory examinations, spirometry (GLI2012 reference ranges), chest X-ray and high resolution CT for children considered to have chronic respiratory disease.

Results: 96 participants were recruited (41 female, 42.7%), median age 11.1 (range 6.1 - 16.1) years, with median age at HIV diagnosis 5.2 (IQR 2.9 - 8.2). Median CD4 was 710 (IQR 458-904). All sputum TB smears were negative.

Children were frequently stunted (n=35, 36.5%). Chronic cough was reported by 20 (20.8%), of which 14 (14.5%) produced sputum spontaneously. Wheeze and dyspnoea were less common (6, 6.3% for each). 40 (41.6%) were previously treated for tuberculosis, and 5 (5.2%) for asthma. Exertional hypoxaemia occurred in 16 (17.7%), and 1 child was hypoxaemic at rest.

Of 82 high quality spirometry traces, obstructive and restrictive abnormalities were demonstrated in 7 (7.9%) and 19 (21.4%) respectively, with poor reversibility. Mean z-scores (SD) for spirometry were: FEV_1 -0.84 (1.17); FVC -0.83 (1.24); FEF25%-75% -0.22 (1.25).

Age at recruitment was significantly negatively associated with FEV_1 and FVC z-scores ($p<0.001$, r^2 =0.12 and 0.11 respectively). Earlier diagnosis was associated with better FEV_1 ($p=0.004$, r^2 =0.08) and FVC ($p=0.02$, r^2 = 0.06), but CD4 count at diagnosis was not.

HRCT demonstrated mosaic attenuation pattern in 14/18 (78%) believed to reflect obliterative bronchiolitis, bronchiectasis in 9/18 (50%) and volume loss in 7/18 (39%). Bronchial wall thickening of varying extent was noted in 16/18, and a minority had ground-glass opacities, cysts, reticulation and consolidation.

Conclusions: We have demonstrated high rates of cough with unknown aetiology, and significantly reduced lung function in older children with vertically acquired HIV. Radiologically, airway abnormalities, and, specifically obliterative bronchiolitis predominate among those with chronic respiratory symptoms. Early HIV diagnosis and treatment is likely to reduce lung function abnormalities.

WEPEB387

Decreased vigorous physical activity in South African HIV-infected school-aged children on antiretrovirals

M. Wong[1], S. Shiau[1], M.T. Yin[1], R. Strehlau[2], F. Patel[2], F. Pinillos[2], A. Coovadia[2], L. Micklesfield[3], L. Kuhn[1], S. Arpadi[1], CHANGES Study Group
[1]Columbia University, New York, United States, [2]University of the Witwatersrand, Empilweni Services and Research Unit, Johannesburg, South Africa, [3]University of the Witwatersrand, MRC/Wits Developmental Pathways for Health Research Unit, Faculty of Health Sciences, Johannesburg, South Africa
Presenting author email: mmw2185@cumc.columbia.edu

Background: Despite potential importance to long-term health outcomes adversely affected by HIV, including bone and cardiometabolic health, physical activity (PA) among people living with HIV has not been well studied. We describe PA in South African HIV-infected and uninfected children.

Methods: Data were obtained from CHANGES (Childhood HAART Alterations in Normal Growth, Genes, and aGing Evaluation Study), a study of perinatally HIV-infected children and uninfected controls in Johannesburg, South Africa from 2012-2014. Age of antiretroviral initiation, HIV-RNA, CD4%, weight-for-age (WAZ) and height-for-age (HAZ) Z-scores, and frequency and duration of physical activities and sedentary behaviors by validated questionnaire were obtained. Metabolic equivalents (METS) of each PA were determined. Moderate-vigorous PA (MVPA) was defined as PA ≥3 METS, while vigorous PA (VPA) was defined as >6 METS. Measures were compared between HIV-infected and uninfected children using chi-squared, t-tests, and linear regression.

Characteristic	HIV-infected	HIV-uninfected	P-Value
N	213	152	
Sex, N (%)			
Male	106 (49.8)	83 (54.6)	0.36
Female	107 (50.2)	69 (45.4)	
Age, Mean (SD)	6.4 (1.3)	7.2 (1.5)	<0.0001
Weight-for-age Z-score, Mean (SD)	-0.80 (0.9)	-0.35 (1.0)	<0.0001[3]
Height-for-age Z-score, Mean (SD)	-1.34 (0.9)	-0.87 (1.0)	<0.0001[3]
Total Moderate-Vigorous PA (hours/week), Mean (SD)	22.7 (16.0)	27.8 (17.6)	0.005
Total VPA (hours/week) Mean (SD)	10.8 (8.9)	14.1 (9.5)	0.001[3,4]
Meets WHO recommendations for PA, %	82.2	88.2	0.12
Sedentary Time (hours/week), Mean (SD)	16.2 (8.9)	18.2 (9.2)	0.035
Sleep Time (hours/week), Mean (SD)	70.2 (7.3)	71.0 (7.1)	0.26
Physical Activities (hours/week), Mean (SD)			
Walking	2.1 (1.5)	1.9 (1.3)	0.13
Running[1]	9.3 (7.0)	11.7 (7.6)	0.004[3,4]
Playing	8.4 (7.3)	9.4 (8.1)	0.25
Active Chores	0.8 (0.6)	0.8 (0.6)	0.5
Skipping[1]	1.5 (1.1)	2.1 (1.6)	0.01[3]
Bicycling[1]	2.3 (1.8)	3.0 (2.3)	0.09
Dancing	1.5 (1.0)	2.0 (1.5)	0.13
Soccer[1]	3.0 (1.9)	3.2 (1.8)	0.65
Sedentary Behaviors (hours/week), Mean (SD)			
Reading	1.8 (1.0)	1.8 (0.9)	0.97
Television	12.1 (7.1)	13.6 (7.7)	0.06
Computer or phone games	2.1 (1.8)	2.4 (1.8)	0.14
Riding in Vehicle	1.9 (1.5)	1.7 (1.4)	0.36

[1] Denotes VPA;
[2] WHO recommends at least one hour of MVPA daily, and VPA at least three times weekly.
[3] Remained significant after adjusting for age; [4] Remained significant after adjusting for age, HAZ, WAZ.

[Table 1. Demographics, anthropometrics, and physical activity (PA) of HIV-infected and HIV-uninfected school-aged children in Johannesburg, South Africa]

Results: 213 HIV-infected and 152 uninfected children aged 6-9 years (83% of target sample) were included. Age, WAZ and HAZ were significantly lower for HIV-infected children. 93.1% of HIV-infected children were virally suppressed (HIV-RNA < 400 copies/mL), had a mean CD4% of 37.4, and were initiated on antiretrovirals at a mean age of 8.9 months (SD

6.7). The most commonly reported activities are listed in Table 1. HIV-infected children spent significantly less time in MVPA and VPA than controls (mean difference of 5.1 and 3.3 hours/week, p=0.005 and 0.001, respectively), including less running and skipping. The proportion of children in both groups meeting WHO recommendations for PA was similar. While HIV-infected children reported significantly less total sedentary time than uninfected children overall, the time spent in the various sedentary behaviors did not differ. Differences in VPA, running, and skipping remained significant after adjusting for age; MVPA differences however were no longer significant (adjusted 3.6 hours/week, p=0.052). When adjusted for age, WAZ, and HAZ, only VPA and running remained significant.

Conclusions: Although HIV-infected children initiated early on antiretrovirals with good virologic suppression have high levels of PA, VPA was significantly lower than healthy controls. Further investigation of reasons for these differences in PA and implications on short and long-term health outcomes throughout life are warranted.

WEPEB388

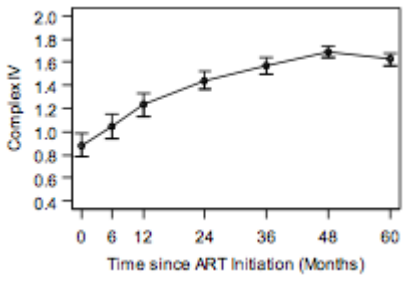
Changes in mitochondrial enzyme function as a predictor of lipodystrophy

M. Foca[1], L. Wang[1], S. Ramteke[2], R. Strehlau[3], S. Shiau[4], F. Pinillos[3], M. Yin[5], F. Patel[3], A. Coovadia[3], S. Arpadi[4], E.J. Abrams[6], L. Kuhn[4], CHANGES Study Group
[1]Columbia University Medical Center, College of Physicians and Surgeons, Department of Pediatrics, Division of Infectious Diseases, New York, United States, [2]Columbia University, Gertrude H. Sergievsky Center, New York, United States, [3]University of the Witwatersrand, Empilweni Services and Research Unit, Rahima Moosa Mother and Child Hospital, Faculty of Health Sciences, Johannesburg, South Africa, [4]Columbia University, Gertrude H. Sergievsky Center, College of Physicians and Surgeons, Department of Epidemiology, Mailman School of Public Health, New York, United States, [5]Columbia University Medical Center, College of Physicians and Surgeons, Department of Medicine, Division of Infectious Diseases, New York, United States, [6]Columbia University, Department of Epidemiology, Mailman School of Public Health, ICAP, New York, United States
Presenting author email: mdf10@columbia.edu

Background: Extended longitudinal data of mitochondrial function in HIV-infected children treated with potent combination antiretroviral therapy (cART) are sparse. We used peripheral blood mononuclear cells to analyze changes in mitochondrial function over a 5-year period. Potential predictors of lipodystrophy were studied.

Methods: We analyzed data on 38 children enrolled in a clinical trial in Johannesburg, South Africa. All children initiated and were maintained on lopinavir/ritonavir-based cART with viral suppression documented through 5 years of treatment. Buffy coat samples were used for isolation of DNA and analysis of mitochondrial enzyme activity. The following markers of mitochondrial function were used: complex IV (CIV) activity (respiratory chain), citrate synthase (CS) activity (mitochondrial mass), the ratios of CIV/CS (respiratory chain function per mass) and mitochondrial to nuclear DNA. DNA measurements were performed by real time PCR. Protein was isolated and activity of CIV and CS were assayed by spectrophotometric methods. CD4%, plasma RNA and standardized clinical assessment of lipodystrophy (LD) were documented throughout follow-up.

A



[Mitochondrial Enzyme Activity]

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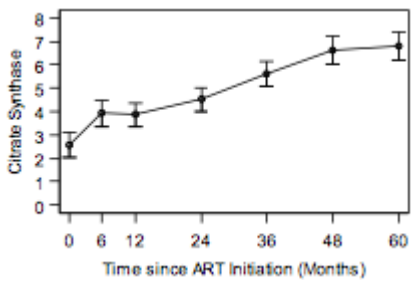

[Mitochondrial Enzyme Activity]

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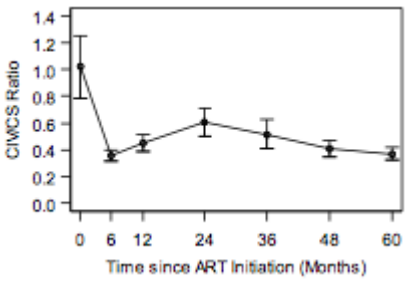


[Mitochondrial Enzyme Activity]

Results: Fifty-three percent of study participants were female. Age at initiation of cART ranged from 2-23 months (mean12 months). Of the 31 children with pretreatment values, median CD4% was 15.3 and 54.8% of participants had a plasma RNA ≥750,000 copies/ml. Eighteen percent developed lipodystrophy, and 71% (5/7) were female. Mitochondrial DNA (mDNA) increased when pre-treatment values were compared to the 5-year time point. CIV and CS activity increased steadily and had not plateaued after 5 years of treatment. Despite these increases, absolute enzyme function did not reach values seen in uninfected children [CIV (2-3 Δ OD/min) and CS (10-12 Δ OD/min)] (Figure). Girls (n=20) and those who developed lipodystrophy (n=7) had early, rapid increases in CIV activity. Pre-treatment CD4% and plasma RNA did not correlate with enzyme function.

Conclusions: Although continuous recovery in mDNA and absolute enzyme activity were observed in these children, they remained below expected levels over 5 years on cART. The more rapid increases in CIV activity observed in those who developed LD suggests mitochondrial recovery may be involved in evolution of LD.

WEPEB389

Early cardio-pulmonary disease in children despite early ART: evidence from CHER cohort

S. Innes[1], M.F. Cotton[1], B. Laughton[1], F. Swart[2], D. Maree[2], Z. Magogotya[1], R.M. Conradie[3], S.H. Browne[4], R. Haubrich[4], R.P. Gie[1]
[1]Stellenbosch University and Tygerberg Academic Hospital, Paediatrics and Child Health, Cape Town, South Africa, [2]Stellenbosch University and Tygerberg Academic Hospital, Respiratory Medicine, Cape Town, South Africa, [3]Stellenbosch University and Tygerberg Academic Hospital, Division of Endocrinology, Department of Medicine, Cape Town, South Africa, [4]University of California San Diego, Division of Infectious Diseases, Dept of Medicine, San Diego, United States
Presenting author email: innes@sun.ac.za

Background: Untreated HIV infection in children is associated with chronic progressive pulmonary and vascular disease. The degree to which early antiretroviral therapy (ART) prevents this is unclear. Maximal oxygen consumption (VO_2max) is the gold standard measure of cardiovascular and respiratory fitness and a sensitive marker of early cardiovascular or respiratory disease.

Methods: In 125 children (77 HIV-infected; 48 uninfected), we performed a standardized 3-minute step test to estimate VO_2max using a previously validated formula for healthy children aged 8-12 years. The HIV-infected children had initiated ART (lopinavir/r, lamivudine, zidovudine) in infancy at median 9.1 (interquartile range, IQR: 7.4 - 11.8) *weeks* of age. We measured fasting lipids, along with fat-free body weight and vertebral bone mineral density (BMD) using dual energy X-ray absorptiometry (DXA). Vertebral BMD z-score for age and gender was used as a surrogate marker of chronic malnutrition, and fasted total cholesterol as a surrogate for high trans-fat / high refined carbohydrate diet, which are common in our local population. Estimated VO_2max was corrected for fat-free body weight before being entered into a multivariate linear regression as the dependent variable.

Results:

Table 1: Description of participants	HIV-infected, N=77	Uninfected, N=48	Univariate p-value
Age (median, range) (years)	7.7 (7.4 - 8.7)	8.5 (7.4 - 8.8)	0.0001
Gender (male/female)	44% / 56%	63% / 38%	0.05
Body mass index	16.2 (12.2 - 20.2)	17.0 (11.5 - 22.4)	0.08
Fat-free body mass (kg)	17.6 (13.0 - 22.3)	18.9 (13.7 - 24.2)	0.007
Unadjusted VO2max (ml/min/kg)	33.6 (23.4 - 43.9)	35.6 (21.0 - 51.1)	0.11
Vertebral BMD z-score	-0.5 (-2.5 - +1.6)	-0.2 (-2.1 - +1.7)	0.14
Total cholesterol (mmol/L)	4.2 (2.7 - 5.7)	3.5 (2.1 - 5.0)	<0.0001
Triglyceride-HDL ratio (median, IQR)	0.7 (0.5 - 1.0)	0.4 (0.3 - 0.7)	<0.0001
Variables are presented as mean (95% confidence interval) unless otherwise stated. IQR = Interquartile range; BMD = bone mineral density			

[Table 1: Description of participants]

On univariate analysis, VO_2max was similar in HIV infected and uninfected children (p=0.16). However, after adjustment for vertebral BMD z-score, total cholesterol, age and gender, HIV-infected children had a significantly lower VO_2max per kg fat-free body weight (p=0.03).
Conclusions: While early ART offers substantial benefit, it may not entirely prevent chronic non-infectious pulmonary and cardiovascular disease in perinatally-infected children.

Mental health and neuro-cognition in children and adolescents

WEPEB390

Better growth at entry to ART is associated with higher neurodevelopmental function at ART and improved post-ART recovery of function in Kenyan children

C.S. Crowell[1], L. Gómez[2], I. Njuguna[3], H. Moraa[3], L. Cranmer[4], V. Otieno[3], D. Chebet[3], E. Maleche-Obimbo[3], D. Wamalwa[3], G. John-Stewart[2], S. Benki-Nugent[2]
[1]University of Washington, Seattle Children's Hospital, Pediatric Infectious Diseases, Seattle, United States, [2]University of Washington, Global Health, Seattle, United States, [3]University of Nairobi, Paediatrics and Child Health, Nairobi, Kenya, [4]University of Washington, Pediatrics, Seattle, United States
Presenting author email: benki@u.washington.edu

Background: There are few prospective studies of neurodevelopmental outcomes in HIV-infected infants initiating antiretroviral therapy (ART) in Africa. We used the Malawi Developmental Assessment Tool (MDAT), to determine baseline and post-ART change in specific domains of developmental functioning in ART naïve hospitalized HIV-infected children initiating ART.
Methods: Children were identified from an ongoing randomized clinical trial (NCT02063880) of hospitalized, ART naïve, HIV-infected children randomized to initiate ART by 48 hours versus 14 days post-enrollment. The MDAT was administered at baseline (up to one month post-enrollment, depending on child's health) and 6-months post-ART. Domain Z-scores were calculated based on data for a Malawian norm population provided by M. Gladstone et al. Baseline and 6-month Z-scores were compared using paired t-tests. Cofactors for change in Z-scores were evaluated using univariate and multivariate linear regression.
Results: Among 46 children with baseline MDAT data 52% were male. Median age and CD4% were 1.8 years and 18%. Median gross motor, fine motor, social, and language z-scores were -0.9, -0.9, -0.5 and -1.0, respectively. At baseline, higher CD4% was associated with higher gross motor (p=0.07) and lower C-reactive protein was associated with higher language (p=0.05). Better nutritional status (weight-for-age (WAZ) and height-for-age (HAZ) Z-scores) was associated with higher MDAT scores with p-values ≤0.05 for all associations except for HAZ and language (p=0.06). Among 32 children with 6-month MDAT data, mean change in Z-scores were 0.3, 0.2, 0.4 and -0.1 for gross motor, fine motor, social, and language, respectively. Adjusting for baseline MDAT scores, higher baseline WAZ was associated with greater increases in MDAT scores following ART for gross motor (p=0.01) and fine motor (p=0.04) scores. Higher increase in weight over 6 months was associated with a higher increase in social score (p=0.03).
Conclusions: Better growth was associated with better neurodevelopment at baseline and improved recovery of neurodevelopment post-ART. Addressing nutritional interventions may be important to optimize long-term ART outcomes.

Clinical issues in sex workers

WEPEB392

Facilitators and barriers to retention in HIV care among female sex workers enrolled in an HIV care program at a community-based organization in Uganda

S. Nakanwagi[1,2], R. Wanyenze[3], F. Kaharuza[4], J. Matovu[3], D. Nabukalu[5], B. Nsangi[2]
[1]Makerere University School of Public Health, Kampala, Uganda, [2]Reach Out Mbuya Parish HIV/AIDS Initiative, Kampala, Uganda, [3]MakSPH-CDC Fellowship Program, Makerere University College of Health Sciences, School of Public Health, Kampala, Uganda, [4]Makerere University College of Health Sciences, Department of Community Health & Behavioral Sciences, Kampala, Uganda, [5]Rakai Health Sciences Program, Kalisizo, Uganda
Presenting author email: sharonshaloam@gmail.com

Background: Few studies have explored the factors influencing retention in HIV care among female sex workers (FSWs). We established facilitators and barriers to retention in HIV care among FSWs enrolled in a community based HIV program.
Methods: A mixed method cross-sectional study was conducted among HIV infected FSWs enrolled at Reach Out Mbuya Parish HIV/AIDS Initiative (ROM) from May 2012 to February 2014. We conducted chart reviews and collected data on age, marital status, treatment type and site, residence, duration in care and ART, CD4 at (enrollment, ART initiation and each clinic visit) and status in care (active, lost to follow and missed appointments) for 111 FSWs. In-depth and key informant interviews were conducted with 29 FSWs and five project staff and 11 peer educators respectively. A parametric model (the Weibull distribution) was adopted to explore factors associated with retention in HIV care. Qualitative data were manually analyzed following a thematic framework approach.
Results: Of the 111 FSWs ever registered in care at ROM; 105(95%) were retained. FSWs with higher CD4 > 351 at enrollment were more likely to be retained compared to those enrolled with CD4 < 200(adj HR; 1.66, 95% CI; 1.18-2.33, P=0.004). However, FSWs with CD4 >200 at each visit had decreased hazards of being retained compared to those with CD4 < 200 (unadj HR; 0.56, 95% CI; 0.48-0.64,
P< 0.001). FSWs enrolled at a static clinic were more likely to be retained compared to the mobile outreach clinics. Facilitators for retention were the good friendly services, follow up by peer educators, encouragement from peers, different models used, being a member of a saving group and need to be healthy. Barriers to retention included stigma, drug side effects, alcohol and drugs, pill burden, multiple service providers, Gender based violence and financial constraints.
Conclusions: Retention in care for FSWs is possible with good friendly care services and intensive follow up. However there is need for continuous counseling to avoid the possible losses along the care continuum.

Clinical issues in transgender populations

WEPEB393

HIV-related health access, health seeking behaviors and health literacy in the Malaysian transgender community

R. Rutledge[1], J. Wickersham[1], B. Gibson[1], V. Pillai[2], A. Kamarulzaman[2], F. Altice[1]
[1]Yale School of Medicine, New Haven, United States, [2]University of Malaya, Centre of Excellence for Research in AIDS (CERiA), Kuala Lumpur, Malaysia
Presenting author email: ronnye.rutledge@yale.edu

Background: Globally, transgender (TG) women are nearly 50 times more likely to be HIV-infected than their non-TG counterparts. In Malaysia, a country with one of Southeast Asia's largest TG populations, HIV prevention efforts have long been undermined by pervasive prejudice and discrimination.
Methods: Using a chain-referral method, transgender women (n=199) and transgender men (n=36) 18 years or older in Kuala Lumpur were recruited and completed a computer-based questionnaire assessing HIV-related knowledge, HIV literacy, and general healthcare utilization.
Results: HIV testing was uncommon, with only 85 (36.2%) having ever been tested, and mean time since last test was 26.2 months. Among those tested, 13 (15.2%) reported being HIV-infected, of which 9 were currently receiving antiretroviral therapy (ART). Sex work was the most common type of employment (68.5%), with most (59.3%) stating it was their primary income source. Among those active in sex work, only 60.5% had ever been HIV tested. While nearly all (99.1%) correctly identified condoms as effective HIV prevention, mosquito bites (51.1%) and meal sharing (40.0%) were incorrectly identified as modes of HIV transmission, with no significant differences in HIV literacy responses based on gender or education level.

Nearly all participants (94.0%) did not have a primary care provider and the majority (86.8%) had not received a general physical exam in the past 12 months. However, 82.1% had seen a medical provider for any health-related need in the past 12 months. Perceptions of providers' knowledge of TG health needs were poor, with 85.1% stating their provider had no knowledge at all of appropriate TG care.

Conclusions: Although TG women and men reported moderate levels of healthcare engagement overall, engagement was low within routine, general care, and HIV/STI testing including among high-risk sex workers. Health literacy regarding modes of HIV transmission was poor. Together, these data support provision of specialty clinical and educational services for the LGBT community, including routine and regular HIV and STI testing. These findings indicate a substantial need for further research to improve HIV knowledge, increase HIV testing through novel strategies to reduce barriers to testing and integrate routine testing into all outpatient environments, including venues for TG-related care.

Clinical issues in indigenous populations

WEPEB394

Disparities in retention in care and virologic suppression rates for Aboriginal persons and persons who inject drugs in Southern Saskatchewan

A. Wong[1,2], B. Hagen[1], C. Allen[1], D. Rodger[1], S. Nasewich[3], C. Benz-Tramer[3]
[1]Regina Qu'Appelle Health Region, Infectious Diseases Clinic, Regina, Canada, [2]University of Saskatchewan, Division of Infectious Diseases, Regina, Canada, [3]Regina Qu'Appelle Health Region, Population & Public Health Services, Regina, Canada
Presenting author email: alexander.wong@usask.ca

Background: Saskatchewan, a Canadian Prairie province, is currently experiencing a unique HIV epidemic characterized by high rates of transmission through injection drug use and disproportionate representation of Aboriginal persons. The Regina Qu'Appelle Health Region Infectious Diseases Clinic (RQHR IDC) provides care for over 430 HIV-positive individuals in southern Saskatchewan. We sought to determine whether disparities exist in HIV care cascade outcomes in the RQHR IDC for Aboriginal persons vs. non-Aboriginal persons, and those with a history of injection drug use vs. those without.

Methods: All non-transferred active HIV-positive individuals in the RQHR IDC were included in the analysis (n=398). Cascade definitions were as follows: linkage to care (seen within 3 months of first reactive HIV serology), retention in care (2 visits in previous 12 months at least 90 days apart), antiretroviral therapy (patient given a prescription for antiretroviral therapy in the previous 12 months), and virologic suppression (HIV viral load < 200 c/mL in the previous 12 months). Cross-tabulations, chi-squared, and logistic regression analyses were performed. Patients with missing data were removed from individual cascade measurements.

Results: Aboriginal persons were less likely to be retained in care vs. non-Aboriginal persons (102/188 [54.3%] vs. 89/125 [71.2%], OR=0.48 [95% CI 0.30-0.78]) and trended towards being less likely to have a suppressed viral load (122/234 [52.1%] vs. 99/163 [60.7%], OR=0.71 [95% CI 0.47-1.07]). Patients with injection drug use as their primary HIV risk factor were significantly less likely to be retained in care (119/214 [55.6%] vs. 67/89 [75.3%], OR=0.40 [95% CI 0.23-0.69]) or have a suppressed viral load (131/252 [52.0%] vs. 74/116 [63.8%], OR=0.61 [95% CI 0.40-0.94]) vs. those without. No differences between groups were observed for either linkage to care or antiretroviral therapy.

Conclusions: Aboriginal persons and persons with a history of injection drug use have suboptimal retention in care and virologic suppression compared to their respective counterparts in southern Saskatchewan. Our clinic population serves as a representative microcosm of the current provincial HIV epidemic, and resources are urgently required to address these disparities and improve cascade outcomes in all patients living with HIV in the province.

Clinical issues in incarcerated populations

WEPEB395

HIV risk and clinical characteristics among HIV-positive individuals involved in the criminal justice system: the CARE+ Corrections trial in Washington, DC

I. Kuo[1], A. Kurth[2], A. Cates[1], C. Trezza[1], L. Bazerman[3], B. Castonguay[1], H. Olsen[1], R. Patrick[1], T. Liu[4], J. Peterson[1], S. Abbott[5], C. Beckwith[6]
[1]George Washington University Milken Institute School of Public Health, Washington, United States, [2]New York University School of Nursing, New York, United States, [3]The Miriam Hospital, Providence, United States, [4]Brown University, Providence, United States, [5]Unity Health Care, Washington, United States, [6]Alpert Medical School of Brown University/The Miriam Hospital, Providence, United States
Presenting author email: bjurhig@gwu.edu

Background: Previously incarcerated individuals, particularly those recently released, have suboptimal linkage and engagement in community HIV care. We are conducting a randomized trial of an mHealth intervention (CARE+ Corrections) to increase linkage to community care among HIV-positive persons involved in the criminal justice (CJ) system. We report on the baseline characteristics of the sample.

Methods: We recruited HIV-positive incarcerated individuals in the District of Columbia jail (7/2014-present) and HIV-positive individuals released from a correctional facility in the previous 6 months through community and street outreach (8/2013-present). Enrollment and follow-up are ongoing. Participants completed a baseline computer-assisted personal interview regarding HIV care and medication adherence, substance use, and sexual behaviors. CD4 and HIV plasma viral load (PVL) testing were performed at baseline or obtained through medical records. Preliminary summary statistics of baseline demographic, behavioral, and HIV-related clinical characteristics are reported.

Results: Of 87 individuals, 68% were enrolled in the community. Mean age was 42 (Range 19-63), 60% were male, 10% were transgender (TG), and 85% were black. Participants had a mean of 8.5 (Range 1-61) previous incarcerations, for a cumulative mean length of 10.5 years (0.1-38). Among men and TG, 63% reported ever having had sex with another man. The majority (77%) met criteria for drug dependence and 36% exhibited high-risk hazardous alcohol use; 15% had ever injected drugs. High proportions of participants reported previous diagnoses of depression (78%), bi-polar disorder (54%), and/or schizophrenia (21%). Prior to the most recent incarceration, 73% reported having an HIV provider and 71% were prescribed HIV medications; among those, only half reported ≥90% adherence. Mean baseline CD4 count was 499 cells/μL (range 17-1186) and 38% were not virally suppressed (HIV PVL≥100 copies/mL). Of note, 21 (24%) self-reported being diagnosed with HCV, yet only four had been treated.

Conclusions: Participants in the CARE+ Corrections trial represent a vulnerable population highly involved in the CJ system with significant substance abuse and mental health co-morbidities. While most have previously been in care, HIV medication adherence and viral suppression remain inadequate. Innovative interventions to link and engage this population in HIV care and improve medication adherence are urgently needed.

Clinical issues in other key populations

WEPEB396

Socio-demographic and clinical characteristics of HIV-infected older children and adolescents diagnosed through optimised provider-initiated HIV testing and counselling in primary healthcare services in Harare, Zimbabwe

R. Ferrand[1,2], G. Mchugh[2], T. Bandason[2], E. Dauya[2], S. Munyati[2], H. Mujuru[3], K. Kranzer[1]
[1]London School of Hygiene and Tropical Medicine, IDEU, London, United Kingdom, [2]Biomedical Research and Training Institute, Harare, Zimbabwe, [3]University of Zimbabwe, Harare, Zimbabwe
Presenting author email: rashida.ferrand@lshtm.ac.uk

Background: Older children and adolescents are an underserved group in HIV programs and HIV-related mortality in this age-group continues to increase. We investigated the socio-demographic and clinical characteristics among 6-15 year olds who were diagnosed following optimum provider-initiated HIV testing and counselling (PITC) in seven primary care clinics in Harare, Zimbabwe.

Methods: HIV testing and counselling was offered to all children aged 6-15 years attending primary care regardless of reason for attendance, with guardian consent. All those who tested HIV-positive underwent a detailed socio-demographic and clinical assessment, including family and clinical history, HIV staging, and evaluation of growth and lung function.

Results: 379 children underwent a clinical assessment. The median age was 11.2 (IQR: 8.7-13.3) years and 48% were male. Nearly all (96%) were infected by mother-to-child transmission and 95% had a missed opportunity for previous HIV testing (see table).

Variable	N (%)
Visit to Primary Care Clinic in the past 6 months	270 (73%)
Previous TB	21 (6%)
Previous hospitalisation	100 (27%)
Parent or natural sibling on ART	244 (64%)
HIV suspected by guardian	253 (87%)
Had any of the above	361 (95%)

[Previous missed opportunities for HIV diagnosis]

221 (59%) were single-or double orphaned and only 53% had a biological parent as their current guardian. More than 50% of children had at least one change in guardianship. While the majority of children (90%) were going to school, 50% had missed a week or more of school in the past three months. Less than 50% of children affirmed knowledge of their HIV status. The median CD4 count was 380 cells/µl, with 34% having a CD4 count> 500 cells/µl. There was a high prevalence of chronic respiratory disease (16% had breathlessness (MRC Dyspnoea scale >1); 53% had cough; 31% were hypoxic (oxygen saturation < 88% at rest or following exercise).

Conclusions: There is significant delay in diagnosis of HIV in older children. HIV-infected children have complex social circumstances with orphanhood, changing guardianship and interrupted schooling and non-disclosure being common. In addition, there is additional morbidity such as chronic lung disease which is currently not addressed systematically by HIV care programs. HIV testing strategies for older children need to be developed and HIV care programs need to address complex social issues and clinical management should focus on co-morbidities as well as on delivery of antiretroviral therapy.

WEPEB397

Outcomes of foreign-born females in an antenatal program of a US HIV clinic

D. McGregor, S. Reddy, S. Sutton, R. Bhatia, B. Taiwo
Northwestern University, Division of Infectious Diseases, Chicago, United States
Presenting author email: d-mcgregor@northwestern.edu

Background: The proportion of foreign-born women in HIV and reproductive health programs in industrialized countries is steadily increasing. Female immigrants may be at particular risk for poor HIV outcomes due to social marginalization, psychological sequelae of trauma and loss, and gender-based violence. Our study aimed to determine if outcomes in pregnant HIV-infected (HIV+) immigrant women (IW) differed significantly from outcomes of United States (US) native-born women (NW) and if IW suffered from disproportionate levels of psychological co-morbidities.

Methods: We retrospectively analyzed medical record data of consecutive HIV+ women receiving outpatient antenatal care in the Northwestern Memorial Hospital Perinatal HIV Program in Chicago, USA in 2007-2012. All patients in the program had comparable insurance coverage and access to medical, social, and mental health services. Univariate analyses were used to compare sociodemographic characteristics, psychological co-morbidities, and clinical parameters of IW versus NW. For the end points that demonstrated a significant association with immigrant status, logistic regression was used to characterize adjusted effect.

Outcome Variable	OR	OR Direction	95% CI	P-Value	Effects For Which OR Is Adjusted
Undetectable Viral Load at week 36 gestation	3.59	Immigrant Women: Native- Born	(1.12, 11.50)	0.0314	Mental Health Diagnosis, DOT During Pregnancy
Employment	1.33	Immigrant Women: Native- Born	(0.64, 2.78)	0.4484	DOT During Pregnancy
Illicit Drug Use	19.39	Native- Born: Immigrant Women	(2.51, 149.59)	0.0045	Employment
Mental Health Diagnosis	2.83	Native- Born: Immigrant Women	(1.26, 6.36)	0.0116	None
DOT During Pregnancy	7.69	Native- Born: Immigrant Women	(1.52, 38.87)	0.0136	HIV RNA <50 at Week 36 Gestation, Employment

[Adjusted Multivariate Analysis]

Results: Our study cohort included 143 women (88 native-born, 55 immigrants). Mean age was 29 years. The majority of IW (63%) was from sub-Saharan Africa. Twelve percent of IW did not speak English. In univariate analysis, IW were significantly less likely than NW to present with mental illness, substance abuse, unintended pregnancy, or to require directly observed antiretroviral therapy (DOT) to ensure treatment adherence. There were no significant differences in timing of presentation for antenatal care, new HIV diagnosis, or AIDS diagnosis at initiation of care among groups. In multivariate adjusted analysis, IW had 3.59 times higher adjusted odds than NW of having an undetectable viral load at week 36 of gestation (95% CI: (1.12, 11.50). The majority of women in the cohort disclosed HIV status to partners (IW 82%; NW 72.2%). Adjusted multivariate analysis results are shown in Table 1.

Conclusions: Contrary to existing data, pregnant IW in our cohort demonstrated reduced odds of psychological co- morbidities or use of DOT during pregnancy and demonstrated significantly better third trimester virologic outcomes than US NW.

Trends in morbidity and mortality

WEPEC596

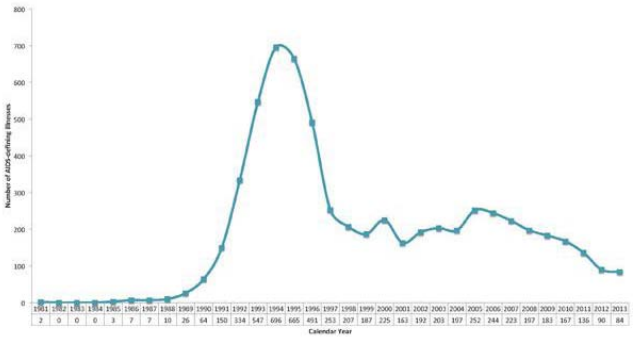
Trends in AIDS incidence and AIDS-related mortality in British Columbia between 1981 and 2013

V.D. Lima, L. Lourenco, B. Yip, R. Hogg, P. Phillips, J.S.G. Montaner
British Columbia Centre for Excellence in HIV/AIDS, Vancouver, Canada
Presenting author email: vlima@cfenet.ubc.ca

Background: Appropriate use of highly active antiretroviral therapy (HAART) can markedly decrease the risk of progression to acquired immunodeficiency syndrome (AIDS) and of premature mortality. We aimed to characterize the trends between 1981 and 2013 in AIDS-defining illnesses (ADIs) and in the number AIDS-related deaths in British Columbia (BC), Canada.

Methods: We included data of 3550 HIV-positive individuals, aged 19 years or older, from different administrative databases in BC. We estimated the relative risk of developing an ADI over time using a Negative Binomial model, and we investigated trends in the percentage of all deaths associated with AIDS using generalized additive models.

Results: The number of ADIs has decreased dramatically to its lowest level in 2013. The peak of the AIDS epidemic in BC happened in 1994 with 696 ADIs being reported (rate 42 ADIs per 100 person-years). Since 1997, the number of ADIs decreased from 253 (rate 7 per 100 person-years) to 84 cases in 2013 (rate 1 per 100 person-years) (p-value equals to zero for the trend in the number of ADIs). We have also shown that out of 22 ADIs considered, only PCP maintained its prominent ranking (albeit with much reduced overall prevalence). Finally, we observed that over time very few deaths were related to AIDS-related causes, especially in the most recent years.



[Overall trend in the number of ADIs]

Conclusions: We showed that the number of new ADIs and AIDS-related mortality have been decreasing rapidly over time in BC. These results provide further evidence that integrated comprehensive free programs that facilitate testing, and deliver treatment and care to this population can be effective in markedly decreasing AIDS-related morbidity and mortality, thus suggesting that controlling and eventually ending AIDS is possible.

WEPEC597

Diabetes mellitus increases death rates among HIV-infected patients in Rio de Janeiro, Brazil

A.G. Pacheco[1], B. Grinsztejn[2], S.W. Cardoso[2], R.I. Moreira[2], S. Ribeiro[2], E. Nunes[2], M.R. Guimarães[2], R.C. Moreira[2], A.A. Paula[1], F.C.Q. Mello[3], V.G. Veloso[2]
[1]Fiocruz, Programa de Computação Científica- PROCC, Rio de Janeiro, Brazil, [2]Fiocruz, Instituto Nacional de Infectologia, Rio de Janeiro, Brazil, [3]Universidade Federal do Rio de Janeiro, Instituto de Doenças do Tórax, Rio de Janeiro, Brazil
Presenting author email: rodrigo.moreira@ini.fiocruz.br

Background: Diabetes mellitus (DM) is a major morbidity worldwide and increases the risk of cardiovascular diseases (CVD) and death. Chronic comorbidities such as DM are becoming increasingly prevalent in the HIV population. We evaluated the prevalence of DM among HIV-infected patients and its association with mortality rates (MR).

Methods: All patients 18 year or older followed in the Instituto Nacional de Infectologia cohort from June 1986 to December 2011 were included. DM was determined through information abstracted from medical charts following Brazilian guidelines. Vital status was determined through information in the charts and recovery using a linkage algorithm. A standardized algorithm (CoDe) was used to classify causes of death (CODs). Time-updated covariables included DM status, calendar year, cART use and CD4 cell counts. Demographic covariables were gender and age at entry. Poisson models were used to calculate rate ratios (RR) with robust variances for mortality.
Results: Among the 4871 patients included, 1192 (24.4%) have died (MR = 4.72/100PY; 95%CI=4.46-5.00). Overall, DM prevalence was 10.2%; median age was 34.4 years and 67.5% were male (Table 1).

	Alive	Dead	Total	p-Value
Total	3679	1192	4871	
Diabetes Mellitus	383 (10.4%)	383 (10.4%)	498 (10.2%)	.49
Male	2413(65.65)	873(73.2%)	3286 (67.5%)	< .001
Schooling 9 years+	832 (23%)	302 (26.7%)	1134 (23.9%)	< .001
White	1944 (53.1%)	649 (54.7%)	2593(53.5%)	< .001
Age	34.4 (28.1,41.7)	35.8 (29.1,43.5)	34.8 (28.4,42.1)	< .001
CD4 counts (cells/mm3)	326 (142,542)	174 (54.5,362)	300 (117,520)	< .001
Ever on cART	3000 (81.5%)	542 (45.5%)	3542 (72.7%)	< .001
CDC criteria	1645(44.7%)	914(76.7%)	2559(52.5%)	< .001

[Table 1- Descriptive statistics]

MR were significantly higher among those presenting DM compared to those who did not (6.16/100PY vs. 4.61/100PY, p=0.001). In the final model, DM was significantly associated with mortality (RR=1.90;95%CI=1.54-2.34;p< 0.001). Male sex, older age, CD4 counts, cART use and higher education were also significantly associated.
When the analysis was restricted to those on cART, the association was even stronger (RR=2.27;95%CI=1.78-2.89;p<0.001). Among the major groups of CODs, AIDS-related conditions accounted for the bulk cases among patients with DM (74.27%) or without DM (58.93%), followed by non-AIDS-related (22.54% vs 34.82%, respectively) and unknown causes (3.19 vs 6.25%, respectively). AIDS malignancies, liver-related diseases and CVD occurred in a higher proportion in patients with DM (14.29%, 4.46% and 6.25%, respectively) compared to those without DM (5.26%, 1.5% and 3.95%).
Conclusions: DM was significantly associated to increased MR even after controlling for HIV-related variables associated to this outcome and also related to a distinct death profile. These findings highlight the need to assess and manage comorbidities in these patients, especially considering the proposal strategy of test and treat.

Measurement and modelling of the HIV epidemics

WEPEC598

Understanding the effects of different HIV transmission models in individual-based microsimulation of HIV epidemic dynamics among people who inject drugs

J.F. Monteiro[1,2], D. Escudero[1], C. Weinreb[1], T. Flanigan[2], S. Galea[3], S.R. Friedman[4], B.D.L. Marshall[1]
[1]Brown University, School of Public Health, Providence, United States, [2]Miriam Hospital, Division of Infectious Diseases, Providence, United States, [3]Boston University, School of Public Health, Boston, United States, [4]National Development and Research Institutes, Institute for Infectious Disease Research, New York, United States
Presenting author email: brandon_marshall@brown.edu

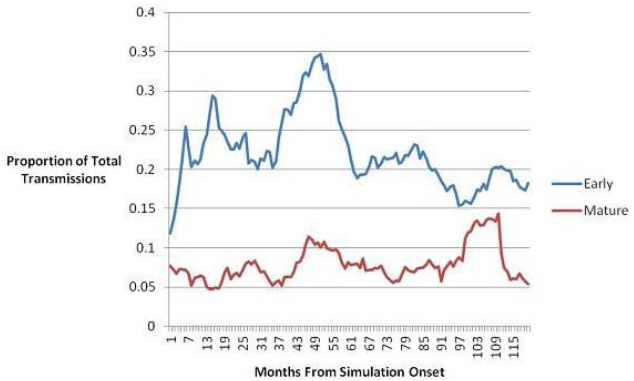
Background: We investigated how different models of HIV transmission, and subsequently various assumptions regarding the distribution of unprotected sex and syringe sharing events in a population, affect quantitative understanding and simulation of the HIV transmission process among people who inject drugs (PWID).
Methods: The individual-based model simulated HIV transmission in a dynamic sexual and injecting network representing an urban, mixed epidemic in North America (New York, 1992-2002). We considered a model for HIV transmission among PWID in which the per-partnership transmission probability followed a binomial distribution, and then constructed more sophisticated HIV transmission models as follows:
Model 1 — numbers of unprotected sex and the syringe sharing acts were constant within partnerships, and the per-act transmission probability varied by stages of HIV disease and by antiretroviral therapy adherence;
Model 2 — the numbers of unprotected sex and syringe sharing acts were random and assigned from Poisson distributions, and the per-act transmission probability was as in Model 1;
Model 3 — the per-act transmission probability was defined based on individual plasma HIV viral load, which has been randomly assigned; Model 4 — same as Model 3, but with two groups of partnerships: those with either higher (primary partner) or lower (casual partners) risk behavior profiles. HIV incidence trajectories outputted by each model were compared to that empirically observed.
Results: Models 1 and 2 were unable to reproduce HIV incidence and prevalence estimates observed among PWID in New York between 1992 and 2002. Overall, models with less heterogeneity were more sensitive to changes in numbers of sexual and parenteral acts, producing HIV incidence up to 4 times higher than that empirically observed. Conversely, Models 3 and 4 produced satisfactory estimates of HIV incidence, and showed less sensitivity to changes in key parameters. Compared to the empirical estimate, we observed a 545% relative bias in HIV incidence among PWID in 2002 from Model 2, compared to 35% for Model 4.
Conclusions: Although all models over-estimated HIV incidence, micro-simulations with greater heterogeneity in the HIV transmission modeling process, specifically transmission determined by individual viral loads, produced more robust results and better reproduced empirical epidemic dynamics.

WEPEC599

The contribution of transmission from acute HIV infection may vary by epidemic stage among people who inject drugs

D.J. Escudero[1], M.N. Lurie[1], C. Weinreb[2], K.H. Mayer[3,4,5], S.R. Friedman[6,7], S. Galea[8], B.D.L. Marshall[1]
[1]Brown University, Department of Epidemiology, Providence, United States, [2]Brown University, Providence, United States, [3]Fenway Health, The Fenway Institute, Boston, United States, [4]Beth Israel Deaconess Medical Center, Boston, United States, [5]Harvard Medical School, Department of Medicine, Boston, United States, [6]National Development and Research Institutes, Institute of Infectious Disease Research, New York, United States, [7]Johns Hopkins Bloomberg School of Public Health, Department of Epidemiology, Baltimore, United States, [8]Boston University School of Public Health, Boston, United States
Presenting author email: brandon_marshall@brown.edu

Background: HIV transmission risk is elevated during acute HIV infection (AHI), but the contribution of AHI to total transmission among people who inject drugs (PWID) remains unknown. Furthermore, the role that epidemic stage plays in determining this contribution has not been investigated. We constructed an agent-based model (ABM) to compare estimates of AHI-attributable infections to overall transmission among PWID in early versus mature epidemic stages.
Methods: The ABM was calibrated to approximate the risk behavior profiles and epidemic dynamics of early (i.e., low prevalence [3%], frequent risk behavior) and mature (i.e., high prevalence [41%], infrequent risk behavior) HIV epidemics within a large urban setting, over a ten-year period. The ABM consists of agents that interact in a dynamic sexual and injecting network representing a population of 100,000. Each agent has a time-dependent probability of transmitting or acquiring HIV, based on risk behavior, partnership characteristics, and engagement in simulated prevention interventions (i.e., HAART, needle/syringe programs), as well as disease stage. Using Monte Carlo stochastic microsimulations, we classified transmission events by disease stage (where AHI was assumed to last three months and have a ten-fold probability of transmission compared to chronic infection), and then compared the AHI transmission events (as a proportion of total transmissions) between the two stages.
Results: The models approximated the conditions of typical early and mature HIV epidemics among PWID over 10 year periods. For the mature epidemic, HIV prevalence decreased from 41% to 18% with an average annual HIV incidence of 2.3% per 100 person-years. In the early epidemic, HIV prevalence increased from 3% to 9% and incidence increased from 0.2% to 2.8% per 100 person-years. On average, AHI accounted for 22% and 8% of total transmissions in early and mature epidemic stages, respectively.



[Figure 1. Proportion of total HIV transmissions attributable to acute HIV infection among PWID, by epidemic stage and month]

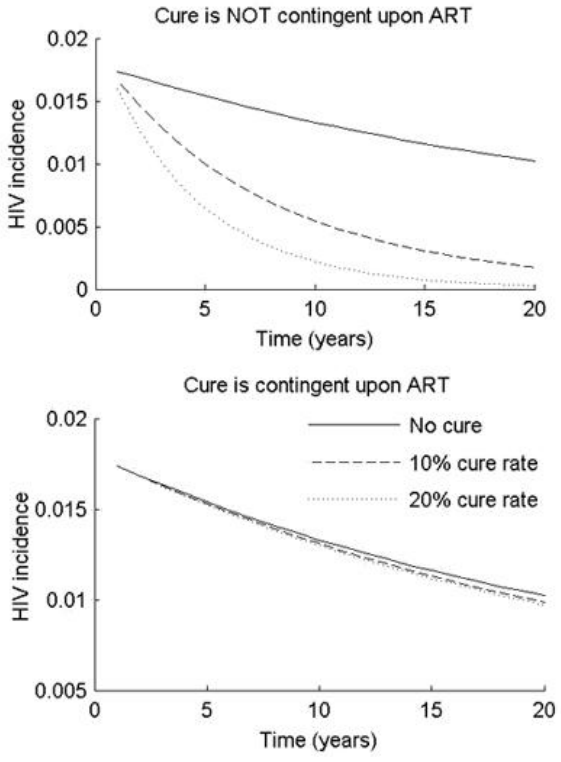
Conclusions: Our results suggest the contribution of AHI to total transmission among PWID varies by epidemic stage. Specifically, the contribution of AHI is greater in an early epidemic setting, compared to mature. These results suggest that prevention strategies seeking to reduce HIV transmission in epidemic growth phases should consider the potentially significant contribution from AHI. Further research is needed to corroborate these results among different epidemic settings.

WEPEC600

Widespread implementation of a curative regimen would have more significant effects on HIV-1 prevalence than incidence

D. Dimitrov[1], H.-P. Kiem[2], K. Jerome[1], J. Schiffer[1]
[1]*Fred Hutchinson Cancer Research Center, Vaccine & Infectious Disease Division, Seatle, United States,* [2]*Fred Hutchinson Cancer Research Center, Clinical Research Division, Seatle, United States*
Presenting author email: dobromir@scharp.org

Background: There is increased optimism that a cure for HIV-1 may be possible. Current strategies aim to achieve complete eradication of latent provirus, or at least provide a functional cure, in which latent HIV-1 is lowered below a threshold necessary for viral replication, progression to AIDS, and transmission. The potential impact of implementing cure programs on HIV-1 prevalence and incidence has not formally been considered.
Methods: We developed a compartmental mathematical model of HIV transmission in a sexually active population to evaluate the independent and synergistic impact of ART, pre-exposure prophylaxis (PrEP) and cure on HIV epidemics in high-prevalence settings. We explored scenarios with and without the assumption that ART treatment and viral suppression is required for cure. We calculated the basic reproduction number (R_0) to evaluate the potential for the HIV epidemic to be eliminated in each scenario. We analyzed the impact of curative treatment on the HIV prevalence and HIV incidence over extended timeframes.
Results: Implementation of curative regimes had limited impact on HIV-1 incidence if ART was a pre-requisite for cure. Treatment alone resulted in R_0 <1 only if more than 16 % of untreated individuals initiated ART annually. Even if 50% of treated patients were cured annually, the ART initiation rate required for elimination of HIV remained above 10%: under these conditions, HIV incidence was virtually unchanged during the first 20 years of cure implementation. Cure implementation had a significant impact on HIV-1 incidence only if pre-treatment with ART was not required (Fig.1). Annual ART and cure rates of 6% were sufficient to reduce R_0 <1 in absence of PrEP. Those rates were reduced to 4% if 60% effective PrEP was used by 20% of the population. Annual curative treatment rate of 10% alone was sufficient to eliminate the HIV epidemic and reduce HIV incidence by 50% over 20 years.
Conclusions: We project that gradual implementation of curative HIV-1 therapies would have a beneficial impact on HIV-1 prevalence but not incidence. Therefore, development of HIV-1 cure technologies should evolve in parallel with ongoing research to expand HIV prevention and ART availability.



[Figure 1]

Risk factors for acquisition of HIV

WEPEC601

HIV prevalence and risk behaviors among university students in Dire Dawa, Ethiopia, 2013

G. Assefa Dessie[1], T. Shenie[2], W. Demissie[3], B. Mengistu[4], L. Slater[5], L. Pessoa-Brandao[6], A.R. Sites[7], M. Argaw[8], W. Bekele[9]
[1]*National Alliance of States and Territorial AIDS Director (NASTAD), Strategic Information Specialist, Addis Ababa, Ethiopia,* [2]*National Alliance of States and Territorial AIDS Director, Country Director, Addis Ababa, Ethiopia,* [3]*National Alliance of States and Territorial AIDS Director, Planning, M&E, Addis Ababa, Ethiopia,* [4]*National Alliance of States and Territorial AIDS Director, Prevention Adviser, Addis Ababa, Ethiopia,* [5]*National Alliance of States and Territorial AIDS Director, Global Director, Washington DC, United States,* [6]*National Alliance of States and Territorial AIDS Directors, Global Program, Washington DC, United States,* [7]*National Alliance of States and Territorial AIDS Director, Country Lead, Ethiopia, Washington DC, United States,* [8]*Dire Dawa University, Medical Faculty Department Head, Dire Dawa, Ethiopia,* [9]*Dire Dawa University, President, Dire Dawa, Ethiopia*
Presenting author email: lpessoa-brandao@nastad.org

Background: HIV infection among young people aged 15-24 years is often attributed to sexual exposure and assumed to be recent infection. Behavioral changes, such as condom use and limiting sex partners, and improving access to HIV prevention services have been shown to reduce new infections.
But in Ethiopia, young people, including university students, are having sex with multiple partners and using condoms inconsistently; these behaviors increase their likelihood of acquiring HIV. This assessment is, therefore, aimed to explore the risk behaviors and HIV prevalence among the students.
Methods: During April 2013, a cross-sectional study was conducted among students of Dire Dawa University, one of 13 Ethiopian universities with 7,938 students enrolled. Using a previously estimated HIV prevalence of 2.5%, 95% confidence level, 80% power, 1% margin of error, and 5% anticipated non-response rate, a representative sample of 983 students was systematically chosen by selecting every eighth student in the sample frame. Data cleaning and analysis were conducted using SPSS 21.0. Ethical approval is obtained from Centers for Disease Prevention and Control Atlanta and from National IRB in Ethiopia.
Results: Of 983 sampled, 967 students participated, a response rate of 98.3%. Of 967 students participating, 961 (99.3%) were tested for HIV; 4 (0.4%) were HIV positive. Half of participants (49.9%) reported ever having sex and 53.0% reported having sex in the past 12 months. Females were more likely to report first having sex after coming to the university and not having used a condom during their first sexual intercourse, and males were more likely to report sex with multiple partners in the past 12 months and having ever used alcohol or drugs.
Conclusions: Despite the low prevalence, this study may inform university policies that address educational needs and environmental factors that can contribute to university students' increase risk of HIV infection. Engaging high school students, prior to their entry to the university setting, to introduce HIV prevention messages earlier may increase students' competency in prevention. Tailoring interventions to both female and male students' educational needs may increase the impact of services.

WEPEC602

Compulsive sexual behavior, substance use, depression and sexual risk-taking among young urban men who have sex with men: the P18 cohort study

E. Storholm[1], D. Satre[1], F. Kapadia[2], P. Halkitis[2]
[1]*University of California, Psychiatry, San Francisco, United States,* [2]*New York University, New York, United States*
Presenting author email: erik.storholm@ucsf.edu

Background: Previous behavioral research has shown that young gay, bisexual and other men who have sex with men (YMSM) are at increased risk for substance abuse, mental health burden, and the Human Immunodeficiency Virus (HIV). As informed by syndemic theory, this analysis sought to further delineate the impact of compulsivity in sexual risk-taking behavior among a new generation of YMSM ages 18-19.
Methods: The current analysis administered the Compulsive Sexual Behavior Inventory (CSBI) as well as additional psychological, psychosocial, alcohol/drug use, and sexual behavior measures to 509 racially and economically diverse, confirmed HIV-negative, YMSM sampled from the New York City metropolitan area. A multivariable model was tested to determine whether the use of alcohol and drugs mediated the relation between compulsive sexual behavior and sexual risk-taking.
Results: Alcohol and drug use were shown to significantly and completely mediate the relation between compulsive sexual behavior and condomless anal sex (b=0.069, t(507) = 1.54, p=0.125). A Sobel test was conducted and found full mediation in the model (z = 2.75, p=0.01). In addition, depression was shown to moderate the relation between compulsive sexual behavior and sexual risk-taking (ΔR^2 =0.008, ΔF(1, 505) = 4.004, p<0.05), where higher rates of

depression were associated with significantly more condomless anal sex among those YMSM who scored high in sexual compulsivity.
Conclusions: Findings suggest that compulsive sexual behavior in concert with depressive symptoms and substance use exacerbate risk for sexual risk-taking among YMSM. Clinicians must take a holistic approach when providing care and need to address the underlying psychological symptoms that exacerbate risk behaviors in order to reduce HIV-risk among this new generation of YMSM.

WEPEC603

Temporary migration, multiple sexual partnerships, and sexual concurrency in the Garífuna population of Honduras

A. Gandhi[1], A. Pettifor[2], C. Barrington[3], S. Marshall[2], F. Behets[2], M.E. Guardado[4,5], E. Ardón[6], G. Paz-Bailey[4]
[1]Columbia University/NY State Psychiatric Institute, HIV Center for Clinical and Behavioral Studies, New York, United States, [2]University of North Carolina at Chapel Hill, Department of Epidemiology, Chapel Hill, United States, [3]University of North Carolina at Chapel Hill, Department of Health Behavior, Chapel Hill, United States, [4]Training Programs in Epidemiology and Public Health Interventions Network (TEPHINET), Guatemala City, Guatemala, [5]Task Force for Global Health, Guatemala City, Guatemala, [6]Ministry of Health, Honduras, Department of STI/HIV/AIDS, Tegucigalpa, Honduras
Presenting author email: adg2185@columbia.edu

Background: Within Latin America, Honduras has historically been one of the countries most severely affected by HIV. The Garífuna, an Afro-indigenous minority group, have been identified as a priority population for HIV prevention and control efforts in Honduras. In 2012, the HIV prevalence among Garífuna adults in Honduras was estimated at 4.1%, while the national prevalence had declined to 0.5%. HIV transmission among the Honduran Garífuna is attributed to high rates of mobility, though empirical evidence is limited. The objective of this study was to assess the relationship between temporary migration and having multiple sexual partnerships or concurrent partnerships among Garífuna men and women.
Methods: Data were collected through a population-based surveillance study of sexual behavior and HIV/STI prevalence in vulnerable populations in Honduras from September-December 2012. Garífuna men and women were recruited from households in randomly-selected urban districts and rural communities, and responded to a comprehensive standardized survey. The primary exposure - recent temporary migration - was defined as spending more than one month away from home in the last 12 months. Primary outcomes were
1) multiple sexual partnerships and;
2) concurrent sexual partnerships in the last 12 months.
Weighted multivariable binomial regression models were used to produce adjusted prevalence ratios (APRs).
Results: We analyzed data from 230 men and 399 women. Fifteen percent of men and 8.5% of women were recent migrants. Men were more likely to report multiple sexual partnerships in the last 12 months compared to women (31.7% vs. 6.2%). Both migrant men and women had an increased likelihood of multiple sexual partnerships in the last 12 months (APR among men 1.7, 95% CI 1.2-2.4; among women APR 3.0, 95% CI 0.7-12.4), compared to non-migrants. Among those with sufficient information on partnerships, 18.0% of men and 2.9% of women reported concurrent sexual partnerships. Migration was associated with concurrency among both men and women, though precision was poor for the corresponding effect estimates.
Conclusions: Multiple and concurrent sexual partnerships were more prevalent among male and female Garífuna migrants compared to non-migrants. Future research focused on HIV/STI vulnerability in Latin America should continue to incorporate measures of short- and long-term mobility.

WEPEC604

Women in peril: high levels of HIV infection risk among the male sex partners of low-income, Black women in the United States

P. Denning, K. Hess, G. Paz-Bailey, for the NHBS Study Group
U.S. Centers for Disease Control and Prevention, Division of HIV/AIDS Prevention, Atlanta, United States
Presenting author email: pdenning@cdc.gov

Background: In the United States (U.S.), black women are disproportionately affected by HIV transmitted through heterosexual contact. To assess the risk of heterosexual transmission to low-income, black women, we sought to determine whether their male sex partners were at high risk for HIV infection.
Methods: We analyzed data from women and their male sex partners who participated in the U.S. National HIV Behavioral Surveillance System (NHBS) in either 2010 or 2013. Participants were 18-60 years old, of low socioeconomic status, and recruited using respondent driven sampling. We restricted our analysis to women who were black, tested HIV-negative, did not have a history of injecting drugs, and had a male sex partner who also participated in NHBS. Men at high risk for HIV infection were defined as men who ever had sex with another man (MSM) and persons who ever injected drugs (PWID). Factors associated with having a high-risk male sex partner were analyzed using generalized estimating equations with a Poisson distribution.
Results: Of the 901 women who met our inclusion criteria, 153 (17%) had a high-risk male sex partner (7% of the male sex partners were MSM, 7% PWID, and 4% both MSM and PWID). In multivariable analysis, factors associated with having a high-risk male sex partner were age 40-60 years (Adjusted Prevalence Ratio [APR]=2.6, 95% Confidence Interval [CI]=1.6-4.1), exchanging sex for money or drugs in the year before interview (APR=1.8, 95% CI=1.3-2.5), and having a household income less than U.S.$10,000 (APR=1.4, 95% CI=1.1-1.8). In a subset of 330 women with additional sex partner data, just 2 (10%) of 20 women with an MSM partner were aware of his history of same-sex behavior and 11 (42%) of 26 with a PWID partner were aware of his history of injecting drugs.
Conclusions: Nearly 1 in 5 black women included in our analysis had a male sex partner at high risk for HIV infection, yet the women's awareness of their partner's risk was low. Older and socially and economically vulnerable women were especially likely to have a high-risk male sex partner. These women would greatly benefit from increased interventions, like couples HIV testing and prevention counseling.

WEPEC605

HIV incidence is low and stable in young adults who inject drugs in San Francisco: UFO study 2000-2014

A. Mirzazadeh[1], J. Evans[2], J. Jain[1], J. Hahn[2], S. Shiboski[2], C. Bentsen[3], K. Shriver[3], M. Dimpasoc[4], M. Stone[4], M.P. Busch[4,5], K. Page[6]
[1]University of California San Francisco, Global Health Sciences, San Francisco, United States, [2]University of California San Francisco, Department of Epidemiology and Biostatistics, San Francisco, United States, [3]Bio-Rad Laboratories, Redmond, United States, [4]Blood Systems Research Institute, San Francisco, United States, [5]University of California San Francisco, Department of Laboratory Medicine, San Francisco, United States, [6]University of New Mexico Health Sciences Center, Epidemiology, Biostatistics & Preventive Medicine, Albuquerque, United States
Presenting author email: ali.mirzazadeh@ucsf.edu

Background: The CDC's National HIV Surveillance System shows that HIV infection among people who inject drugs (PWID) has been declining. We assessed HIV incidence, trends and primary risk factors from data collected in an ongoing prospective observational study (The UFO Study) of young adult PWID in San Francisco.
Methods: Young (< 30 years) PWID who were HCV negative were enrolled the study with survey and blood specimens collected quarterly. For this analysis we included all those who were HIV negative at baseline, enrolled and followed between 2000 and 2014, who had ≥2 visits. Date of incident HIV infection was estimated as the midpoint between last documented seronegative and first seropositive blood sample. Negative participants were censored at the last study visit date. Risk exposures were based on self-reported data. HIV infection was determined using GS HIV Combo Ag/Ab EIA (4th gen assay) with GS HIV-1 Western Blot confirmation.
Results: Overall, 10 seroconverters were identified over the 1074.8 py follow up time in 561 individuals, for an estimated HIV infection rate of 0.9/100 py (95% CI, 0.5-1.7). HIV incidence was highest among Latino or Hispanic 7.9/100py (95% CI 3.3-19.0), African-American 4.7/100py (95% CI 1.2-18.7), followed by men who reported any sex with men (MSM) (3.0/100py; 95% CI 1.5-6.0). HIV incidence was stable between 2000-2 (0.6%, 95% CI 0.2-2.5) and 2012-14 (1.1%, 95% CI 0.3-4.2), with a pick in 2003-5 (2.3%, 95% CI 0.9-5.4). The IRR of MSM vs. non-MSM was 11.4 (95% CI, 2.4-53.8; P< 0.001).
Conclusions: HIV infection rates were low (under 1%) in young PWID in San Francisco over the observation period. However rates were high in young male PWID who also report sex with men, Latino and African-Americans. These results show the ongoing risk of HIV in association with overlapping drug and sexual exposures. The trends overall are comparable to those seen nationally, reflecting declines. HIV prevention efforts in San Francisco and elsewhere should be scaled up to reach this younger high risk population, who are also experiencing high rate of other blood borne infections, including viral hepatitis.

WEPEC606

Household socioeconomic status, sexual behavior, and prevalence of HIV and HSV-2 among sexually experienced South African school girls: HPTN 068

N. Nguyen[1], H. Thirumurthy[2], X. Gomez-Olive[3,4], C. MacPhail[5,6], J. Hughes[7], E. Piwowar-Manning[8], A. Selin[9], R.G. Wagner[3], K. Kahn[3,10,11], A. Pettifor[1]
[1]University of North Carolina, Epidemiology, Chapel Hill, United States, [2]University of North Carolina, Health Policy and Management, Chapel Hill, United States, [3]MRC/Wits Rural Public Health and Health Transitions Research Unit (Agincourt), Johannesburg, South Africa, [4]INDEPTH-Network, Accra, Ghana, [5]University of New England, School of Health, Armidale, Australia, [6]Wits Reproductive Health and HIV Institute, Johannesburg, South Africa, [7]University of Washington, Biostatistics, Seattle, United States, [8]Johns Hopkins University, School of Medicine, Pathology, Baltimore, United States, [9]University of North Carolina, Chapel Hill, United States, [10]Umeå University, Umeå Centre for Global Health Research, Division of Epidemiology and Global Health, Department of Public Health and Clinical Medicine, Umeå, Sweden, [11]INDEPTH Network, Accra, Ghana
Presenting author email: nadia.nguyen@unc.edu

Background: Poverty is hypothesized to increase young women's risk of HIV infection; however, little is known about the association between socioeconomic status (SES) measures and HIV risk among adolescent girls in sub-Saharan Africa.
Methods: Within a randomized controlled trial of conditional cash transfers to reduce HIV risk among adolescent girls (HPTN 068), we used baseline data to determine the association between three indicators of SES and self-reported sexual behavior as well as prevalent HIV and HSV-2 infection. The study took place in the Agincourt Health and Socio-Demographic Surveillance Site in South Africa, a rural area characterized by high poverty; 80% of households receive income support from the national Child Support Grant (CSG) - a non-contributory social support grant. We measured household SES using three indicators: monthly per-capita consumption expenditures, asset ownership, and parent/guardian education. We used logistic regression to estimate prevalence odds ratios (OR), controlling for orphan status, age, CSG receipt, and the other SES indicators.
Results: Among 693 sexually experienced high school girls, those from households with more assets had significantly lower odds of HSV-2 infection (OR=0.68, 95%CI: 0.48, 0.98), pregnancy (OR=0.76, 95%CI: 0.58, 0.99) and had lower odds of HIV infection (OR=0.61, 95%CI: 0.36, 1.015). Girls whose parent/guardian obtained any education had significantly lower odds of sexual debut before age 15 (grade 1-11: OR=0.57, 95%CI: 0.36, 0.90; grade 12 and above: OR=0.50, 95%CI: 0.27, 0.94; among girls 15+), and had lower odds of HIV and HSV-2 infection and pregnancy (results not statistically significant). The associations with consumption expenditures were generally not significant, but higher expenditures were associated with lower odds of HIV and HSV-2 infection and pregnancy.
Conclusions: In this study, greater household wealth, measured by asset holdings, and parent/guardian education was associated with decreased odds of HIV infection and sexual risk factors. However, the specific SES measure used and the widespread coverage of social protection programs such as the CSG may be critically important in determining the association with HIV risk outcomes. SES measures that are typically used to measure poverty, such as consumption expenditures, may have a weaker association with HIV risk due to the effect of social protection programs.

WEPEC607

How common and frequent is heterosexual anal sex among South Africans? A systematic review and meta-analysis

B.N. Owen[1], R.F. Baggaley[2], I. McGowan[3], B. Shacklett[4], M.-C. Boily[1]
[1]Imperial College London, Department of Infectious Disease Epidemiology, London, United Kingdom, [2]London School of Hygiene and Tropical Medicine, Department of Infectious Disease Epidemiology, London, United Kingdom, [3]University of Pittsburgh School of Medicine, Department of Medicine, Pittsburgh, United States, [4]University of California, Department of Medical Microbiology and Immunology, Davis, United States
Presenting author email: b.owen11@imperial.ac.uk

Background: HIV is transmitted more effectively during anal intercourse (AI) than vaginal intercourse. However, the role that AI plays in heterosexual HIV epidemics remains incompletely understood. We aimed to determine the proportion of adults in South Africa (SA) reporting heterosexual AI and how frequently it is practised.
Methods: We searched PubMed for studies published from 1990 to December 2014 reporting data on the proportion of SA adults (aged 18+) practising heterosexual AI (i.e. AI prevalence) and on the number of AI acts (i.e. AI frequency). Where two or more estimates were available, we pooled estimates of AI prevalence using random-effects models.
Results: Of the 1367 records identified, 27 articles were included. Twelve reported on higher-risk populations, mainly FSW [N=5] and STI patients [N=4]. Nineteen reported on females, 10 on males, and 5 on genders combined. The 27 articles included 47,104 study participants aged 18-59. Fourteen articles reported on AI frequency and 15 on AI prevalence.
Pooled AI prevalence tended to be higher over shorter recall periods (lifetime[N=2]=2.3% [95%CI:1.5-3.1]; past month[N=2]=10.4% [95%CI:2.5-18.3]; with current partner[N=2]=17.8% [95%CI:7.5-28.2]) among the general population (Figure). This appeared to be confounded by confidentiality of interview method.

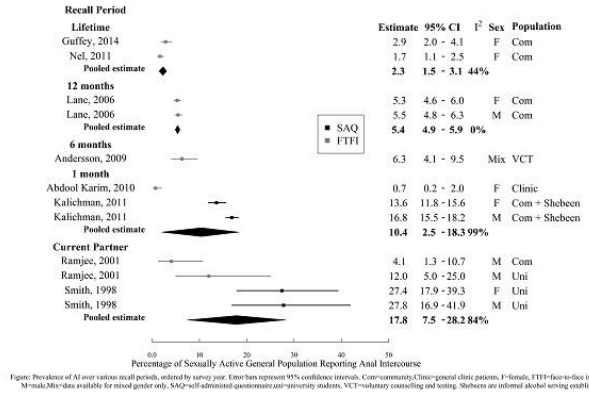


Figure: Prevalence of AI over various recall periods, ordered by survey year. Error bars represent 95% confidence intervals. Com=community;Clinic=general clinic patients; F=female, FTFI=face-to-face interview, M=male;Mix=data available for mixed gender only, SAQ=self-administered questionnaire,uni=university students, VCT=voluntary counselling and testing. Shebeens are informal alcohol serving establishments.

[ForestPlot_AI_in_SA]

Among higher-risk respondents, AI prevalence was reported across too many different recall periods to pool (female range[N=4]=5.8-42.8%; male range[N=2]=21.6-28.4%).
Among the general population, the reported number of total AI and unprotected AI (UAI) acts ranged between 0.3-1.3 and 0.1-0.7 per month, respectively (N=4). The fraction of all sex acts that were AI among whole samples (i.e. including those reporting no AI) was 4.4-16.7% across studies [N=6]. The fraction of all unprotected acts that were UAI ranged from 4.5% to 21.0% [N=8]. Among higher-risk respondents, number of AI acts/month was 0.1-16.8, with 1.6-29.2% [N=4] of all sex acts being AI, and 0.1-40.0% of unprotected acts being UAI [N=4].
Conclusions: AI is common and frequent among South Africans and could therefore be a determinant in the country's HIV epidemic. Given its higher transmission risk and common practice, it is imperative that messaging on safe AI be included in HIV interventions and that products which enable safer AI be developed.

WEPEC608

Association of condom use with changing sexual roles among MSM, transgenders and hijras in India: findings from the midline study of the Global Fund-supported Pehchan programme

A. Biswas[1], N. Kumar Mattipalli[1], B. Ubarhande[1], K. Biswas[1], R. Sarkar[2], A. Aher[2], S. Mehta[2], J. Robertson[3]
[1]India HIV/AIDS Alliance, Strategic Information, New Delhi, India, [2]India HIV/AIDS Alliance, Programme, New Delhi, India, [3]India HIV/AIDS Alliance, New Delhi, India
Presenting author email: anindita.b25@gmail.com

Background: HIV prevalence among MSM and transgenders is disproportionately high at 4.43% and 8.82% respectively in comparison to the national prevalence of 0.3% in India. India HIV/AIDS Alliance in consortium with five partner organizations implements the five-year Global Fund-supported Pehchan programme in 18 Indian states to build the capacity of 200 CBOs to serve as effective HIV prevention partners with the National AIDS Control Programme and reach more than 450,000 MSM, transgenders and hijras (MTH) using a community-driven and rights-based approach. Pehchan conducted a midline study (2012) to determine the effectiveness of the programme's strategy for priority interventions including condom use, sexual behaviours, and HIV risk reduction strategies.
Methods: A mixed method of evaluation was adopted using a cross-sectional study that sampled 601 MSM, transgender and hijra respondents covering 23 districts across six states in community-based organisations that had provided services through Pehchan for at least six months. Probability Proportion to Size (PPS) method and systematic random sampling were used. Qualitative techniques of data collection namely 72 focus group discussions, 84 key informant interviews, 24 in-depth interviews, and five case studies were used. Descriptive and correlation analysis was done using SPSS.
Results: Anal sex with regular partners and non-regular partners was reported to be 96% and 95% respectively. Consistent condom use during anal sex in the previous month in which respondents were engaged in a receptive role with regular partners and non-regular partners was reported to be 58% and 64% respectively. Consistent condom use during anal sex in the previous month in which respondents engaged in an insertive role with regular partners and non-regular partners stood significantly lower at 30% and 34% respectively. Average sexual acts when MSM, TG/H played receptive role with regular and non-regular partners ranged from 5 to 9 and 8 to 16 respectively. When MTH played an insertive role, average sexual acts ranged from 1 to 3 with varied partners
Conclusions: Data suggest that MTH vary condom practices with changing sexual roles, especially reduced condom use by those in insertive roles increasing vulnerability to HIV. Appropriate interventions including targeted prevention messaging must be undertaken to address high-risk practices among MTH.

WEPEC609

Mental health and sexual risk behaviors among networks of young men in Dar es Salaam, Tanzania

L. Hill[1], S. Maman[1], M.N. Kilonzo[2], L.J. Kajula-Maonga[2]
[1]UNC Chapel Hill, Health Behavior, Chapel Hill, United States, [2]Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania, United Republic of
Presenting author email: hilllm@email.unc.edu

Background: 7% of the population of Dar es Salaam is living with HIV, and youth account for 60% of new HIV infections in Tanzania. Young men in Tanzania report infrequent condom use and high levels of sexual partner concurrency, both important risk factors for HIV-infection. Though there is evidence that mental health may be an important predictor of these behaviors, this has rarely been shown in the sub-Saharan context. We examined the associations between mental health (anxiety and depression) and sexual risk behaviors (condom use and concurrency) in a population of young men in Dar es Salaam.
Methods: Participants in this study are male members of 60 "camps," or social groups occupying designated physical spaces where they socialize regularly, in Dar es Salaam, Tanzania. After random selection of camps, eligible members completed a computer assisted personal interview in the fall of 2013. Measures of condom use and concurrency were self-reported. Anxiety and depression were measured using sub-scales of the Hopkins Symptom Checklist-25. Hypotheses were tested using hierarchical linear modeling to account for the nested structure of the data.
Results: A total of 1280 men were interviewed at baseline. Using common clinical cutoffs, 21% of men displayed symptoms of anxiety, and 22% showed symptoms of depression. On average, men reported condom use for 42% of sex acts (SD=16) and 20% of men reported ever engaging in sexual partner concurrency. Controlling for key demographic variables, both anxiety and depression significantly predicted condom use (β= -0.12 and -0.11, respectively; p< .0001 in both cases), and concurrency
(β= 0.83 and 0.69, respectively; p< .0001 in both cases). Specifically, as levels of anxiety or depression increased, frequency of condom use decreased and the likelihood of reporting concurrency increased.
Conclusions: These findings further our understanding of the mental health determinants of HIV risk in a population of high risk young men. Our results indicate intervention targeting mental health as a potential strategy to reduce key HIV risk behaviors among the growing population of male youth in sub-Saharan urban areas.

WEPEC610

Newly HIV-infected gay, bisexual, and other men who have sex with men (MSM) in Vancouver, British Columbia: preliminary findings of the Momentum Health study

N. Lachowsky[1,2], K. Stephenson[3], A. Rich[1], A. Lal[1], Z. Cui[1], G. Colley[1], P. Sereda[1], J. Brown[4], J. Jollimore[5], D. Hall[3], J. Montaner[1,2], E. Roth[6,7], R. Hogg[1,8], D. Moore[1,2]
[1]British Columbia Centre for Excellence in HIV/AIDS Research, Vancouver, Canada, [2]Faculty of Medicine, University of British Columbia, Vancovuer, Canada, [3]Vancouver Coastal Health, Vancouver, Canada, [4]YouthCo Society for HIV and Hep C, Vancouver, Canada, [5]Health Initiative for Men, Vancouver, Canada, [6]Department of Anthropology, Faculty of Social Sciences, University of Victoria, Victoria, Canada, [7]Centre for Addictions Research BC, Victoria, Canada, [8]Faculty of Health Sciences, Simon Fraser University, Burnaby, Canada
Presenting author email: arich@cfenet.ubc.ca

Background: We measured HIV incidence among participants in a prospective cohort of MSM in Vancouver, British Columbia and explored characteristics associated with HIV seroconversion.
Methods: The Momentum Health Study employs respondent-driven sampling to recruit participants into a longitudinal bio-behavioural cohort study with 6-monthly visits. At baseline, participants completed a computer-assisted questionnaire and nurse-administered sexual health check-up including a point-of-care HIV test. Seroconvertors were participants who tested HIV-negative at baseline and HIV-positive at a subsequent study visit or another testing source between visits. Behavioural data are drawn from their most recently completed questionnaire prior to HIV diagnosis. Comparisons between HIV seroconvertors and men who remained HIV-negative were made using non-parametric statistical tests (p< 0.05).
Results: As of December 7, 2014, 378 MSM who tested HIV-negative at baseline contributed a mean follow-up time of 1.27 years. The HIV incidence rate was 1.25 per 100 person-years (6 MSM seroconverted; 95% CI 0.56-2.77). Although not significantly different when compared with MSM who remained HIV negative, all seroconvertors identified as gay, 5/6 as Caucasian, and 5/6 were aged ≤30 years. The HIV incidence rate for MSM aged ≤30 was 2.40 per 100 person-years (95% CI 0.90-5.17). Compared with MSM who remained HIV-negative, MSM who seroconverted reported a greater median number of sexual partners in the past six months (15.5 vs 4.0, p=0.01), reported a greater median number of anal sex events with sexual partners in the past six months (47.5 vs 7.0, p=0.02), and felt at high risk for HIV (50.0% vs 8.0%, p< 0.01). Five sero-convertors had heard about Treatment as Prevention, four of post-exposure prophylaxis, and two of pre-exposure prophylaxis. There were no significant differences in the proportion of participants reporting any condomless anal intercourse, other socio-demographics, substance use patterns, mental health diagnoses, or reported prevention / risk reduction practices.
Conclusions: Recent HIV seroconvertors were younger MSM with frequent partner change and greater rates of anal intercourse who appeared to understand that they were at higher risk for HIV acquisition. The level of awareness regarding effective biomedical prevention strategies among HIV seroconvertors was incomplete. These findings can help target further HIV prevention programs towards such individuals.

WEPEC611

Experiences with food insecurity and risky sex among low-income people living with HIV/AIDS in the San Francisco Bay Area: a qualitative study

H. Whittle[1], K. Palar[2], E. Frongillo[3], L. Lemus Hufstedler[2], T. Napoles[2], R. Hecht[2], S. Weiser[2]
[1]University of California, Global Health Sciences, San Francisco, United States, [2]University of California, Division of HIV/AIDS, Department of Medicine, San Francisco, United States, [3]University of South Carolina, Department of Health Promotion, Education, and Behavior, Arnold School of Public Health, Columbia, United States
Presenting author email: sheri.weiser@ucsf.edu

Background: Forty-nine million individuals are classified as food insecure in the United States, where both food insecurity and HIV/AIDS are prevalent among the urban poor. Previous studies have demonstrated that food insecurity is associated with risky sexual practices among people living with HIV/AIDS (PLHIV). However, no qualitative studies to date have explored the mechanisms underlying this relationship either in a resource-rich setting or among populations that include men who have sex with men (MSM).
Methods: Semi-structured in-depth interviews were conducted with 28 male and 6 female low-income PLHIV receiving food assistance from a non-profit organization in the San Francisco Bay Area. The interviews explored experiences with food insecurity and perceived associations with sexual risk behaviors. Interviews were conducted in English, audio-recorded and transcribed verbatim. Transcripts were coded and analyzed according to content analysis methods using an inductive-deductive approach.
Results: Food insecurity was reported to be a strong contributor to risky sexual practices among both MSM and female participants. Individuals described engaging in transactional sex (both sex work and more opportunistic encounters with casual partners) in order to alleviate food insecurity, exchanging sex for food or money to buy food and sometimes also obtaining shelter during the encounter. Transactional sex often co-occurred with destitution and homelessness. Participants also described how the experience of food insecurity could lead to unprotected sexual activity despite knowledge of and desire to engage in safe sexual practices. Specifically, hunger could compromise an individual's ability to insist on condom use with a casual partner, largely because the need to obtain food in the short-term was prioritized over the need to use protection.
Conclusions: Our data extend previous research by demonstrating that food insecurity may contribute to risky sexual practices among urban poor individuals in the resource-rich context, including among MSM. The mechanisms describing how food insecurity may contribute to transactional and unsafe sex underscore the importance of public health intervention efforts focused on structural inequalities.

WEPEC612

Low frequency of consistent condom use during heterosexual intercourse in prison among male inmates in a State Prison System in Mexico

P. Belaunzarán-Zamudio[1,2], J. Mosqueda-Gómez[3,4], A. Macias-Hernandez[4], J. Sierra-Madero[5], A. Saifuddin[6], C. Beyrer[7]
[1]Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Infectious Diseases, Mexico, Mexico, [2]Johns Hopkins Bloomberg School of Public Health, International Health, Baltimore, United States, [3]Centro de Ambulatorio de Prevención y Atención en SIDA e Infecciones de Transmisión Sexual León, León, Mexico, [4]Universidad de Guanajuato, León, Mexico, [5]Instituto Nacional de Ciencias Médicas y Nutrción Salvador Zubirán, Infectious Diseases, Mexico, Mexico, [6]Johns Hopkins Bloomberg School of Public Health, Baltimore, United States, [7]Johns Hopkins Bloomberg School of Public Health, Epidemiology, Baltimore, United States
Presenting author email: p_belaunzaran@yahoo.co.uk

Background: Inmates are at high-risk for HIV and STIs. To prevent the sexual transmission of HIV and STIs inside prisons, conjugal visits have been recommended in prisons where sex is forbidden. However, little is known about condom use in prisons where conjugal visits are in place.
Methods: Cross-sectional study to estimate the proportion of male inmates who always use condom use for heterosexual intercourse during imprisonment, and identify factors associated to unsafe sex. We collected data on sex behavior with structured interviews from inmates

in the 10 prisons of the state of Guanajuato, Mexico (Sep 2011-Feb 2012). Condom use and other variables are described as weighted proportions, using regression models to identify factors associated with consistent condom use.
Results: Among 2,107 participants, 1,670 (63.8%, 95%CI=58.8-68.9) have had sex in prison, most of them (1,628, 97.8%, 95% CI=95.6-99.8) with women. Only 149 inmates (8.9%, 95%CI=5.2-12.6) consistently used condom for heterosexual intercourse and 984 (56.5%, 95%CI=48.1-64.9) never did so. In the multivariate analysis, those who reported using drugs during incarceration, had decreased odds of having always used condom for sex with women (OR=0.5, [95%CI=0.3-0.9]) and a slightly decreased odds of having any condom use (OR=0.8, [95%CI=0.7-0.9]), independently of age, education, self-perceived risk of HIV, previous incarcerations, time of incarceration and consistency of condom use before incarceration. Increasing age and longer time of incarceration were also associated to lower consistent condom use. Inmates who answered having always used condom before incarceration used it more likely (OR=7, 95%CI=4.4-11.3) for sex with women during incarceration than those who reported not having always used condom before incarceration.
Conclusions: Most inmates in these prisons with conjugal visits are sexually active during their imprisonment and the vast majority had consensual heterosexual sex, but less than 10% consistently used condoms with their female partners. Drug use was associated with inconsistent condom use. Preventive programs should include improved education, and clear policy for open, free and discreet condom distribution as well as drug use therapy.

Risk factors for infectivity, progression and transmission of HIV

WEPEC613

Health insurance, ADAP and HIV viral load among women in the Women's Interagency HIV study, 2006-2009

C. Ludema[1], S.R. Cole[2], J.J. Eron Jr.[1], A. Edmonds[2], G.M. Holmes[3], K. Anastos[4], J. Cocohoba[5], M.H. Cohen[6], H. Cooper[7], E.T. Golub[8], S. Kassaye[9], D. Konkle-Parker[10], L. Metsch[11], J. Milam[12], T.E. Wilson[13], A.A. Adimora[1]
[1]University of North Carolina, Medicine, Chapel Hill, United States, [2]University of North Carolina, Epidemiology, Chapel Hill, United States, [3]University of North Carolina, Health Behavior and Health Education, Chapel Hill, United States, [4]Albert Einstein College of Medicine, Medicine and Epidemiology & Population Health, New York, United States, [5]University of Caifornia, Clinical Pharmacy, San Francisco, United States, [6]Cook County Heath and Hospital System and Rush University, Medicine, Chicago, United States, [7]Emory University, Behavioral Sciences and Health Education, Atlanta, United States, [8]Johns Hopkins Bloomberg School of Public Health, Epidemiology, Baltimore, United States, [9]Georgetown University, Medicine, Washington DC, United States, [10]University of Mississippi Medical Center, Infectious Diseases, Jackson, United States, [11]University of Miami, Epidemiology and Public Health, Miami, United States, [12]University of Southern California, Medicine, Los Angeles, United States, [13]State University of New York Downstate Medical Center, Community Health Sciences, Brooklyn, United States
Presenting author email: ludema@email.unc.edu

Background: Health insurance is crucial for optimizing health outcomes for those with HIV. While research has shown that health insurance and the AIDS Drug Assistance Program (ADAP) provide needed access to antiretroviral therapy (ART), the effect of insurance on viral load has not been explored. To provide a comparator for future research on the effects of the Affordable Care Act (ACA), we provide estimates of the effects of health insurance on HIV viral load among women prior to ACA implementation.
Methods: For all HIV infected participants active in the Women's Interagency HIV Study (WIHS) (n=1,481), insurance data were categorized into non-overlapping groups at the index date in 2006. We used Cox proportional hazards models to estimate the time from 2006 to unsuppressed viral load (>200 copies/mL) among those with Medicaid, private, Medicare/other public insurance, and no insurance, stratified by use of ADAP. We did not adjust for ART and included participants regardless of ART use as medication access is a consequence of health insurance and is part of its effect.
Results: In 2006, 65% of women had Medicaid; 18% had private insurance, and 14% reported no health insurance. Approximately 70% of women in each insurance group reported receiving ART at the index date. ADAP coverage was reported by 270 women (20%); 56% of uninsured participants reported ADAP coverage. After adjustment for study site, age, race, lowest observed CD4, and type of health insurance and viral load before the index date, those who were privately insured without ADAP had a hazard of 0.77 (95% CI: 0.60-0.98) for unsuppressed viral load compared to those on Medicaid without ADAP (referent group). Among the uninsured, those with ADAP had a marginally lower relative hazard of unsuppressed viral load (HR, 95% CI: 0.80, 0.59-1.08) than those without ADAP (HR, 95% CI: 0.94, 0.69-1.28). When restricted to women with a nadir CD4< 350, similar results, though less precise, were observed.
Conclusions: While women with private insurance are the least likely to experience unsuppressed viral load, ADAP also contributes to viral load suppression. Continued funding for ADAP is recommended, and may be especially critical for states that have not expanded Medicaid.

WEPEC614

Decrease in the proportion of HIV-positive MSM followed up in hospital likely to transmit HIV between 2003 and 2011 in France: results from national representative surveys (ANRS VESPA-1 and VESPA-2)

M. Suzan-Monti[1,2,3], B. Demoulin[1,2,3], R. Dray-Spira[4,5], F. Lert[6], B. Spire[1,2,3], ANRS-VESPA2 Study Group
[1]INSERM, UMR 912 (SESSTIM), Marseille, France, [2]Aix Marseille Université, UMR_S 912, IRD, Marseille, France, [3]ORS PACA, Observatoire Régional de la Santé Provence-Alpes-Côte d'Azur, Marseille, France, [4]INSERM, UMR_S 1136, Pierre Louis Institute of Epidemiology and Public Health, Team Research in Social Epidemiology, Paris, France, [5]Sorbonne Universités, UPMC Univ Paris 06, UMR_S 1136, Pierre Louis Institute of Epidemiology and Public Health, Team Research in Social Epidemiology, Paris, France, [6]Centre de Recherche en Épidémiologie et Santé des Populations, Inserm U 1018, Villejuif, France
Presenting author email: marie.suzan@inserm.fr

Background: In France, men who have sex with men (MSM) still remain the population most at risk of HIV infection, with no decrease in HIV incidence being observed. We aimed to assess changes in sexual behavior among HIV-positive MSM attending outpatient clinics using data from two national representative surveys, conducted in 2003 and 2011, respectively, by considering indicators reflecting the diverse factors that might impact HIV sexual transmission in this population.
Methods: ANRS VESPA-1 and -2 were cross-sectional surveys conducted among adult PLWH attending French hospitals. Socio-behavioural and medical data were collected. The present analysis included men who self-reported they were gay, bisexual or had had at least one male partner in the previous year (n=1117 VESPA-1, n=1337 VESPA-2). HIV-negative or unknown status partners were considered serodiscordant. The outcome was inconsistent condom use for oral or anal sex with a serodiscordant steady partner in the previous 12 months, or with a serodiscordant casual partner during their last sexual encounter. Chi^2 tests were performed on weighted and calibrated data.
Results: Compared with MSM included in 2003, those in 2011 were significantly ($p< 10^{-3}$) older, were diagnosed with HIV longer, and reported less sexual activity. However, they had better immunovirological status (CD4>500 cells/mm^3 and undetectable viral load (VL)). Globally, between 2003 and 2011, the proportion of MSM reporting inconsistent condom use with a serodiscordant steady (79% vs 86% for oral sex; 23% vs 25% for anal sex, respectively) or casual partner (76% vs 80% for oral sex; 23% vs 18% for anal sex, respectively) did not differ significantly. However, the proportion of MSM with a detectable VL engaging in unprotected intercourse with serodiscordant main (23% vs 9% for oral sex; 7% vs 1% for anal sex, respectively) and casual partners (28% vs 7% for oral sex; 8% vs 4% for anal sex, respectively) decreased noticeably.
Conclusions: The proportion of HIV-positive MSM likely to transmit HIV decreased between 2003 and 2011 despite no increase in condom use. To have an impact on HIV epidemic, acting on behavioral changes will not be enough without achieving an undetectable viral load in all treated seropositive people.

WEPEC615

HIV risk perception and sexual risk behavior among HIV-infected married couples in rural Uganda

J. Matovu[1], J. Todd[2], R. Wanyenze[1], F. Wabwire-Mangen[1], D. Serwadda[1]
[1]Makerere Univ. School of Public Health, Kampala, Uganda, [2]London School of Hygiene and Tropical Medicine, London, United Kingdom
Presenting author email: matovujkb@gmail.com

Background: Studies show that married couples are at an elevated risk of HIV infection. However, few studies have explored HIV risk perception and sexual risk behaviors of HIV-infected married couples.
Methods: This cross-sectional study was conducted among 832 married couples aged 15-49 years, resident in three geographical strata in Rakai district, southwestern Uganda. Data collection took place between November 2013 and February 2014. HIV risk perception was defined as a respondent's perception of the likelihood that their sexual partner might be at risk of HIV infection. Data were collected on self-reported alcohol use before sex, engagement in non-marital sex and condom use at last non-marital sex. HIV testing was done using rapid HIV antibody tests. We conducted descriptive statistics to assess HIV risk perception and sexual risk behaviors among 697 couples for whom complete HIV status data were available. Data were analyzed using STATA version 11.0.
Results: Of 697 couples, 43 (6.2%) were HIV-discordant while 41 (5.9%) were HIV positive. Men in HIV-discordant (53.5% vs. 20.9%, P=0.002) and those in HIV-positive (46.4% vs. 21.9%, P=0.02) relationships were more likely than women to believe that their partners were not at risk of HIV infection. However, a higher proportion of women in HIV-discordant (79.1% vs. 46.5%) and those in HIV-positive (78% vs. 53.7%) relationships were more likely to believe that their male partners were very or somewhat likely to be at risk of HIV infection. Men in HIV-discordant

(34.9% vs. 7%, P=0.002) and those in HIV-positive (29.3% vs. 12.2%, P=0.06) relationships were more likely to report extra-marital relationships. However, only 13% of men and 0% of women who engaged in extra-marital relationships used a condom at last non-marital sex. Alcohol use before sex was reported more by men than women in both HIV-discordant (46.5% vs. 37.2%) and HIV-positive (56.1% vs. 26.8%) couples.
Conclusions: Men had a lower perception of their female partners' HIV risk but were more likely to engage in high-risk behaviors than women. These findings suggest a need for gender-responsive interventions to increase HIV risk perception and reduce sexual risk behaviors particularly among married men.

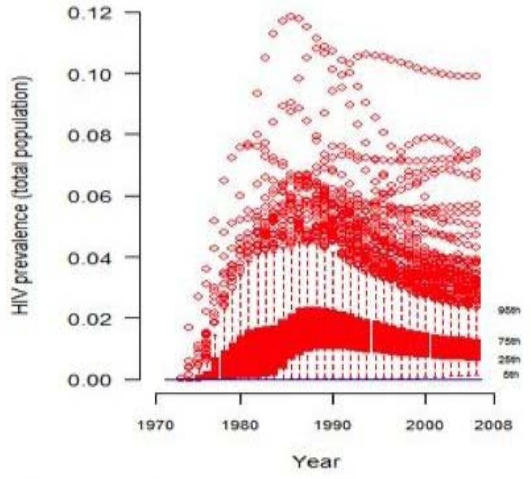
Epidemiology of HIV in the general population

WEPEC616

How high can a population's overall HIV prevalence driven by female sex work reach? Insights from mathematical modelling

M.-C. Boily[1], M. Pickles[1], S. Baral[2], P. Vickerman[3], J.F. Blanchard[4], S. Moses[4], M. Alary[5,6], S. Mishra[7]
[1]Imperial College London, Infectious Diseases Epidemiology Department, London, United Kingdom, [2]Johns Hopkins School of Public Health, Center for Public Health and Human Rights, Department of Epidemiology, Baltimore, United States, [3]University of Bristol, School of Social and Community Medicine, Bristol, United Kingdom, [4]University of Manitoba, Centre for Global Public Health, Department of Community Health Sciences, Winnipeg, Canada, [5]Centre de Recherche du CHU de Québec, Axe Santé des Populations et Pratiques Optimales en Santé, Quebec, Canada, [6]Université Laval, Département de Médecine Sociale et Préventive, Quebec, Canada, [7]University of Toronto, Department of Medicine/Division of Infectious Diseases, Toronto, Canada
Presenting author email: mc.boily@ic.ac.uk

Background: HIV epidemics have been classified as "concentrated" among key populations if overall HIV prevalence was below 1%, and as "generalised" otherwise. These surveillance criteria have often been used to inform HIV prevention policies and resource allocation. We aimed to objectively demonstrate the limitation of this definition and improve our understanding of HIV transmission dynamics by determining how high a population's overall HIV prevalence can reach in epidemics solely driven by unprotected female sex work (SW) (an epidemic that would have been prevented if the needs of FSWs had been addressed and transmission during sex work had been completely prevented at the onset).
Methods: We developed a deterministic model of HIV transmission specific to West and Central Africa (WCA) to simulate 1,000 plausible HIV epidemics where SW is the sole behavioral driver. The model was parameterized based on a comprehensive extraction of biological, epidemiological and sexual behavior parameters for WCA. We determined the range of plausible overall population HIV prevalence over time and the population attributable fraction (SW-PAF) of HIV due to unprotected SW over different time periods.



[Figure. Ranges of overall HIV prevalence across 1000 plausible HIV epidemics solely driven by sex work in West and Central Africa]

Results: In 1988 and 2008, overall HIV prevalence across the 1,000 plausible concentrated HIV epidemics ranged (5th-95th percentile) between 0.1%-4.2% and 0.1%-2.8%, respectively. The maximum HIV prevalence peaked at 10-12% in mid 80's to mid 90's(Figure). The SW-PAF measured from 2008 was < 5%-18% over one year compared to 16-59% (median=32%) over twenty years, with the latter accounting for long chains of secondary HIV transmissions originally related to sex work. The PAF was larger when measured earlier in the HIV epidemic (median SW-PAF from 1988-2008: 58%[20-100%]).
Conclusions: These results challenge our previous understanding of HIV epidemics. Even high HIV-prevalence epidemics can be solely driven by unprotected SW. Overall HIV prevalence and the short-term PAF are poor markers of underlying transmission dynamics and underestimate the role of SW in HIV epidemics, and thus should not be used alone to inform HIV policies and programmes. Although this model was calibrated with data from WCA, the findings have similar implications for understanding the transmission dynamics of HIV in higher East and South African prevalence settings.

WEPEC617

Is HIV prevalence declining in Uganda? Results from a home-based testing project

J. Gonzalez Perez[1], G. Ojamuge[1], M. Kahungu[1], J. Kiwanuka[1], J. Ssali[1], L. Buzaalirwa[1], K. Ssamula[1], T.M. Ford[2], P. Iutung Amor[1]
[1]AIDS Healthcare Foundation, Kampala, Uganda, [2]AIDS Healthcare Foundation, Los Angeles, United States
Presenting author email: Terri.Ford@aidshealth.org

Background: The Masaka region has been in the epicenter of the HIV epidemic in Uganda for more than 2 decades. Three surveys carried out in the decades of 1990 and 2000 reported prevalence between 8.2% and 11.2%. In the last two national surveys, prevalence in the Masaka area was 8.5% (2004) and 10.6% (2011). AIDS Healthcare Foundation (AHF) implements since 2011 a Test and Treat project aimed to cover 80% of the population of Masaka. Here we present data on HIV prevalence from that project.
Methods: Since April 2013, AHF has tested over 140,000 individuals in 13 sub-counties in Masaka using a home based approach. For this study we selected data from three of those sub-counties based on population size and testing coverage. A census of all residents was conducted and all households visited by a clinical team offering counseling and testing to residents older than 18 months of age.
Results: A total of 93,512 individuals, 49% of whom were adults (15 years and older) was listed in the census. Out of the adult population, 32,489 (70.1%) were tested. Testing coverage was higher among women (75.2% of all censused women tested versus 64.6% of men) and in the age group 15-34 years (73.7% versus 65.1% in the group over 35 years). By sub-county, testing coverage ranged between 63.8% and 76.8%. Overall adult HIV prevalence was 3.8% (95% CI 3.6-4.0). Prevalence was significantly higher in women (4.0% versus 3.5% in men, p=0.02) and increased with age, reaching a peak earlier (6.9% at 25-29 years) than in men (7.1% at 30-34 years).
Conclusions: All the surveys conducted in the Masaka region since 1990's have found prevalence above 8%. The last national survey documented an increase in prevalence (up to 10.6% in the Masaka area) due to longer survival of patients on ART and high incidence of HIV infection. Our testing results differ from those figures and show a prevalence of around 4%. These findings suggest that actual prevalence in the region may have decreased in the last years as a result of intensive efforts in HIV prevention implemented by AHF and other organizations in the ground.

Epidemiology of HIV in youth and adolescents

WEPEC618

HSV-2 and HIV infection among vulnerable adolescent girls in Zambia

P. Hewett[1], E. Soler-Hampesjek[2], J. Digitale[2], K. Austrian[3]
[1]Population Council, Zambia Office, Lusaka, Zambia, [2]Population Council, New York, United States, [3]Population Council, Nairobi, Kenya
Presenting author email: phewett@popcouncil.org

Background: Adolescent girls are recognized as having an elevated risk of STI and HIV acquisition in high prevalence countries, such as Zambia. The Adolescent Girls Empowerment Programme (AGEP) is an intervention that was designed to address the heightened vulnerability of 10,000 Zambian adolescent girls 10-19 by providing them social, health and economic assets through a 'Safe Spaces' model. Such assets can be drawn upon on to reduce vulnerabilities and expand opportunities, increasing their delaying sexual debut, unintended pregnancy and acquisition of STIs.
Methods: Embedded within the AGEP intervention, a randomized cluster evaluation with longitudinal observation over 4 years is being implemented to obtain a rigorous assessment of the impact of AGEP. Girls were selected for the program and research based on a vulnerability indicator that captures household and individual deprivations. Baseline data collection was completed in 2014; survey information was collected from 5,241 adolescent girls 10-19. HSV-2

and HIV status was obtained from girls aged 15-19. Multivariate logistic regression of HIV and HSV-2 status by sub-group and with socio-economic and risk behaviors will be explored and presented; the association between vulnerability, sexual behavior and STI acquisition will be delineated.

Results: The baseline response rate was 88% percent of the eligible population, 85% among those 15-19; 91% among those 10-14. Approximately 40% of the adolescents 15-19 were sexually active, with 17% having had sex prior to the age of 15 years. About 30% of the sample reported having had a previous HIV test. HIV testing was completed among 96% of the sample who took part in the baseline survey, while HSV-2 specimen collection was completed among 95% of the sample. The HIV prevalence in the sample was 3.1% (1.9% in rural areas and 4.2% in urban areas), while the HSV-2 prevalence observed in the sample was 7.6%.

Conclusions: Little detailed information exists about HSV-2 and HIV infection among adolescent girls in Zambia. the prevalence of HIV and HSV-2 is only modest in the baseline sample, the data will provide useful information as to the distribution of HIV and STI infection in Zambia and the risks associated with acquisition.

Epidemiology of HIV in male, female and transgender sex workers

WEPEC619

Characterizing the contribution of sex work to HIV epidemics in sub-Saharan Africa: a systematic review, meta-analysis, and mathematical modelling study

S. Mishra[1], S. Moses[2], M.-C. Boily[3], L. Mckinnon[4], W. John[3], A. Michel[5], H. Prudden[6], A. Low[6], W. Odek[2], M. Becker[2], V. Peter[7], C. Watts[6], J. Blanchard[2]
[1]University of Toronto, Infectious Diseases, Toronto, Canada, [2]University of Manitoba, Winnipeg, Canada, [3]Imperial College, London, United Kingdom, [4]CAPRISA, Durban, South Africa, [5]Universite Laval, Quebec City, Canada, [6]London School of Hygiene and Tropical Medicine, London, United Kingdom, [7]Bristol University, Bristol, United Kingdom
Presenting author email: sharmistha.mishra@utoronto.ca

Background: Few countries with large "generalized" HIV epidemics implement HIV prevention programmes for female sex workers (FSWs) and clients to scale. We aimed to quantify the contribution of unprotected sex work to HIV epidemics in Sub-Saharan Africa (SSA).

Methods: We systematically reviewed published (Medline, EMBASE, PsychInfo, Scopus) and grey literature, and used random-effects meta-analyses, to estimate the population size and HIV prevalence/incidence of FSWs and/or clients, by SSA country/region and year of data collection (2002-2013). We estimated the odds ratio (OR) of prevalent HIV in FSWs/clients compared to adult females and non-clients using national HIV prevalence estimates by year of data collection, the classic population attributable fraction (PAF) of sex work on prevalent HIV in males and females by country; and used a dynamic mathematical model of HIV transmission to explore the utility of the classic PAF when appraising the contribution of sex work.

Results: Of 4,004 unique records identified in the empiric-data search, 213 were included. The median size of FSW and client populations were 1.8% (range, 0.25-11.5%, 35 countries) and 3.0% (range, 0.025-30.0%, 36 countries) respectively. Pooled HIV prevalence in FSWs and clients was 28.2% (95% CI: 24.6-31.9, N=79, 34 countries) and 6.4% (95% CI: 4.3-8.9%, N=39, 27 countries) respectively. Pooled OR among FSWs was 9.7 (95% CI: 7.9-11.9), decreasing over time: 13.4, 9.8, and 5.6 in 2002-2005, 2006-2009, and 2010-2013 respectively. Pooled OR among clients was 2.0 (95% CI: 1.4-2.8). The classic PAF of sex work on prevalent HIV infections in females and males ranged from 0.4 to 71.2% and 0 to 88.0% respectively. Dynamic model analyses showed that the classic PAF considerably underestimates the medium- to long-term contribution of sex work to HIV epidemics.

Conclusions: In SSA, a high proportion of women and men sell and purchase sex, and both continue to experience a disproportionately higher burden of HIV. Unprotected sex work account for a larger burden of HIV acquisition and onward transmission than would be suggested by existing approaches of appraising the contribution of sex work to HIV epidemics. Preventing HIV in FSWs/clients is critical to the HIV response, even in countries labeled as experiencing "generalized" HIV epidemics.

WEPEC620

Stigma as barriers to healthcare among high-risk groups for HIV transmission in Burkina Faso

H.-Y. Kim[1], A. Grosso[1], O. Ky-Zerbo[2], M. Lougue[2], G. Ouedraogo[3], S. Kouanda[3], S. Baral[1]
[1]Johns Hopkins School of Public Health, Epidemiology, Baltimore, United States, [2]Programme d'Appui au Monde Associatif et Communautaire, Ouagadougou, Burkina Faso, [3]Institute de Recherche en Sciences de la Sante, Ouagadougou, Burkina Faso
Presenting author email: hkim207@jhu.edu

Background: Female sex workers (FSW) and men who have sex with men (MSM) have a disproportionately high burden of HIV transmission in Burkina Faso. However stigma and discrimination may prevent them from seeking healthcare services.

Methods: FSW practicing sex work as the primary source of revenue and MSM reporting anal intercourse with another man within the past 12 months were recruited in Bobo-Dioulasso, Burkina Faso by respondent driven sampling. All participants were aged ≥18 years and lived in Bobo-Dioulasso for ≥ 3 months. Perceived healthcare stigma was defined as being afraid to go to health services or avoiding going to health services. Stigma related to police, social support or past experience of healthcare stigma as well as baseline characteristics were examined as potential risk factors. Factor analysis and logistic regression were used.

Results: A total of 350 FSW and 330 MSM were recruited and consented to participate in the study. The prevalence of perceived healthcare stigma was 17.4% and 32.7% in FSW and MSM, respectively. Experienced healthcare stigma was much lower in both groups (3.1% in FSW and 5.2% in MSM). Longer years of being FSW or participating in any HIV prevention or community group were significantly associated with higher odds of perceived healthcare stigma among FSW. In multivariate analysis, perceived healthcare stigma was associated with higher odds of verbal harassment due to selling sex (OR=3.91; 95% CI 1.06, 9.43) as well as being forced to have sex (OR=2.04; 95% CI 1.06-3.93) and feeling rejected by friends (OR=2.53; 1.27-5.06) among FSW. Similarly, MSM who reported perceived healthcare stigma had a higher odds of being forced to have sex (OR=3.07; 95% 1.38-6.82) and were more likely to experience police refusing to protect them or being arrested, being scared to walk in public places or being blackmailed.

Conclusions: In these two key populations, perceived healthcare stigma was high and associated with experienced stigma, mainly being forced to have sex as well as social stigma among FSW and stigma from police and general public among MSM. Interventions to increase utilization of health services in these key populations may need to be targeted with different strategies.

Epidemiology of HIV in MSM

WEPEC621

Factors associated with high incident HIV in a high-risk cohort in Lima, Peru

K. Konda[1,2], C.C. Bristow[3], S.R. Leon[2], J.A. Flores[2], B. Brown[4], C.F. Caceres[2], J.D. Klausner[1]
[1]UCLA, Medicine, Division of Infectious Diseases, Los Angeles, United States, [2]Universidad Peruana Cayetano Heredia, Public Health, Lima, Peru, [3]Fielding School of Public Health, University of California Los Angeles, Department of Epidemiology, Los Angeles, United States, [4]University of California, Irvine, Irvine, United States
Presenting author email: kkonda@mednet.ucla.edu

Background: HIV incidence in Latin America is concentrated among men who have sex with men (MSM) and male-to-female transgender women (TW). Despite substantial documentation of increased HIV prevalence in these populations, HIV incidence estimates and factors associated with incident HIV are rare.

Methods: We conducted an observational cohort study among MSM and TW recruited based on high-risk characteristics including having condomless sex with a male partner in Lima, Peru. Blood samples were collected and tested for HIV infection at baseline and then every 3 months, using an algorithm that included a 3rd generation HIV antibody rapid Point of Care (POC) (Determine, Alere Medical Co, Japan) and a 4th generation Ag/Ab HIV EIA serum test (Genscreen ULTRA HIV Ag-Ab, Bio-Rad, Redmond, WA) with Western Blot (WB) confirmation (Genetic Systems HIV-1 Western Blot, Bio-Rad, Redmond, WA). HIV positives at baseline were excluded from this analysis. Variables considered for the analysis included socio-demographics and risk behaviors. Cox regression was used to examine baseline factors associated with HIV incidence; for the multivariable model all variables with a bivariate p-value< 0.2 were included. All analyses were conducted in Stata 13.0.

Results: During the 222 years of follow-up included in the cohort, there were 22 cases of incident HIV infection, yielding an HIV incidence of 9.9 cases per 100 person years (95% CI 5.9 - 13.8). In multivariable analysis the risk of HIV infection decreased with age (aHR 0.90, 95% CI 0.84 - 0.97) and increased if participants reported having had anal sex 2-3 times in venues

like a discotheque or sauna or during an orgy (aHR 3.89, 95% CI 1.03 - 14.62). Incident HIV infection was not associated with reporting condomless receptive anal sex, having an increased number of sex partners, being a transgender woman, or being a sex worker (all p-values>0.05).

Variable		HIV cases	Total person-time (years)	Crude HR	95%CI	Adjusted HR	95%CI
Age (years)				**0.89**	**0.83 - 0.96**	**0.90**	**0.84 - 0.97**
Sex Role during anal sex	Insertive	2	49.7	Ref		Ref	
	Receptive	10	70.1	3.23	0.71 - 14.76	3.29	0.72 - 15.10
	Both insertive and receptive	10	102.2	2.19	0.48 - 9.99	1.57	0.33 - 7.49
Had recent syphilis infection		5	26.1	2.07	0.76 - 5.61	2.30	0.75 - 7.02
No. of risky situations for anal sex	0-1	3	78.8	Ref		Ref	
	2-3	10	66.6	**3.87**	**1.06 - 14.09**	**3.89**	**1.03 - 14.62**
	4+	9	76.7	2.99	0.81 - 11.07	3.25	0.84 - 12.50
Bolded p-values ≤0.05, *Risky situations for anal sex: reporting anal sex in a discotheque or sauna or during an orgy							

[Risk factors for HIV incidence]

Conclusions: The HIV incidence among MSM/TW documented in this study was substantial. Within this high-risk group, standard individual-level risk characteristics may not be associated with HIV incidence. The identification of risky venues and behaviors associated with incident HIV infection suggest targeted locations for HIV prevention interventions such as testing, condom promotion and referral for PrEP.

WEPEC622

HIV testing and diagnosis among young Asian-born men who have sex with men in Victoria, Australia: understanding needs and vulnerability

J. Asselin[1], A.L. Wilkinson[1,2], H. Nasra[3], M. Stoove[1,2], M. Hellard[1,2], C. El-Hayek[1]
[1]Burnet Institute, Centre for Population Health, Melbourne, Australia, [2]Monash University, Department of Epidemiology and Preventative Medicine, Melbourne, Australia, [3]Victorian Department of Health, Health Protection Branch, Melbourne, Australia
Presenting author email: hellard@burnet.edu.au

Background: Asian-born migrant men who have sex with men (MSM) are disproportionately represented among notifications of HIV in many Western countries. Poor sexual health knowledge, social isolation and barriers to health services may be increasing risk. As migration from men from this region increases, there is a need to better understand the epidemiology of HIV in this population.
Methods: HIV registry data (2007-2012) from Victoria, Australia described new diagnoses by country of birth, time since arrival and exposure to HIV. Recently arrived migrants were defined as arriving in Victoria < 5 years prior to HIV diagnosis. Testing and behavioural data (2007-2012) captured via a network of sentinel surveillance sites from MSM testing for HIV in Victoria were also analysed; stratified by Asian-born and Australian-born.
Results: Of the 1639 HIV notifications, 32% were born overseas (n=531), of which 43% were recently arrived migrants (n=230). Among recently arrived migrants, 50% were MSM, 49% of whom were from SE Asia, China and India; 61% reported acquiring their infection in Victoria. From the sentinel surveillance network, 25,038 tests were recorded among Australian-born MSM and 4,963 tests among Asian-born MSM. At one in five (22%) tests among Asian-born MSM, they reported >10 partners in the previous 12 months and in 47% of tests, Asian-born MSM reported unsafe sex. The proportion that tested HIV positive among Asian-born MSM was higher compared to Australian-born MSM (2.6% vs 1.9%) and more Asian-born MSM were diagnosed on their first test within the sentinel network (58% vs 30% in 2011).
Conclusions: These results highlight the potential vulnerability of Asian-born MSM to HIV upon arrival to Australia. The evidence that Asian-born MSM were more likely to be diagnosed on their first test suggests less routine testing when compared to Australian-born MSM, and require a need to focus on access to HIV prevention, testing and care among this group.

WEPEC623

HIV and syphilis among male clients of male sex workers in China: the hidden epidemic

L. Chen[1], T. Mahapatra[2], G. Fu[3], J. Xu[4], J. Tucker[5], B. Yang[6], J. Zhao[7], W. Tang[8], R. Detels[2]
[1]Guangdong Provincial Center for Skin Diseases and STIs Control, Guangzhou, China, [2]University of California Los Angeles, Los Angeles, United States, [3]Jiangsu Provincial Center for Disease Control and Prevention, Nanjing, China, [4]China Medical University, China, Shengyang, China, [5]University of North Carolina Project-China, Guangzhou, China, [6]Guangdong Provincial Center for Skin Diseases and STI Control & Prevention, Guangzhou, China, [7]The Global Fund to Fight AIDS, Tuberculosis and Malaria, Geneva, Switzerland, [8]University of North Carolina at Chapel Hill, Project-China, Guangzhou, China
Presenting author email: xjjbeijing@gmail.com

Background: High risk of HIV/syphilis transmission from male sex workers (MSWs) was emphasized in recent studies; still male clients of these MSWs (MCM) were never studied. A detailed investigation was thus called for, to determine the burden and socio-behavioral determinants of HIV and syphilis among these MCM and compare them with other men who have sex with men (MSM) in China.
Methods: In a multi-center cross-sectional study, using respondent-driven and snow-ball sampling, 2958 consenting adult MSM were recruited, interviewed and tested for HIV and syphilis. Distribution of socio-demographics, behavior and HIV/syphilis prevalence were determined along-with comparison between MCM and other MSM regarding these parameters using SAS-9.3.
Results: Among recruited MSM, 5.0% (n=148) were MCM. HIV prevalence for MCM and other MSM were 7.4% and 7.7%, while syphilis prevalence were 18.9% and 14.0%, respectively. Condomless anal intercourse (CAI) was reported among 59.5% MCM and 48.2% MSM. Multivariate logistic regression revealed that compared to other MSM, MCM were more likely to have less education [for ≤elementary level, adjusted odds ratio (aOR)=3.13, 95% confidence interval (95%CI)=1.42-6.90], higher income (for >$500 /mth, aOR=2.97, 95%CI=1.53-5.77), found partners at park/restroom (aOR=4.01, 95%CI=2.34-6.85), reported CAI (aOR=1.49, 95%CI=1.05-2.10), larger network (for ≥10, aOR=2.70, 95%CI=1.44-5.07) and higher odds of syphilis (aOR=1.54, 95% CI=1.00-2.38).
Conclusions: Compared to other MSM, similarly high prevalence of HIV and higher burden of risk behaviors and syphilis were observed. Our study indicated that HIV/syphilis prevention programs in China need to address MCM as a separate sentinel group especially focusing on their education, venues, network size and condom use.

WEPEC624

Factors associated with sex at "high parties" in men who have sex with men, Bangkok

W. Thienkrua[1], A. Varangrat[1], E.F. Dunne[1,2], W. Wimonsate[1], T. Chemnasiri[1], W. Sukwicha[1], K. Satumay[1], S. Lertpruek[1], A. Chitwarakorn[3], T.H. Holtz[1,2]
[1]Thailand MOPH - U.S. CDC Collaboration, Nonthaburi, Thailand, [2]U.S. Centers for Disease Control and Prevention, Division of HIV/AIDS Prevention, Atlanta, United States, [3]Thailand Ministry of Public Health, Department of Disease Control, Nonthaburi, Thailand
Presenting author email: tkh3@cdc.gov

Background: Studies have demonstrated that drugs and alcohol are often associated with sexual practices that may increase the risk of HIV acquisition or transmission. We describe factors associated with having sex while under the influence of (being "high" on) drugs or alcohol in the Bangkok Men Who Have Sex with Men Cohort Study (BMCS), Thailand.
Methods: From April 2006 to November 2010, we enrolled Thai men aged ≥18 years from the Bangkok metropolitan area who reported penetrative oral or anal sex with another man in the past 6 months. Men were followed-up every 4 months with HIV testing and audio computer-assisted self-interview behavioral questions. Men were asked if they had participated in a "high party", defined as "a party when two or more men come together to have sex while high on drugs." We evaluated factors associated with high party using logistic regression.
Results: Among 1337 men aged 18-56 years (median age of 26 years), 223 (16.7%) had participated in a high party, 826 (61.8%) reported using the Internet to find a sexual partner, and 410 (30.7%) reported used the Internet to have online sex (cam sex). When adjusted for age, educational level, and employment status at enrollment, factors associated with participating in a high party were using the Internet to find a partner [Adjusted Odds Ratio (AOR) 2.7, 95% Confidence Interval (CI) 1.6-4.5], ever used the Internet to have online sex ("cam sex") (AOR 1.8, 95% CI 1.2-2.7), being drunk 2-3 times per week or more (AOR 1.6, 95% CI 1.1.9-2.5), ever using crystal methamphetamine (MDMA) (AOR 1.8, 95% CI 1.1-3.1), ever using methamphetamine (AOR 9.6, 95% CI 6.1-15.0), ever using inhaled nitrates (AOR 2.4, 95% CI 1.5-3.7), ever using erectile dysfunction drug (AOR 2.0, 95% CI 1.3-3.0), and ever having had group sex (AOR 1.9, 95% CI 1.2-2.9).
Conclusions: Sexual encounters while high on drugs were common in this cohort. These encounters occurred more often in men who had a history of substance use or participation in group sex or the Internet used to find a partner. HIV prevention interventions targeting this group are needed, especially via the use of social media.

WEPEC625

HIV incidence in young men who have sex with men exposed to club drugs and 'high parties' and associated risk factors from the Bangkok MSM cohort study, Thailand, 2006-2014

W. Thienkrua[1], P. Mock[1], W. Sukwicha[1], E.F. Dunne[1,2], K. Pancharoen[1], S. Lertpruek[1], W. Chonwattana[1], S. Winaitham[1], A. Chitwarakorn[3], T.H. Holtz[1,2], T. Chemnasiri[1]
[1]Thailand MOPH - U.S. CDC Collaboration, Nonthaburi, Thailand, [2]U.S. Centers for Disease Control and Prevention, Division of HIV/AIDS Prevention, Atlanta, United States, [3]Thailand Ministry of Public Health, Department of Disease Control, Nonthaburi, Thailand
Presenting author email: hpu4@cdc.gov

Background: Increasing club drug use and exposure to 'high parties' among young men who have sex with men (YMSM) in Bangkok have been documented in several studies. We assess HIV incidence among YMSM exposed to club drugs and 'high parties' and factors associated with HIV incidence.
Methods: Between 2006-2008 and 2009-2010 we enrolled Thai men and transgender women aged ≥18 years from the Bangkok metropolitan area reporting penetrative oral or anal sex with men in the past 6 months into the Bangkok MSM Cohort Study (BMCS). HIV testing was performed on oral fluid, with serologic confirmation of all reactive specimens. Participants provided socio-demographic, sexual risk, and drug use behavior data by audio computer-assisted interview. We defined a 'high party' as two or more men coming together to have sex while high on drugs.
We calculated incidence from participants who were HIV-negative at enrollment and returned for 4-month follow-up visits to a maximum of 60 months . We evaluated factors associated with HIV incidence using Cox proportional hazard analysis.
Results: Among 1744 BMCS participants followed from 2006-2014, 1372 tested HIV-negative at baseline, including 561 (40.8%) YMSM aged 18-24 years with 1647 person-years. Among these YMSM, we detected 122 seroconversions and determined the HIV incidence to be 7.4 per 100 Person-Years (PY). Stratifying among high-risk subgroups, we found the crude HIV incidence to be highest among YMSM using club drugs to enhance sexual pleasure (23.6/100 PY), those using erectile dysfunction drug in combination with club drugs (19.4/100 PY), those using nitrates inhalation (13.9/100 PY), those who had group sex (12.6/100 PY), those joining 'high parties' with men met via the Internet (11.5/100 PY), and those joining any 'high party' (10.3/100 PY).
In multivariate analysis, using club drugs to enhance sexual pleasure (Adjusted Hazard Ratio [AHR] 3.5, 95% CI 1.9-6.6) and engaging in group sex (AHR 1.7, 95% CI 1.03-2.7) were statistically significantly associated with increased HIV incidence in YMSM.
Conclusions: HIV incidence was high among YMSM in our study. Recreational drug use and having group sex increased the risk of acquiring HIV among Thai YMSM. Comprehensive HIV prevention packages targeting this group are urgently needed.

WEPEC626

Risky sexual practices in casual partnerships while traveling internationally

H.-H.M. Truong[1,2], Y.-H. Chen[3], M. Grasso[3], T. Robertson[3], L. Tao[3], A. Curotto[1], W. McFarland[1,3], R.M. Grant[1,2], R. Fatch[1], H.F. Raymond[3], W.T. Steward[1]
[1]University of California, San Francisco, Medicine, San Francisco, United States, [2]Gladstone Institute of Virology and Immunology, San Francisco, United States, [3]San Francisco Department of Public Health, San Francisco, United States

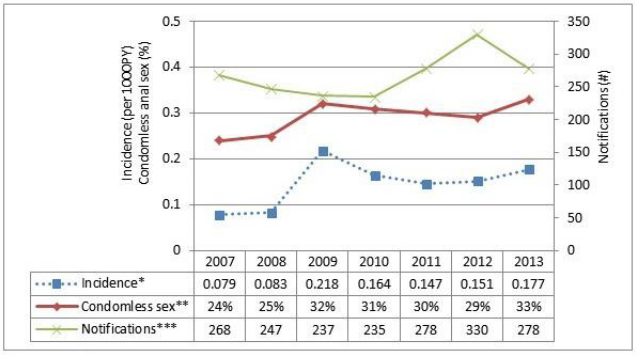
Background: International travel provides an opportunity to meet new sexual partners while in the destination countries. We assessed partnership type, where partners were met and sexual practices that occurred while traveling internationally.
Methods: A probability-based sample of men who have sex with men (MSM) from the San Francisco Bay Area who traveled internationally in the previous 12 months was recruited (N=501). Detailed partnership-level data were collected for up to three sexual partnerships per international country visited, for up to two countries. Partnerships were classified as "casual" if it was not a committed relationship and the respondent knew how to re-contact the partner or as "anonymous" if it was one-time sexual encounter and the respondent did not know how to re-contact the partner.
Results: Respondents reported on 344 casual and 456 anonymous partnerships. They met 98% of anonymous and 82% of casual partners in the country they were visiting. Casual partners were met most often on the Internet (32%) and anonymous partners at a sex club or bathhouse (41%). Respondents were more likely to know the partner's HIV serostatus in casual partnerships compared to anonymous ones (77% vs. 27%, p<0.01), disclose their own HIV status (57% vs 24%, p<0.01) and have an easier time communicating (86% vs. 63%, p<0.01). Unprotected insertive anal intercourse (UIAI) (16% vs. 7%; p=0.01) was more likely to occur in casual partnerships than anonymous ones, as were unprotected receptive anal intercourse (URAI) (15% vs. 5%; p<0.01), oral-anal contact (35% vs. 22%; p=0.03) and drug use before or during intercourse (55% vs. 36%; p=0.01).
Respondents were more likely to disclose their HIV status to casual partners who shared a common language (p<0.01).
Conclusions: MSM engaged in riskier sexual practices in casual partnerships than anonymous ones while traveling internationally. They more often knew the casual partner's HIV serostatus and disclosed their own serostatus, which may be related to ease of communication. The findings suggest that interventions to reduce HIV transmission risk while traveling need to focus on partnerships that are established and recur in a foreign country rather than on partnerships that consist only of one-time sexual encounters.

WEPEC627

HIV incidence estimates from repeat testing are closely related to trends in HIV risk behaviour and can identify epidemic changes earlier than HIV notifications

D. Callander[1], H. Wand[1], L. Watchirs Smith[1], M. Chen[2,3], M. Hellard[4], C. O'Connor[1,5], A. Grulich[1], C. Fairley[2,6], D. Wilson[1], M. Holt[7], V. Knight[8], C. Selvey[9], J. Kaldor[1], H. Ali[1], B. Donovan[1,8], R. Guy[1]
[1]UNSW Australia, Kirby Institute, Sydney, Australia, [2]Melbourne Sexual Health Centre, Melbourne, Australia, [3]Monash University, Central Clinical School, Carlton, Australia, [4]Burnet Institute, Centre for Population Health, Melbourne, Australia, [5]Royal Prince Alfred Hospital, Sexual Health Service, Camperdown, Australia, [6]Monash University, Carlton, Australia, [7]UNSW Australia, Centre for Social Research in Health, Sydney, Australia, [8]Sydney Sexual Health Centre, Sydney, Australia, [9]New South Wales Ministry of Health, Sydney, Australia
Presenting author email: d.callander@unsw.edu.au

Background: In high-income countries, trends in HIV notifications and behavioural risk are widely used in the evaluation of population-level HIV prevention programs. Direct estimates of HIV incidence are the ideal indicator for this purpose but can be difficult to obtain. We estimated trends in HIV incidence among gay, bisexual and other men who have sex with men (GBM) using repeat testing data from a large clinical network and compared it to trends in sexual risk practices and passive HIV notifications.
Methods: Our analysis utilised HIV test data extracted from a network of 33 sexual health clinics in New South Wales (NSW) from 2007 to 2013. HIV incidence among GBM was calculated based on those who had an initial negative test for HIV followed by a repeat test during the study period Annual HIV notifications associated with male homosexual exposure in NSW were obtained from Australia's national registry. The behavioural indicator of 'condomless anal sex with casual partners in the past 6 months' was sourced from annual cross-sectional community surveys of GBM. Spearman's statistics were used to assess correlations between pairs of indicators.
Results: Between 2007 and 2013 there were 150 incident infections of HIV in GBM at participating clinics. During this period, HIV incidence increased significantly from 0.79/100PY in 2007 to 2.18/100PY in 2009 (p=0.03) before decreasing at a non-significant rate to 1.77/100PY in 2013 (p=0.13; see Figure 1). The trend for condomless sex with casual partners was remarkably similar and from 2007 to 2013, HIV incidence was strongly correlated with this behavioural indicator (r=0.93, p=0.02). HIV notifications, however, were not correlated with other indicators until we introduced a 3-year lag to the notification data, after which strong correlations were observed between HIV notifications and condomless sex (r=0.95, p=0.05) and HIV incidence (r=0.95, p=0.05).
Conclusions: Trends in HIV notifications reflect changes in transmission that occurred up to three years prior. HIV incidence calculated using repeat testing methods is a more immediate indicator for evaluating the impact of HIV prevention programs.



	2007	2008	2009	2010	2011	2012	2013
Incidence*	0.079	0.083	0.218	0.164	0.147	0.151	0.177
Condomless sex**	24%	25%	32%	31%	30%	29%	33%
Notifications***	268	247	237	235	278	330	278

*Adjusted for scale
** Source: Hull P, Mao L, Kolstee J, Duck T, Prestage G, Zablotska I, de Wit J, Holt M. *Gay Men Community Periodic Survey: Sydney 2014*. 2014. Sydney, NSW: Centre for Social Research in Health, UNSW Australia
*** Source: New South Wales Ministry of Health. *NSW HIV Strategy 2013 Annual Data Report*. Sydney, NSW: NSW MoH

[Figure 1. HIV incidence among GBM sexual health attendees in NSW, HIV notifications among GBM in NSW, and condomless anal sex with casual partners among GBM in NSW, by year, 2007-2013]

WEPEC628

HIV prevalence among men who have sex with men in Malawi: informing national strategies through research from seven urban and rural districts

A. Wirtz[1,2], G. Trapence[3], V. Gama[3], D. Kamba[3], R. Chalera[3], L. Klein[2], R. Kumwenda[4], T. Chikoko[5], M. Mangochi[6], S. Baral[2]
[1]Johns Hopkins Medical Institute, Department of Emergency Medicine, Baltimore, United States, [2]Johns Hopkins Bloomberg School of Public Health, Epidemiology, Baltimore, United States, [3]Center for the Development of People, Lilongwe, Malawi, [4]UNDP, Lilongwe, Malawi, [5]UNAIDS, Lilongwe, Malawi, [6]Department of Nutrition and HIV/AIDS, Lilongwe, Malawi
Presenting author email: awirtz1@jhu.edu

Background: The nation of Malawi has made great progress in efforts to prevent HIV and provide treatment those living with HIV in the general population. Key populations remain at high risk of infection and only recent, limited research studies have been conducted among men who have sex with men (MSM). Though same sex practices are criminalized, national HIV programs have sought to understand the population to inform programmatic decisions and resource allocations.
Methods: A cross-sectional study of MSM living in Malawi was conducted between 2011 and 2014 in urban and rural districts: Blantyre, Lilongwe, Mzuzu, Nkhata Bay, Mangochi, Chikwawa, and Mulanje. Data collection was implemented by a local community-based organization. A total of 2,454 MSM (350/site) were recruited via respondent-driven sampling to participate in a sociobehavioral survey and HIV and syphilis testing. Unique object multiplier and wisdom of the crowd methods were used for population size estimation. Bivariate and multivariable regression analysis to investigate correlates of HIV infection.
Results: Across the districts, the estimated sizes of the MSM populations were heterogeneous. Overall, the MSM population was estimated to represent 1.84% (95%CI: 0.65%-6.2%) of the male population, aged 20-39 years in Malawi. HIV prevalence was also heterogeneous and ranged from 5.4% in Mzuzu City to a high of 24.9% in Mulanje. Two to 8.7% of MSM had an active syphilis infection. In all but one low prevalence district, at least 90% of MSM living with HIV were unaware of their infection. Lifetime history of HIV testing ranged from 22.7%-62.7%. Correlates of infection were diverse across districts and related to behavioral and structural risks, including: sexual identity, young age of first same sex intercourse, inconsistent condom use with male partners, use of condom incompatible or no lubricants during anal sex, and lifetime history of jail/prison.
Conclusions: HIV prevalence among MSM is high and geographically heterogeneous. Geographic patterns are reflective of the general adult population, though relatively higher. The majority of MSM who are living with HIV are unaware of their infection status, largely reflective of low lifetime history of HIV testing. Findings provide insight into gaps and opportunities for informing future, national HIV prevention programs.

Epidemiology of HIV in serodiscordant couples

WEPEC629

"Testing machines can lie and be faulty": perceptions of serodiscordance and ART by Ugandan serodiscordant couples and their communities

J. Kim[1], M. Nanfuka[2], D. Moore[1,3], M. Shafic[2], M. Nyonyitono[2], F. Galenda[2], R. King[4]
[1]B.C. Centre for Excellence in HIV/AIDS, Vancouver, Canada, [2]The AIDS Support Organization, Jinja, Uganda, [3]University of British Columbia, Faculty of Medicine, Vancouver, Canada, [4]University of California, Global Health Sciences, San Francisco, United States
Presenting author email: rachel.king@ucsf.edu

Background: The primary driver of the HIV epidemic in sub-Saharan Africa remains heterosexual transmission. Serodiscordant couples in long term relationships represent a significant source of new HIV infections in this region. However, serodiscordance is often poorly understood in those affected. This study investigated perceptions and attitudes of serodiscordant couples regarding their status, and some of the social and sexual factors driving serodiscordance or seroconversion.
Methods: In-depth, gender-matched interviews were conducted from June 2013 to December 2014 with 28 heterosexual, initially serodiscordant couples (57 individuals) attending The AIDS Support Organization in Jinja, Uganda as part of an ongoing study of serodiscordant couples and treatment as prevention. 14 of the HIV negative participants in these couples seroconverted by the first of 5 in-depth interviews.
Thematic framework analysis of the baseline interview transcripts resulted in dominant themes regarding prevention methods, attitudes and knowledge about serodiscordance and antiretroviral treatment (ART).
Results: Participant ages ranged from 27-71 years. Couples were mixed regarding disclosing their serodiscordance, but those who had not cited stigma as a dominant factor in not disclosing. Almost all couples had adequate access to condoms, but adherence to-and use of condoms varied widely. Inconsistent condom-use was felt to have contributed to seroconversion in some cases. Participants' understanding of serodiscordance was varied, and many cited extensive education and multiple tests as positive factors. However, there were misconceptions about whether serodiscordance is possible, exemplified by the belief in "strong" or "heavy" blood which can resist HIV infection. Individuals cited that their communities' understanding of discordance was limited, and many members dismissed the concept of discordance entirely. ART is perceived negatively by many community members stating it comes with "shovels and axes" (burial tools), although individuals on ART acknowledge benefits. Beliefs were varied as to whether ART could prevent HIV infection.
Conclusions: Although affected individuals in a serodiscordant relationship have a fair understanding of serodiscordance and treatment, stigma and misinformation remains widespread in the community. A focus on further education about serodiscordance and the benefits of ART should be considered in efforts to minimize heterosexual transmission, and accelerate the destigmatization of HIV and serodiscordance.

Epidemiology of HIV in transgender persons

WEPEC630

Gendered vulnerabilities: HIV prevalence and correlates of transgender and feminine gender identity among natal males who have sex with males in Burkina Faso, Gambia, Lesotho and Malawi

T. Poteat[1], A. Grosso[1], A. Wirtz[1], D. Diouf[2], G. Ouedraougo[1], S. Baral[1], T. Mothopeng[3], N. Taruberekera[4], G. Trapence[5], V. Jumbe[6], S. Ketende[1], C. Nuha[7], N. Ceesay[7], K.-Z. Odette[8], J. Loum[9], H. Gautier[10]
[1]Johns Hopkins School of Public Health, Epidemiology, Baltimore, United States, [2]Enda Sante, Dakar, Senegal, [3]Matrix Support Group, Maseru, Lesotho, [4]PSI, Johannesburg, South Africa, [5]CEDEP, Blantyre, Malawi, [6]University of Malawi, College of Medicine, Blantyre, Malawi, [7]UNAIDS, Joint United Nations Programme on HIV/AIDS, Mbabane, Swaziland, [8]PAMAC, Ouagadougou, Burkina Faso, [9]Network of AIDS Service Organizations, Banjul, Gambia, [10]Research Institute of Health Sciences, Ouagadougou, Burkina Faso
Presenting author email: tpoteat123@gmail.com

Background: Where data is available, it indicates that transgender women worldwide bear a heavy and disproportionate burden of HIV, with an estimated prevalence of 19% and 49 times the odds of infection compared to the general population. However, data are notably missing from sub-Saharan Africa, the region with the heaviest overall burden of HIV. This study examined the prevalence and correlates of gender diversity and HIV in at 6 sites in 4 African countries.
Methods: This cross-sectional analysis included participants from integrated HIV bio-behavioral surveillance (IBBS) studies with natal males who have sex with males in Burkina Faso (n=673), Lesotho (n=530), Gambia (n=206), and Malawi (n=338). Regression modeling was used assess the relationships between gender identity, HIV vulnerabilities, and HIV status by site. Correlates were not assessed in Gambia due to the low number of gender variant participants (n=4).
Results: The proportion of respondents identifying as women included 23% in Bobo-Dioulasso, 19% in Blantyre, 8% in Maseru, 7% in Ouagadougou, 6% in Maputsoe, and 2% in Banjul. In the three sites where asked, the proportion of transgender-identified respondents were 13% in Maseru, 9% in Maputsoe, and 3% in Blantyre. Across sites, gender variance was significantly associated with greater likelihood of reporting discrimination, such as rejection by family or friends, verbal harassment, physical assault, and forced sex. Women-identified participants were more likely to report problem alcohol use, depressive symptoms, receptive anal sex, and a higher number of male partners. Condom use was lower in all sites except Bobo-Dioulasso. Laboratory-confirmed HIV prevalence was much higher among gender variant respondents in all sites, but only reached statistical significance in Lesotho (60-64% versus 28-33%).
Conclusions: These data suggest that women-identified and transgender natal males may represent a considerable proportion of the "MSM" included in current IBBS studies and that they differ from male-identified participants in structural HIV vulnerabilities, HIV risk behavior, and HIV prevalence. Filling the gap in understanding gender diversity in Africa is essential to the ability to accurately measure and interpret data as well as develop appropriate interventions for the prevention, care, and treatment of HIV.

	Bobo-Dioulasso, Burkina Faso	Ouagadougou, Burkina Faso	Banjul, Gambia	Blantyre, Malawi	Maputsoe, Lesotho	Maseru, Lesotho
Woman or Transgender	12/201 (6%)	10/241 (4%)	18/199 (9%)	44/305 (14%)	63/192 (33%)	80/285 (28%)
Man	3/75 (4%)	2/21 (10%)	2/4 (50%)	8/33 (24%)	12/20 (60%)	16/25 (64%)

[Proportion with HIV by gender and site]

Epidemiology of HIV in other populations

WEPEC631

HIV prevalence and sexual behaviours among people with disabilities (PWD) in four states in Nigeria

S. Adebajo[1], W. Tun[2], A. Oginni[1], G. Eluwa[1], S. Sangowawa[1], J. Njab[1], O. Idogho[3]
[1]Population Council, Abuja, Nigeria, [2]Population Council, Washington, DC, United States, [3]Society for Family Health, Abuja, Nigeria
Presenting author email: sadebajo@popcouncil.org

Background: PWD have often been overlooked in the context of HIV risk, prevention, and services as it is commonly assumed that they are not at risk for HIV. However, PWD are indeed at risk for HIV and have been found to be at equal or greater, risk for HIV compared to non-disabled persons.
This study measured prevalence of HIV, sexual behaviors and identified barriers to access and use of HIV prevention services among people with hearing, vision, and physical impairments in specialized schools and in the community.
Methods: A cross-sectional survey with HIV testing was conducted among PWD recruited through staff of Disabled Persons Organizations (DPO) from specialized schools and the community in Lagos, Calabar, Kaduna and Benue states in Nigeria.
Results: A total of 624 individuals (53.7% females and 46.3% males) participated with median age of 25.0 (IQR, 20.0—31.0) years. Two-thirds had at least secondary level education (67.6%), were single (69.6%), and resided in urban (62.3%) areas. Nearly half lived with at least one parent while 32.4% lived on their own. Seventy-one percent had ever had sex of which 74.4% had sex in the last year and nearly 20% had their sexual debut before 15 years. In the last year, 26% males and 17% females had multiple sex partners and 15% engaged in transactional sex. Only 63% ever used a condom, 36% currently used and 50% used condoms during higher-risk sex. PWD displayed low comprehensive knowledge and self-perceived risk of HIV and a high level of gender-based violence was reported by female PWD. Only 43% ever tested for HIV and received their results. Overall, HIV seroprevalence was 2%, higher among females (2.4%) than males (1.4%).
Conclusions: This is the first study to estimate the sero-prevalence of HIV and risk behaviors among PWD in Nigeria. It highlights that PWD are sexually active and they engage in behaviours that increase their vulnerability to HIV. While the HIV prevalence is lower than in the general population in Nigeria (3.4%), 2% is not negligible. This study also found that female PWD experience sexual violence that put them at risk for HIV.

WEPEC632

Factors related to seeking prison-based medication assisted therapy for opioid addiction

T. Mukherjee[1], J. Wickersham[2], V. Pillai[3], A. Kamarulzaman[3], F. Altice[2]
[1]Yale School of Public Health, New Haven, United States, [2]Yale University School of Medicine, AIDS Program, New Haven, United States, [3]University of Malaya, Centre of Excellence for Research in AIDS (CERiA), Kuala Lumpur, Malaysia
Presenting author email: tmukher1@gmail.com

Background: Criminalization of drug use in Malaysia has led to a concentrated epidemic of HIV and substance use disorders within prisons. In response, Malaysia introduced prison-based methadone maintenance therapy (MMT) programs to treat opioid dependence, reduce risk behaviors, and prevent relapse to drugs post-release. Despite the introduction of this program, MMT uptake has been suboptimal in prison settings. Therefore identifying individual-level factors associated with MMT initiation is key to improving uptake.
Methods: A total of 200 incarcerated individuals with a history of opioid use in the 12 months prior to incarceration were enrolled in a study to identify attitudes and behaviors associated with MMT-seeking. Inclusion criteria were: 18 years of age or older, current incarceration for at least 30 days, and the ability to speak English or Bahasa Malaysia. Sampling was stratified by HIV status (HIV-positive=96; HIV-negative=104).
Results: Only 18 (9.0%) participants were currently enrolled in the MMT program and 69 (39.9%) were interested in enrolling in the MMT program. Pre-incarceration poly-substance use (OR=1.92) and injecting drug use (OR=2.80) were both associated with greater MMT seeking (p< 0.05). In regards to psychosocial factors, greater addiction severity (OR=1.20) and depression (OR=1.70) were associated with greater MMT seeking (p< 0.05).
Additionally, those with greater treatment knowledge and more positive attitudes towards MMT were 1.50 times more likely to seek MMT (p< 0.001). Age, ethnicity, religion, marital status, education, and income were unrelated to MMT-seeking. Those without previous incarcerations, however, were 5.80 times more likely to seek MMT when compared to those with prior incarcerations (p=0.005).
Conclusions: Results show that interest in MMT initiation is largely driven by risky drug use behavior, treatment knowledge and attitudes, and prior incarceration history. Incarceration provides a unique window of opportunity to initiate MMT, and previous findings suggest that prison-initiated MMT is associated with greater treatment retention and anti-retroviral (ARV) adherence post-release. Further investigation into how pre-incarceration drug use behavior affects MMT interest is warranted, especially in the context of prisons. Despite efforts to introduce MMT into the prison system, successful uptake of MMT will not be possible without addressing how treatment knowledge and attitudes impair MMT seeking.

Epidemiology of sexually transmitted infections (STI) and HIV co-infection

WEPEC633

Factors associated with HIV and syphilis co-infection among men who have sex with men in Brazil

M.D.C. Guimaraes[1], C. Kendall[2], I. Dourado[3], A.M. Brito[4], G.M. Rocha[5], L.R.F.S. Kerr[6]
[1]Federal University of Minas Gerais, Department of Preventive and Social Medicine, Belo Horizonte, Brazil, [2]Tulane University School of Public Health and Tropical Medicine, Center for Global Health Equity, New Orleans, United States, [3]Federal University of Bahia, Instituto de Saúde Coletiva, Salvador, Brazil, [4]Oswaldo Cruz Foundation, Centro de Pesquisas Ageu Magalhães, Recife, Brazil, [5]Federal University of São João del Rei, Divinopolis, Brazil, [6]Federal Univerity of Ceará, Fortaleza, Brazil
Presenting author email: mark.guimaraes@gmail.com

Background: HIV and Syphilis share many common factors and syphilis may increase the likelihood of HIV transmission. Syphilis is increasing among men who have sex with men (MSM) in several countries. This work aimed at assessing the prevalence and factors associated with HIV-syphilis co-infection, HIV only, or syphilis only among MSM in Brazil.
Methods: Respondent Driven Sampling cross-sectional study of 3738 MSM aged 18 years or older residents in ten large Brazilian cities. Data on sociodemographic and behavioral characteristics were collected using hand-held devices. HIV and syphilis serology were performed using standard methods. Estimates were weighted by the inverse of the probability proportional to the size of the social network and the proportion of MSM in each city. Number (>5) and type of sex partners (commercial, fixed, casual), and irregular condom use during anal intercourse in the past year were combined into a sexual risk score. Weighted prevalence rates with 95% confidence intervals (95% CI) were estimated. Observations with missing data on HIV or syphilis serology were excluded. The magnitude of the associations with HIV only, Syphilis only, or HIV-Syphilis co-infection, each compared to participants with no infection, was estimated by the prevalence rate ratio (PRR) using Poisson regression, with a significance level of 0.05.
Results: Prevalence rates and Adjusted PRR are shown in Table 1. Older age and past history of syphilis were independently associated with all outcomes. Not knowing ones risk of acquiring HIV was strongly associated with HIV only or with co-infection. Median risk score was 4 (rage 0-36), while moderate-high sexual risk score (> 2) was associated with co-infection only. Prior HIV testing and sex with men only was associated with HIV infection only.

Characteristics	HIV Only	Syphilis Only	HIV-Syphilis Co-infection
Prevalence Rate	6.7% (5.8 - 7.5)	9.5% (8.5 - 10.5)	4.4% (3.7 - 5.0
	PRR (95% CI)	PRR (95% CI)	PRR (95% CI)
Age (> 24 y.o.)	2.46 (1.55 - 3.91)	2.12 (1.16 - 3.88)	4.81 (1.70 - 13.59)
History of syphilis	1.76 (1.02 - 3.02)	2.39 (1.30 - 4.37)	8.46 (3.92 - 18.25)
History of Any STD	1.66 (1.01 - 2.74)	2.51 (1.41 - 4.46)	-
Not knowing ones risk of acquiring HIV	4.11 (2.69 - 6.29)	-	4.10 (1.91 - 8.78)
Sex with men only	2.06 (1.11 - 3.82)	-	-
Prior HIV Testing	2.50 (1.38 - 4.50)	-	-
Moderate-High sexual risk score	-	-	2.61 (1.20 - 5.69)

[Table 1- Prevalence and Adjusted PRR according to]

Conclusions: The prevalence of HIV and syphilis, alone or as co-infections, was high among this RDS sample of MSM in Brazil. Despite availability of free treatment and access to testing within the public health system in Brazil, treatment and prevention efforts may not be reaching those at higher risk. Public health workers and non-governmental organizations should be aware of the rising number of syphilis cases and co-infection among MSM to improve prevention and treatment nationwide.

WEPEC634

Sexually transmitted infection (STI) incidence in men who have sex with men (MSM) followed since primary infection stage in the French ANRS-PRIMO cohort

K. Champenois[1], R. Seng[1,2,3], A. Persoz[1], A. Essat[1], C. Goujard[1,2,4], L. Meyer[1,2,3], ANRS PRIMO Cohort Study Group
[1]Inserm UMR 1018, CESP-4, Epidemiology of HIV and STIs, Le Kremlin Bicêtre, France, [2]South-Paris University, South-Paris Medical School, Le Kremlin Bicêtre, France, [3]AP-HP, Bicêtre Hospital, Epidemiology and Public Health Service, Le Kremlin Bicêtre, France, [4]AP-HP, Bicêtre Hospital, Internal Medicine Department, Le Kremlin Bicêtre, France
Presenting author email: remonie.seng@inserm.fr

Background: In France, in a context of rising at-risk sexual behaviour in MSM, we estimated the incidence rate of STIs in HIV-infected MSM followed since primary HIV infection. We compared these incidence rates according to the viral load of patients at the visit preceding the STI diagnosis.
Methods: In 1996-2014, 1,226 MSM have been enrolled in the ANRS-PRIMO cohort during primary HIV-infection. Patients are followed every 6 months. At each visit, a clinical questionnaire is completed with lab measurements, antiretroviral treatment and clinical information including STI occurrence since the last visit.
We focused on syphilis, gonorrhea, *Chlamydia trachomatis* infections, and other suspected bacterial infections such as unspecified uretritis, rectitis, epididymitis, orchitis and balanitis. We assumed that two episodes of the same STI were distinct infections if separated by ≥3 months, and by ≥1 year for syphilis. We assessed the evolution over time in incidence rates and their association with the viral load of the patients measured at the visit preceding the STI diagnosis with a regression model of Poisson taking into account longitudinal data.
Results: We observed 412 incident STIs in MSM, i.e. an incidence rate of 6.67/100 patient-years (PY) [95%CI: 6.05-7.34], including 215 syphilis (incidence rate: 3.61/100PY [3.16-4.13]) and 197 other bacterial STIs (incidence rate: 3.19/100PY [2.77-3.66]).
The syphilis incidence rate was null before 2000 and increased afterwards of 9% per year on average (p< 0.0001) up to 4.91/100PY in 2013. As well, the other STIs incidence rate increased over time of 4% per year (p=0.006) up to 4.40/PY in 2013.
Considering all STIs together throughout 1996-2014, the incidence rate during the periods when MSM had an undetectable viral load was lower compared with the periods with detectable viral load (6.08/100PY versus 7.72/100PY, p=0.02).
Conclusions: In these HIV-infected MSM, STIs incidence has risen over calendar time, in syphilis as well as in other bacterial infections. Although they may be underestimated because of under-reporting or under-diagnosis, these incidence rates were high, particularly when the viral load is detectable. With the diffusion of the concept of Treatment as HIV Prevention, efforts should be done to help MSM to prevent transmission of other STIs.

WEPEC635

Prevalence of STI and HIV RNA levels in ano-genital compartments among Thai MSM and transgender women after antiretroviral therapy: implication for treatment as prevention program

S. Pattanachaiwit[1], T. Pankam[1], P. Chamnan[2], P. Pathipvanich[3], S. Thongpaen[4], J. Jantarapakde[1], S. Pengnonyang[1], N. Teeratakulpisarn[1], M. Kongkabpan[1], J. Jitrach[1], D. Trachunthong[5], T. Sungsing[1], S. Naowajit[1], K. Parasate[2], S. Seeneewong Na Ayutthaya[3], K. Trairat[6], C. Lertpiriyasuwat[7], P. Phanuphak[1], N. Phanuphak[1]
[1]The Thai Red Cross AIDS Research Centre, Bangkok, Thailand, [2]Sanpasitthiprasong Hospital, Ubonratchathani, Thailand, [3]Lampang Hospital, Lampang, Thailand, [4]Mahasarakam Hospital, Mahasarakam, Thailand, [5]The HIV Netherlands Australia Thailand Research Collaboration (HIV-NAT), Bangkok, Thailand, [6]Mahasarakam Hospital,, Mahasarakam, Thailand, [7]Ministry of Public Health, Department of Disease Control, Nonthaburi, Thailand

Background: Sexually transmitted infections (STI) are very common among men who have sex with men (MSM) and transgender (TG) women, especially in those with HIV infection. Prior to antiretroviral therapy (ART) initiation, we previously demonstrated the correlation between STI and HIV RNA detectability in ano-genital compartments among Thai MSM and TG. We evaluated this correlation again after 12 months of ART.
Methods: Thai MSM and TG aged ≥18 years who tested HIV-positive at enrollment were offered immediate ART. Syphilis serology, oropharyngeal/rectal swab, urine collection for gonorrhea and chlamydia nucleic acid amplification testing, and HIV RNA measurement in blood, semen and rectal samples were performed at baseline and after 12 months of ART.
Results: Of 111 HIV-positive MSM/TG who reached month 12 after ART, median (IQR) age was 23.5 (21.2-29.2) years. At month 12 after ART, median (IQR) CD4 count was 484 (361-661) cells/mm^3, 16% reported having >1 partners and 15% did not use condom in the past month. 32% had reactive syphilis serology, 18% had gonorrheal infection (oropharyngeal 12%, rectal 12%, urethral 1%) and 30% had chlamydial infection (oropharyngeal 7%, rectal 23%, urethral 1%). At baseline, detectable HIV RNA (>50 copies/mL) was found in 100% of blood, 61% of semen and 67% of rectal samples. At 12 months after ART, detectable HIV RNA was found in 3.5% (3/86) of blood, 1.2% (1/83) of semen and 1.4% (1/72) of rectal samples. No participant had detectable HIV RNA in more than one compartment. STI was not found in participants with detectable HIV RNA in semen or rectal sample. Higher proportion of participants with detectable HIV RNA after ART had HIV RNA >100,000 copies/mL in blood at baseline (100% vs. 42%, p=0.02), had < 95% ART adherence (75% vs. 23%, p=0.05) and had baseline resistance mutations to first-line ART used (20% vs. 2%) than those with undetectable HIV RNA.
Conclusions: HIV-positive MSM/TG continued to have high prevalence of STI after ART. ART effectively reduced HIV RNA in all compartments. Correlation between STI and detectable HIV RNA in ano-genital compartment was not seen after ART. Adherence remains crucial to achieve the prevention benefit of ART.

Epidemiology of viral hepatitis and HIV co-infection

WEPEC636

Elevated hepatitis C incidence among youth, women co-infected with HIV/STIs and sex workers who use crack cocaine in Vancouver, Canada: gaps and opportunities for HCV prevention and treatment

S. Goldenberg[1,2], K. Deering[1,2], P. Nguyen[1], S. Dobrer[1], M.E. Socias[1,3], S. Guillemi[2,4], J. Montaner[2,5], K. Shannon[1,2]
[1]Gender and Sexual Health Initiative, BC Centre for Excellence in HIV/AIDS, Vancouver, Canada, [2]University of British Columbia, Department of Medicine, Vancouver, Canada, [3]University of British Columbia, Interdisciplinary Studies Graduate Program, Vancouver, Canada, [4]Clinical Education and Training Program, BC Centre for Excellence in HIV/AIDS, Vancouver, Canada, [5]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada
Presenting author email: sgoldenberg@cfenet.ubc.ca

Background: Given the dearth of incidence data on hepatitis C virus (HCV) among female sex workers, potential for dual sexual and drug risk pathways, and the opportunities posed by new HCV therapies in 2014, we aimed to characterize incidence and predictors of HCV infection among female sex workers (SWs) who use and do not use substances in Metropolitan Vancouver, BC.
Methods: Data were drawn from a prospective cohort of 723 SWs recruited through street, indoor and online outreach ("An Evaluation of Sex Workers' Health Access") from 01/2010 - 08/2013. At baseline and semi-annually, participants completed questionnaires and voluntary HIV, STI and HCV testing by a project nurse with education and referrals to HIV, STI and HCV prevention, treatment and care. Cox regression was used to longitudinally model predictors of time to HCV seroconversion.
Results: Of 715 SWs included in the analysis, HCV prevalence was 43.6%, with higher odds of HCV infection among women who were HIV-positive, had a recent acute STI infection, older, of Aboriginal/Indigenous ancestry, engaged in sex work for longer, and solicited clients outdoors (vs. indoor/online). HCV incidence density and predictors of time to infection were calculated among 256 SWs who were HCV-seronegative at baseline and had at least one follow-up visit. During the 3.5-year observation period, the HCV incidence density was 4.28 events/100 person-years (95% CI: 2.73-6.72), with highest rates among SWs who inject drugs (SW-PWID) (24.05 events/100 person-years, 95% CI: 13.57-42.63) and SWs who use non-injection drugs (7.02 events/100 person-years, 95% CI: 4.39-11.21). In a multivariate Cox model, age (Hazard Ratio (HR): 0.91, p=0.04), STI co-infection (HR: 3.45, p=0.04), and non-injection crack use (HR: 4.24, p=0.05) remained independent predictors of time to HCV seroconversion; in a separate model, HIV co-infection also independently predicted time to HCV seroconversion.
Conclusions: While HCV incidence was highest among SW-PWID, STIs and non-injection stimulant crack use appear to be major pathways to HCV infections, suggesting dual sexual and drug transmission of HCV. Younger women and those co-infected with HIV/STIs face enhanced risk of HCV acquisition, highlighting the need for integration of HCV services within sexual health and HIV/STI programmes for youth, women and sex workers.

WEPEC637

Benzodiazepine use is a risk factor for hepatitis C infection in a prospective cohort of persons who inject drugs

P. Bach, G. Walton, K. Hayashi, M.J. Milloy, H. Dong, T. Kerr, J. Montaner, E. Wood
St. Paul's Hospital, British Columbia Centre for Excellence in HIV/AIDS, Vancouver, Canada
Presenting author email: paxbach@gmail.com

Background: Intravenous drug use is associated with an increased risk of acquiring blood-borne infections such as HIV and hepatitis C (HCV). While the diversion and abuse of prescription drugs has been has been the source of growing public health concern, benzodiazepines have received relatively less attention in comparison to prescription opioids. Therefore, the present study examined for a possible association between benzodiazepine use and HCV infection in a prospective cohort of persons who inject drugs (PWID).
Methods: The Vancouver Injection Drug Users Study is a prospective cohort of PWID in Vancouver, British Columbia. In the present study we investigated the relationship between benzodiazepine use and HCV seroconversion using a Cox proportional hazards regression.
Results: Between May 1996 and November 2013, 441 participants were included in our study sample. At the time of enrollment the median age of participants was 29.5, 300 (68.0%) were male, and 253 (57.4%) were Caucasian. 271 (61.5%) reported benzodiazepine use within the past 6 months. In a multivariate Cox regression model, after adjusting for potential confounders, benzodiazepine use remained independently associated with an increased risk of HCV seroconversion (Adjusted Hazard Ratio = 2.42; 95% Confidence Interval = 1.59 - 3.69).
Conclusions: This study highlights the high prevalence of illicit benzodiazepine use in a population of PWID, and demonstrates an independent association with increased risk of HCV infection. These data highlight the need for physician education regarding the limited evidence-based clinical indications for benzodiazepine prescription and greater recognition of the safety concerns related to benzodiazepine diversion.

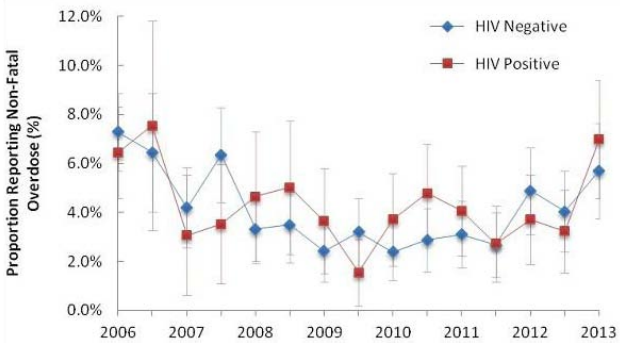
Epidemiology of Serious Non-AIDS events

WEPEC638

No association between HIV serostatus and risk of non-fatal overdose among people who inject drugs within the ACCESS and VIDUS2 cohorts in British Columbia

D.J. Escudero[1], B.D.L. Marshall[1], T. Kerr[2,3], C. Feng[2], S. Guillemi[2], R. Hogg[2], J. Montaner[2,3], E. Wood[2,3], M.-J. Milloy[2,3]
[1]Brown University, Department of Epidemiology, Providence, United States, [2]British Columbia Centre for Excellence in HIV/AIDS, Vancouver, Canada, [3]University of British Columbia, Division of AIDS, Department of Medicine, Vancouver, Canada
Presenting author email: brandon_marshall@brown.edu

Background: HIV infection among people who inject drugs (PWID) may contribute additional risk of experiencing an accidental drug overdose. A 2012 meta-analysis, which found a positive association between HIV infection and overdose, summarized possible causative pathways for this association, including immunosuppression and poorer physical health. We sought to replicate this finding by estimating the association between HIV serostatus and risk of non-fatal overdose (NFOD) using seven years of data from two community-recruited cohorts of HIV-positive and -negative PWID.
Methods: Data were collected from the ACCESS (HIV-positive) and the VIDUS2 (HIV-negative) parallel open prospective cohorts in Vancouver, Canada. We included all participants who completed at least one baseline or follow-up questionnaire during the study period (2006-2013). During each follow-up assessment, participants were asked whether they had experienced an NFOD (i.e., "a negative reaction from using too much drugs") within the previous six months. We plotted the proportion reporting at least one NFOD during each assessment, stratified by HIV status
(**Figure 1**). Then, bivariable and multivariable generalized mixed-effects regression models were used to determine the longitudinal unadjusted and adjusted association between HIV status and likelihood of NFOD.
Results: 1760 participants completed at least one questionnaire, producing 15,070 unique assessments. Among these observations, 649 (4.3%) included a report of a NFOD within the previous six months (4.4% among seropositive and 4.3% among seronegative individuals). Results of the bivariate analysis of serostatus and risk of NFOD were null (Odds Ratio [OR]: 1.05, *p*=0.853). This persisted in multivariate analysis adjusted for potential confounders such as ancestry, risk behavior, and exposure to violence (Adjusted OR [AOR]: 1.19, *p*=0.474). Additionally, secondary multivariate analysis estimating the association between detectable plasma viral load (compared to undetectable or negative serostatus) and NFOD yielded a null result (AOR: 1.30, *p*=0.290).



[Figure 1. Proportion of ACCESS and VIDUS2 participants reporting NFOD, by assessment period and HIV serostatus]

Conclusions: Using longitudinal data from two large, long-running and community-recruited prospective cohorts of PWID, we did not observe a significant relationship between HIV status and overdose. Potential differences in study settings or methods may have contributed to our results differing from those previously observed. Further research is needed to test the relationship between HIV status and risk of overdose.

Molecular epidemiology

WEPEC639

Transmission clusters among newly diagnosed HIV patients in the country of Georgia

N. Dvali[1], M. Karchava[1], N. Chkhartishvili[1], L. Sharvadze[1], I. Burjanadze[2], M. Parker[3], J. De Hovitz[4], K. Nelson[5], T. Tsertsvadze[1]
[1]Infectious Diseases, AIDS and Clinical Immunology Research Center, Tbilisi, Georgia, [2]National Center for Disease Control and Public Health (NCDC), Tbilisi, Georgia, [3]Wadsworth Center, Albany, United States, [4]SUNY Downstate Medical Center, Brooklyn, United States, [5]Bloomberg School of Public Health, Johns Hopkins University, Baltimore, United States
Presenting author email: natia_dvali@yahoo.com

Background: For years the HIV epidemic in Georgia was driven by injection drug use (IDU). Recent trends indicate an increase in sexually acquired infections, including emergence of an epidemic among men who have sex with men (MSM). We aimed to characterize the molecular epidemiology of HIV in Georgia and identify possible transmission clusters.
Methods: Multiple alignments of HIV-1 *pol* sequences were created with CLUSTAL W and phylogenetic analyses were conducted using MEGA software. The Neighbor Joining method and Kimura two-parameter model with reliability estimated from 1000 bootstrap replicates were used for tree construction. Branches consisting of ≥2 sequences showing bootstrap value of ≥70% and intra-cluster genetic distance ≤0.015 were considered reliable and defined as "cluster".
Results: Among 218 newly diagnosed HIV patients included in the study the median age was 35 years and 138 (63.3%) were men. Slight majority (53%) were infected via heterosexual contact, IDU accounted for 37.6% and MSM to 6.9% of cases. 195 (89.4%) patients carried subtype A virus; 15 (6.9%) had subtype B and 6 (2.7%) had subtype G viruses; there was a single case each of subtype F (0.5%) and recombinant form AB_03 (0.5%). Overall 93% of IDUs and heterosexually infected persons had subtype A and 60% of MSM had subtype B. All viruses within subtypes A and B formed major clusters, with bootstrap values of 86% and 98% respectively. A total of 49 sequences grouped into 17 smaller clusters, the majority of which (71%) were pairs. The largest cluster of 8 sequences was dominated by MSM. There was significant clustering between viruses from IDUs and heterosexually infected females. Viruses from MSM and IDUs did not cluster together. In multivariate analysis, factors associated with membership in a cluster included: age < 25 (RR 2.44, p=0.014), MSM (RR 2.16, p=0.015), subtype B virus (RR 2.56, p=0.002).
Conclusions: Our study shows that subtype A is predominant HIV strain circulating in Georgia. Our findings confirm surveillance data showing emergence of HIV in the MSM population. There is strong linkage between IDU and heterosexual epidemics. Viruses from IDUs and MSM do not cluster together, thus suggesting independent evolution of epidemics in these populations.

WEPEC640

Genetic characterization of a large panel of diverse HIV-1 strains at six international sites

B. Hora[1], S. Keating[2,3], Y. Chen[1], A.M. Sanchez[1], E. Sabino[4], G. Hunt[5], J. Hackett Jr.[6], P. Swanson[6], I. Hewlett[7], V. Ragupathy[7], S.V. Vemula[7], P. Zeng[8], K.-K. Tee[9], W.Z. Chow[9], T.N. Denny[1], M.P. Busch[2,3], F. Gao[1]
[1]Duke Human Vaccine Institute, Medicine, Durham, United States, [2]University of California, Blood Systems Research Institute, San Francisco, United States, [3]University of California, Department of Laboratory Medicine, San Francisco, United States, [4]Instituto de Medicina Tropical, Sao Paolo, Brazil, [5]National Institute of Communicable Diseases, Johannesburg, South Africa, [6]Abbott Laboratories, Infectious Diseases Research, Abbott Park, United States, [7]Food and Drug Administration, Center for Biologics Evaluation and Research, Silver Springs, United States, [8]Chinese Academy of Medical Sciences, Institute of Blood Transfusion, Chengdu, China, [9]University of Malaya, Centre of Excellence for Research in AIDS, Faculty of Medicine, Kuala Lumpur, Malaysia
Presenting author email: bhavna.hora@duke.edu

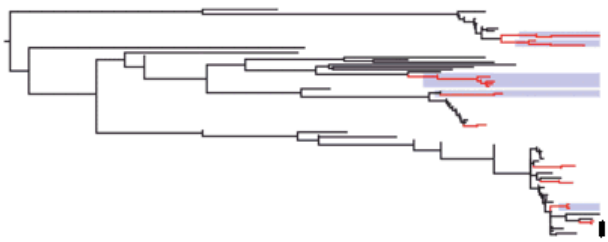
Background: Genotyping for HIV-1 subtypes and drug resistance are determined by many international surveillance groups including the Recipient Epidemiology and Donor Evaluation Study-III (REDS-III) network. However, results from different sites are variable. A systematic comparison of results from multiple sites is needed to determine if a standardized protocol is required for consistent and accurate data analysis.
Methods: A panel of well-characterized viruses (N=50) from the External Quality Assurance Program Oversight Laboratory (EQAPOL) was assembled for evaluation at six international sites (Brazil, South Africa, USA {2 sites},China, and Malaysia). The panel represented 7 subtypes, 6 circulating recombinant forms (CRFs), 9 unique recombinant forms (URFs) and 3 group O viruses. Seven viruses contained 10 major drug resistance mutations (DRMs). The virus isolates were prepared at 10^7 copies/mL, compiled into blinded panels. Genotypes and DRMs were determined with partial *pol* sequences at five sites or whole genome sequences generated by next generation sequencing (NGS) at one site. Results (genotypes, DRMs and sequences) were reported, decoded, and compared to full-length genome sequences generated by EQAPOL.
Results: Five sites targeting partial *pol* gene obtained positive PCR products from the majority (89.4%-93.6%) or all of 47 group M viruses. 95.1%-98% of the viruses were genotyped correctly for the partial *pol* sequences. However, many viruses contained additional recombination at unsequenced regions that could not be predicted by the partial *pol* sequences. All 10 major DRMs in 7 viruses were correctly detected at these 5 sites. All 50 viruses were also analyzed by NGS by one site. Four group M viruses were not amplified, and 3 recombinant viruses were not genotyped correctly. In addition, NGS missed 5 major DRMs but detected one additional major DRM. No group O viruses were amplified, except at one site that used additional PCR primers specific for group O viruses.
Conclusions: While major DRMs in protease and reverse transcriptase can be detected by partial *pol* sequences, the PCR conditions and subtyping program should be standardized to more efficiently amplify diverse viruses and more consistently assign virus genotypes, which is critical for accurate global subtype surveillance.

WEPEC641

Molecular analysis of HIV-infected individuals in a network-based intervention (TRIP): phylogenetics identify HIV-infected individuals with risk links

D. Paraskevis[1], J. Schneider[2], B. Skaathun[2], M. Psichogiou[3], P. Smyrnov[4], E. Pavlitina[1], A. Korobchuk[4], M. Malliori[5], A. Hatzakis[1], S.R. Friedman[6], G. Nikolopoulos[7]
[1]Medical School, University of Athens, Department of Hygiene Epidemiology and Medical Statistics, Athens, Greece, [2]University of Chicago, Departments of Medicine & Public Health Sciences, Chicago, United States, [3]Laikon General Hospital, Department of Propedeutic Medicine, Athens, Greece, [4]International HIV/AIDS Alliance, Odessa, Ukraine, [5]Medical School, University of Athens, Athens, Greece, [6]National Development and Research Institutes (NDRI), New York, United States, [7]Hellenic Center for Disease Control and Prevention, Athens, Greece
Presenting author email: gknikolopoulos@gmail.com

Background: TRIP is a three-city network-based intervention which aims to decrease HIV spread by the recently infected. Here we estimate patterns of viral spread among persons who inject drugs (PWID) recruited in TRIP, Athens, and explore correlations between transmission links as estimated by phylogenetic analysis and risk networks.
Methods: Phylogenetic trees were inferred from HIV sequences generated from TRIP participants using as references, sequences from PWID sampled during the HIV outbreak (2011-2014) in Athens. Highly supported clusters (subnetworks) are those received >75% bootstrap support. Risk network links were determined based on standard network survey methods.
Results: We recruited 339 individuals (89% PWID) including negative controls; recently infected persons; long-term infected controls; and the first and second degree risk network members of recently infected and controls. Among them, 143 were HIV(+). To date, we have sequenced 96 HIV(+) individuals (males 77%, mean age 36.8 years). We identified three categories of phylogenetic clusters: Those whose members belong to previously identified PWID transmission networks in Athens outbreak (n=78, 82.1%: CRF14_BG, CRF35_AD, subtypes A and B), unique recombinant forms consisting of partial sequences from previously-identified PWID clusters (n=10, 10.4%); and those whose sequences are tied to non-PWID transmission trees (n=8, 8.3%: CRF56_cpx, subtype A). Further phylogenetic analyses in all sequences suggested the existence of nine phylogenetic clusters (subnetworks) including 2-5 individuals in each cluster (figure). We identified 24 (25.0%) PWID within the subnetworks. Five of these subnetworks included 15 people who also had risk ties with at least another member of their cluster (figure). Specifically, one subnetwork consisted of people who were all homeless or incarcerated.



[Figure. Phylogenic tree of sequences from TRIP participants. Highly supported clusters (subnetworks) are shown in red. Five subnetworks who also had risk ties with at least another member of their cluster are highlighted in purple]

Conclusions: Risk networks are known to affect the probability of getting or transmitting HIV. Our data suggest that molecular methods can identify infected people with a risk link in about half of the clusters. The lack of congruence between data sources may be due to older strains, to clients' not naming all risk ties, or both. Regardless, PWID molecular methods can be used to identify some clusters of individuals linked by risk which may be useful for further targeting of biomedical HIV prevention.

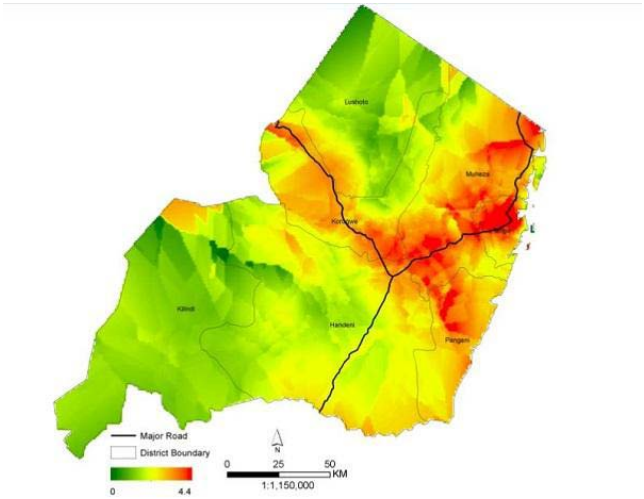
Geographical information systems and HIV

WEPEC642

A geographic approach to better understand HIV at a sub-regional and sub district level in Tanzania

I. Wanyeki[1], B. Mitto[1], L. Nganga[1], T. Tuhama[2], J. Nondi[3]
[1]Futures Group, Nairobi, Kenya, [2]Futures Group, Dar es Salaam, Tanzania, United Republic of, [3]National AIDS Control Program, Dar es Salaam, Tanzania, United Republic of
Presenting author email: ian.wanyeki@mail.mcgill.ca

Background: Significant variations in adult HIV prevalence have been observed at a Regional level in Tanzania, however variations in HIV disease burden at a sub-regional and sub district level are not well understood. We describe a pragmatic approach for examination of variations in HIV burden, identification of potential hotspots and cold spots), as well as ART coverage at a sub-district level through the use of routinely collected clinic level program data from PMTCT and ART clinics.
Objectives:
1. Describe sub district level variations in estimates of HIV prevalence derived from 2013 PMTCT clinic level data.
2. Describe variations in estimates of ART coverage as of June 2014 at the following levels of aggregation (District level and clinic catchment level).
Methods: HIV positivity data was obtained from 523 PMTCT clinics located across 2 regions of Tanzania. 104 clinics which tested less than 50 women and were excluded from the analysis. Annual HIV positivity in 2013 for women attending PMTCT clinics was calculated at each of the remaining 419 PMTCT clinics along with estimates of clinic level HIV prevalence through adjustment with the 2011 population based survey. The geocodes of the clinics were linked to the program data and HIV clinic level prevalence estimates were plotted. Interpolation of clinic level HIV prevalence using universal kriging was performed to create a predicted map of HIV prevalence in 2013. This gridded map of HIV prevalence was multiplied by a gridded map of population to obtain estimates of people living with HIV at a $1km^2$ resolution. Hot and cold spots were determined through the use of the Getis ord Gi statistics tool. ART coverage estimates were then calculated at each clinic catchment area.
Results: Significant district level and sub district level variations in HIV prevalence were observed.
Conclusions: This approach allows an examination of variations in HIV burden at a very fine level of granularity through the use of routinely collected clinic level data. When thinking about resource allocation it is also important to also take into account population distribution and absolute numbers of PLHIV. It helps provide an evidence base that allows for appropriate targeting of resources.



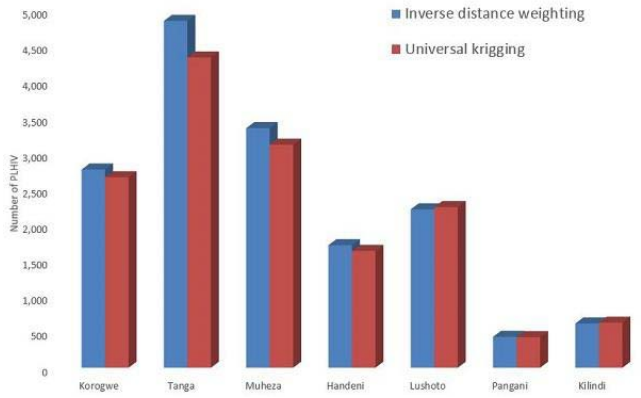
[HIV prevalence estimate surface]

WEPEC643

Interpolation of HIV estimates using off the shelf options, what's the difference?

B. Mitto[1], T. Tuhama[2], I. Wanyeki[1]
[1]Futures Group, Nairobi, Kenya, [2]Futures Group, Dar es Salaam, Tanzania, United Republic of
Presenting author email: ian.wanyeki@mail.mcgill.ca

Background: Understanding disease burden at the lowest level of aggregation is important to enable an appropriate response to managing HIV. Prevalence surveys provide estimates at a national level or provincial level and routinely collected clinic data can provide reasonable estimates of HIV prevalence at a clinic level. To obtain a smoothed surface of HIV prevalence point prevalence estimates can be converted to pixel based estimates through a process known as interpolation.
We evaluated two interpolation methods to examine how the various interpolation methods affect estimates of PLHIV.
Methods: Using routinely collect PMTCT clinic data from 216 PMTCT clinics in the Tanga region of Tanzania, HIV positivity among women in 2013 was calculated and after adjustment, estimates of HIV prevalence among adults were generated. Two interpolation methods (IDW and Universal Kriging) were used to create a smooth surface of HIV prevalence and then two gridded population surfaces of PLHIV were calculated. Performance of the two interpolators was evaluated through two internal validations (Partitioned data holdback and leave one out cross validation). Results were aggregated to the district level and absolute differences in PLHIV examined.
Results: The two interpolation methods produced relatively similar results when the information was aggregated up to the district level. Differences observed in the numbers of PLHIV at the district level ranged from a low of five in Pangani district to a high of 511 in Tanga.



[PLHIV comparison using 2 different methods]

Universal krigging performed better during both internal validations with a RMSE of 4.12 compared to 4.22 in the portioned data holdback, and 0.97 compared to 4.9 in the leave one out cross validation.
Conclusions: An appropriate interpolation method that provides the best estimates of PLHIV at a lower resolution is an important prerequisite for analysis that requires a detailed examination of HIV at a very fine resolution. Different methodologies, tools and models have been developed to estimate HIV prevalence from point data. These methods vary in complexity and accuracy in prediction. It is essential that a user select an interpolator that minimizes the prediction error and also provides an estimated errors of prediction. Our evaluation found universal kriging to be a more suitable interpolator.

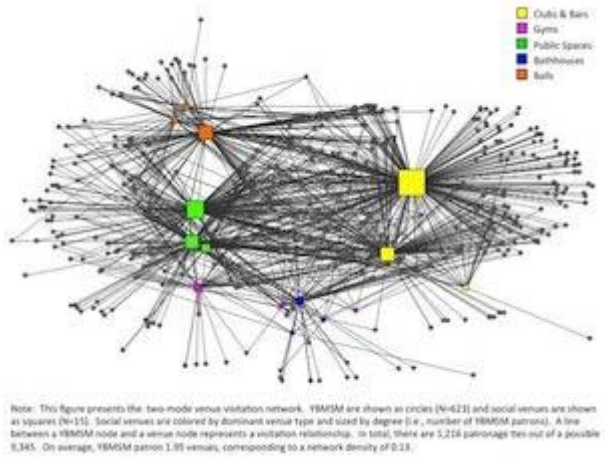
Network studies of risk behaviours and their implications for prevention

WEPEC644

The organizing potential of risk behaviors: sexual risk behaviors as social cues that motivate where young black men who have sex with men (YBMSM) go to meet and socialize

L.E. Young[1,2], S. Michaels[3], A. Khanna[1,2], B. Skaathun[2,4], E. Morgan[2,4], P. Schumm[4], J.A. Schneider[1,2,4], The UConnect Study Team
[1]University of Chicago Medicine, Section of Infectious Diseases and Global Health, Chicago, United States, [2]Chicago Center for HIV Elimination, Chicago, United States, [3]NORC at the University of Chicago, Chicago, United States, [4]University of Chicago, Public Health Sciences, Chicago, United States
Presenting author email: youngl@uchicago.edu

Background: HIV programs focus on social venues that MSM frequent as sites where risk behaviors are practiced and "hotspots" for intervention. But, the impact of established risk tendencies (e.g., sex-drug use) on venue visitation is not well understood. We determine the extent that three types of risk behaviors drive venue visitation amongst a population sample of YBMSM. Understanding the relationship between risk behaviors and venue visitation is critical for understanding how risk emerges in these settings.
Methods: From 2013-2014 data were collected from a respondent-drive sample (RDS) of YBMSM (16-29 years) in Chicago (N=623). The outcome of interest is a 623x15 YBMSM-to-venue visitation network (see Figure). Risk behaviors include inconsistent condom use, sex-drug use, and group-sex. To determine the likelihood of a visitation tie conditioned on YBMSM risk behaviors, we used exponential random graph models (ERGMs), a network analytic technique that examines the prevalence of specific patterns within the network by assessing their statistical likelihood.



[The Two-mode YBMSM-to-Venue Visitation Network]

Results: Of the 623 YBMSM, 46% used condoms inconsistently, 40% used sex-drugs and 21% engaged in group-sex. Clubs & bars were the most visited venues (61%); bathhouses were the least visited (9%). ERGM results reveal that venue visitation, when modeled as an isolated choice, was no more or less likely to be informed by any of the three risk behaviors. However, when YBMSM who:
(a) used condoms inconsistently, or
(b) used sex-drugs, or
(c) engaged in group sex visited venues, they were statistically more likely in all three cases ($p < .05$) to choose places that attracted other YBMSM who practiced the same behaviors.
So, when the influence of other YBMSM is considered, risk behaviors emerge as a socializing force.
Conclusions: Findings demonstrate that sexual risk behaviors provide social cues that YBMSM draw from to make their visitation decisions. HIV prevention programs that target social venues for intervention should examine whether visitors' desires to act on their risky tendencies by being with other MSM that behave similarly informs where they socialize. With this information, it becomes possible to see social venues on a spectrum of enacted risk versus risky in and of themselves.

WEPEC645

Some mediators contribute critically to transmit HIV-1 subtype B to various MSM communities in Japan

T. Shiino[1], K. Sadamasu[2], M. Nagashima[2], J. Hattori[3], A. Hachiya[4], W. Sugiura[4]
[1]National Institute of Infectious Diseases, Infectious Disease Surveillance Center, Tokyo, Japan, [2]Tokyo Metropolitan Institute of Public Health, Department of Microbiology, Tokyo, Japan, [3]National Institutes of Health, National Cancer Institute, Bethesda, United States, [4]Nagoya Medical Center, Clinical Research Center, Nagoya, Japan
Presenting author email: tshiino@nih.go.jp

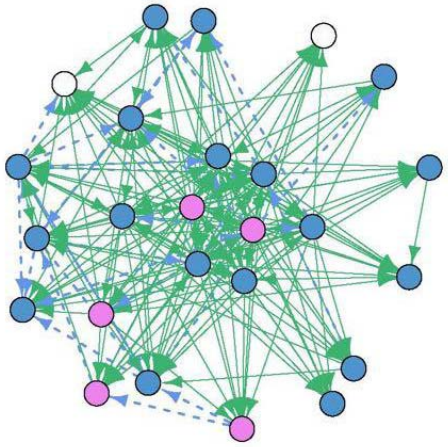
Background: Investigation of transmission network features through conventional epidemiological method are of limited in HIV-1 which has a long incubation period between transmission and disease state and a low transmission rate per contact. To clarify an HIV transmission network of men who have sex with men (MSM) population in Japan, we conducted a phylogenetic-based transmission clustering followed by a network analysis.
Methods: Cases newly diagnosed as HIV-1 infected and registered in the Japanese Drug Resistance HIV-1 Surveillance Network between 2002 and 2012 were enrolled in the analysis. Protease-reverse transcriptase sequences from individuals newly diagnosed as HIV-1 seropositive were collected and their subtypes were determined. Phylogenetic relationships of subtype B sequences were inferred by 3 different methods: distance-matrix, maximum likelihood and Bayesian inference. Transmission clusters were identified based on the following criteria: >95% in interior branch test, >95% in Bayesian posterior probability and < 10% in depth-first searches for sub-tree partitions. Time of the most recent common ancestor (tMRCA) of the transmission clusters were estimated by Bayesian inference. The transmission networks were estimated by linking two individuals (nodes) in a cluster whenever their sequences showed less than 1.5% genetic distance, and degree- and betweenness-based centrality indexes were calculated.
Results: Of 5018 cases collected between 2002 and 2012, 4398 (87.6%) were classified as subtype B. Of the 312 clusters found, 121 (38.8%) were large clusters with >5 individuals, and the largest cluster consisted of 256 individuals. 292 clusters (93.6%) showed a MSM behavior for their major transmission risk. Especially, all of 121 large clusters had the MSM risk. Most clusters had tMRCA between 1995 and 2005, suggesting that subtype B viruses expanded among MSM in the second half of the 1990s. Based on sample collection areas, clusters appeared to associate with specific geographic regions. Node centrality analysis of transmission networks in some large clusters revealed a few core individuals were connecting different communities.
Conclusions: Our study suggests that a few mediators connect different transmission networks. To prohibit further spread of HIV-1 infections and expansions of the transmission networks, such mediators and their communities should be targeted for prevention interventions.

WEPEC646

Sociocentric networks of urban Tanzanian youth enrolled in an HIV prevention trial

M. Mulawa[1], T. Yamanis[2], C. Barrington[1], L. Kajula[3], S. Maman[1]
[1]University of North Carolina at Chapel Hill, Health Behavior, Durham, United States, [2]American University, School of International Service, Washington, United States, [3]Muhimbili University of Health and Allied Sciences, Psychiatry and Mental Health, Dar es Salaam, Tanzania, United Republic of
Presenting author email: smaman@unc.edu

Background: Sociocentric network studies can advance our understanding of the structure and function of social relationships, and the mechanisms through which social networks shape HIV risk behaviors. Compared to egocentric network studies, which depict relationships of an actor's contacts and his/her perceptions of relationships between those contacts, sociocentric network studies aim to collect comprehensive data on the direct and indirect relationships between all individuals within bounded populations. This information may be leveraged to enhance the efficiency and effectiveness of HIV prevention efforts. Despite their potential for improving HIV prevention efforts, sociocentric network studies are lacking in sub-Saharan Africa. Our team is conducting a cluster-randomized HIV prevention trial with youth who socialize in urban social networks called camps in Dar es Salaam, Tanzania. Our objective is to describe the network structure of youth within these camps.
Methods: We defined the network boundaries through membership in one of our 60 study camps.
Of the 1,950 individuals enumerated via camp rosters, 1,514 (77.6%) agreed to participate.
Each participant was asked to identify all members known to him/her from his/her roster, and then, among known members, whether the member was a friend, acquaintance, or somebody they didn't get along with. Network variables were created using the igraph R package.
Results: Networks had an average of 32.5 members (SD = 12.3) and contained 457 relationships (SD = 370). On average, the camp networks were closely connected, with an average density (representing the overall connectedness within networks) of 0.4 (SD = .19). The cohesion within camps was also high, with an average transitivity (a proxy for cohesion describing the probability that two camp members connected to the same individual are also connected to each other) of 0.7 (SD=.18). Finally, networks were fairly decentralized with an average degree centralization (a measure assessing the degree to which networks revolve around a single individual) of 0.35 (SD =.08).



[Sociocentric network of study camp with average density]

Conclusions: The networks in our HIV prevention intervention trial are closely connected, cohesive, and decentralized, allowing for efficient transmission of HIV prevention information. Longitudinal network data will help us assess whether and how network structures mediate or moderate the intervention effect.

WEPEC647

Sexual risk behaviors and STI prevalence among social networks of young men in Dar es Salaam, Tanzania

S. Maman[1], L. Hill[1], P. Balvanz[1], L. Kajula[2]
[1]University of North Carolina at Chapel Hill, Health Behavior, Chapel Hill, United States, [2]Muhimbili University of Health and Allied Sciences, Psychiatry and Mental Health, Dar es Salaam, Tanzania, United Republic of
Presenting author email: smaman@unc.edu

Background: HIV/AIDS continues to eliminate generations of youth in sub-Saharan African settings, such as Tanzania. Young men in Tanzania report infrequent condom use and high levels of sexual partner concurrency, however little is known about whether and how men's sexual risk behaviors in this context are influenced by their social networks.
Methods: We used baseline data from an ongoing cluster randomized HIV prevention trial with 1,280 men to describe men's STI prevalence and sexual risk behaviors. We recruited men who are members of groups called "camps" Camps are venues in Dar es Salaam where networks of young men meet regularly. Behavioral measures were self-reported among all men and STIs were assessed among a sub-sample of the sexually active men at baseline. Descriptive statistics were calculated in SAS v 9.4 as were intraclass correlations, which were calculated based on parameters from null hierarchical linear models.
Results: Most men were sexually active (89%) and the mean age at first sex was 17 years. The median number of lifetime sex partners was 4 (mean=8) and the average number of sex partners over the past 12 months was 1.3. 36% of men reported using a condom at last sex. When asked about unprotected sex with partners in the past one month, 53% of men reported never using condoms, 14% reported sometimes using condoms and 33% always used condoms. Further, 20% of men reported ever engaging in sexual partner concurrency. 13.3% of men tested positive for any STI, including 4.4% Trichomonas vaginalis, 4.1% Neisseria gonorrhea, and 5.8%, Chlamydia. Significant clustering by camp was found for total number of sex partners (ICC=2.8%, T_{00}=10.30, p=0.023) and sex partners over the past 12 months (ICC= 2.0%, T_{00}=0.08, p=0.033), as well as condom use at last sex (ICC= 6.8%, T_{00}=0.23, p= 0.012), and frequency of condom use (ICC=5.4%, T_{00}=0.011, p= 0.0063).
Conclusions: STI prevalence was lower than anticipated, but sexual risk behaviors showed significant clustering by camp. Clustering in these behaviors may be related to normative, environmental, and other contextual influences. Further research is needed to determine group-level determinants of sexual risk behaviors to inform appropriate intervention.

WEPEC648

Relationships between improvements in neighborhood conditions and sexual network dynamics among adults relocating from public housing

S. Linton[1], H. Cooper[1], R. Luo[2], C. Karnes[3], K. Renneker[4], D. Haley[1], E. Dauria[5], J. Hunter-Jones[1], Z. Ross[6], G. Wingood[1], A. Adimora[7,8], L. Bonney[9], R. Rothenberg[10]
[1]Rollins School of Public Health at Emory University, Department of Behavioral Sciences and Health Education, Atlanta, United States, [2]School of Public Health at Georgia State University, Epidemiology & Biostatistics, Atlanta, United States, [3]AT&T, Mobility, Marketing Science & Insights, Atlanta, United States, [4]The Task Force for Global Health, Neglected Tropical Diseases Support Center, Atlanta, United States, [5]Warren Alpert Medical School of Brown University, Department of Psychiatry and Human Behavior, Providence, United States, [6]ZevRoss Spatial Analytics, Ithaca, United States, [7]University of North Carolina Gillings School of Global Public Health, Department of Epidemiology, Chapel Hill, United States, [8]University of North Carolina School of Medicine, Chapel Hill, United States, [9]Emory University School of Medicine, Division of General Medicine, Atlanta, United States, [10]School of Public Health at Georgia State University, Atlanta, United States
Presenting author email: sabriya.linton@emory.edu

Background: Extensive literature places risk of HIV acquisition and other sexually transmitted infections (STIs) in a socio-ecological framework, with social network and neighborhood characteristics associated with transmission. Instability and turnover in sexual networks have been associated with higher HIV risk behaviors, but few studies investigate the influence of neighborhood conditions on sexual network stability over time.
Methods: This longitudinal multilevel study uses seven waves of data (2009-2014) from a predominantly substance-using cohort of 172 adults relocated from public housing in Atlanta, GA, to determine the potential implications of post-relocation neighborhood change on the overall stability of sexual networks over time, and the extent to which sexual network members enter and leave participants' sexual networks. At each wave, individual-and network-level characteristics were captured via survey; administrative data from the US Census Bureau and local agencies were analyzed to describe the census tracts where participants lived. According to the distribution of each outcome, multilevel logistic regression was used to model overall sexual network stability; multilevel poisson regression was used to model the number of new sexual partners entering sexual networks; and multilevel binomial regression was used to model the number of sexual partners leaving sexual networks.
Results: On average, participants relocated to neighborhoods that had less economic deprivation, social disorder, and renter-occupied housing, and to neighborhoods that had greater racial diversity and more equitable male-to-female sex ratios. No place characteristic was associated with overall sexual network stability over time. Reduced alcohol outlet density was associated with lower rates of new partners entering participants' sexual networks between waves (beta=0.03, CI= -0.001, 0.058, p-value=0.06); this association was borderline statistically significant. Reduced perceived community violence was associated with a higher probability of partners leaving participants' sexual networks between waves (beta=-0.113, CI=-0.236, 0.010, p-value=0.07); this association was also borderline statistically significant.
Conclusions: Improvements in social context may lead to lower sex partner turnover. Research should be expanded to investigate the impact of neighborhood characteristics on social network characteristics, a key determinant of HIV/STI epidemics.

Determination of HIV incidence

WEPEC649

Reconstructing HIV incidence curves by incorporating estimated seroconversion time for each reported infection

S.S. Lee[1], O.T.Y. Tsang[2], K.H. Wong[3], M.P. Lee[4], N.S. Wong[1,5], D.P.C. Chan[1]
[1]Chinese University of Hong Kong, Stanley Ho Centre for Emerging Infectious Diseases, Hong Kong, China, [2]Princess Margaret Hospital, Department of Medicine and Geriatrics, Hong Kong, China, [3]Hong Kong Special Administrative Region Government, Department of Health, Hong Kong, China, [4]Queen Elizabeth Hospital, Department of Medicine, Hong Kong, China, [5]South China-UNC STI Research Training Center, Guangzhou, China
Presenting author email: iseewong@gmail.com

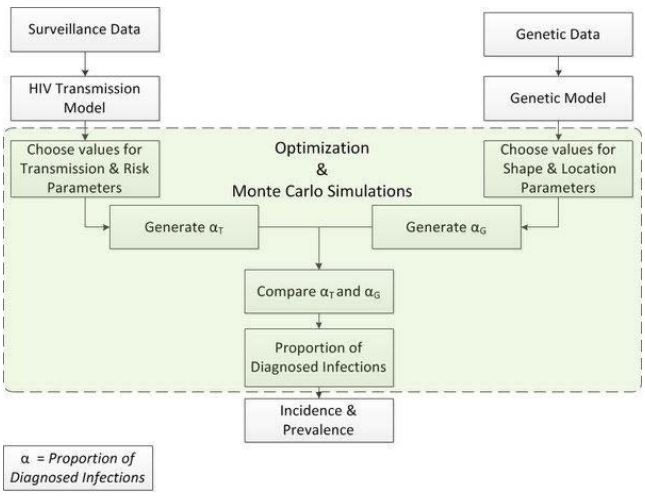
Background: In the past, HIV incidence was normally estimated by back-calculation using such data as incubation period and AIDS diagnoses. With the advent of highly antiretroviral therapy (HAART), new approaches are needed to account for treatment effects. In this study, we estimate seroconversion time at individual level for assessing temporal changes of HIV incidence.
Methods: Longitudinal clinical data of patients in Hong Kong were collected from HIV specialist clinics where almost all reported HIV cases are managed. A combination of methods was used to determine the seroconversion time. The mid-point of the interval between last HIV- and first HIV+ date was used if such interval was < 2 years. Otherwise, they were estimated from CD4 trajectories of the patient, or from reference cases depending on the number of pre-treatment CD4 measurements available. Crude estimation was made If there were no CD4 records. The incidence curve of heterosexual and MSM subpopulations was then reconstructed by plotting patients' seroconversion time by year.
Results: By 2012, 69,996 clinical measurements of 3712 patients diagnosed in 1991-2010 were collected. Mid-point calculation was applied in only 529 (14%) of the patients while CD4 trajectories were used for estimation in 2949 (79%). The incidence of heterosexual, by individuals' seroconversion year, reached its peak in early-1990s which then declined. The peak was 6 years ahead of that for new diagnoses. The HIV incidence curve of MSM gave a different shape for seroconversion year compared to diagnosis year. There were 2 plateaus in 2001-2002 and 2005-2006, whereas reported new diagnosis curve gave a continuing rising trend.
Conclusions: By making full use of clinical dataset available, the seroconversion time of each patient could be computed to allow incidence curves to be redrawn. The epidemiology of HIV infection in different subpopulations could be better reflected through the application of the new data, providing a more realistic reflection of HIV transmission dynamics in the population. With seroconversion time, population viral load, a measure which includes viral burden of both diagnosed and undiagnosed individuals in respective time points, can be assessed longitudinally to describe HIV epidemiology effectively.

WEPEC650

A new method for estimating HIV incidence that uses optimization to reconcile and validate two models based on independent data sources for the same population

A. Nadaf[1,2], A. Rutherford[1,2], B. Ramadanovic[2], K. Vasarhelyi[2,3,4], B. Yip[4], A. Poon[4], R. Liang[4], R. Harrigan[4,5], M. Gilbert[5,6], R. Witternberg[1], J. Montaner[4,5]
[1]Simon Fraser University, Mathematics, Burnaby, Canada, [2]IRMACS Centre, Burnaby, Canada, [3]Simon Fraser University, Faculty of Health Sciences, Burnaby, Canada, [4]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada, [5]University of British Columbia, Faculty of Medicine, Vancouver, Canada, [6]Ontario HIV Treatment Network, Toronto, Canada
Presenting author email: anadaf@sfu.ca

Background: HIV incidence is difficult to estimate due to the long asymptomatic disease stage which delays diagnosis. We developed an optimization-based method utilizing surveillance data and HIV genetic data to simultaneously estimate incidence and validate these estimates.
Methods: Mathematical models were developed for estimating HIV incidence for British Columbia (BC), Canada during 2000-2009, a time period preceded and followed by major expansions in antiretroviral coverage. The approach is summarized in the figure. First, a differential equation for the diagnosed proportion (α) was obtained using an HIV transmission model informed by surveillance data on new diagnoses, death rate, net immigration of diagnosed individuals, and number of people on antiretroviral therapy from the BC Centre for Disease Control and the BC Centre for Excellence in HIV/AIDS (BC-CfE). HIV transmission rate and risk behavior reduction upon diagnoses were left as un-estimated free parameters.
The second model was based on viral genetic distance calculated from genotypic drug resistance data from the BC-CfE, which reflected the probability of a new infection sharing high genetic similarity with a previously diagnosed infection in the database. This model also contained free parameters ("shape and location parameters" in the figure). Using a Tabu Search numerical optimization method, we determined values for all free parameters from the models that minimized the sum of the weighted squared differences between the two 2000-2009 time series for the diagnosed proportion of the HIV-positive population. A Monte Carlo simulation with 200 iterations was used to generate 90% confidence intervals.



[Combined modelling approach]

Results: Monthly time series were generated for free parameters from both models, which were used to produce a single time series for the proportion of diagnosed infections and HIV incidence. Our model suggests that HIV incidence (new infections per year) declined from 594± 1 in 2000 to 534± 2.3 in 2009 in BC. Our estimates are consistent with independent estimates by the Public Health Agency of Canada.
Conclusions: Our method for estimating HIV incidence from routinely collected surveillance and patient-monitoring data is potentially widely applicable. A particular advantage of the approach is that it integrates an internal validation method through reconciling models based on independent data sets.

WEPEC651

HIV incidence in Recife, Brazil, 2013, through the application of laboratory testing algorithm for detection of recent HIV infections

A. Brito[1], O. Ferreira Jr[2], A.M. Silva[3], A.M.S. Cavalcanti[4], L.C.B. Albuquerque[3], D.M. Salustiano[4], J.C. Silva[4], P.R.B. Souza Jr[5], A.B. Santos[5], C.L. Szwarcwald[5]
[1]Centro de Pesquisas Aggeu Magalhaes, Fiocruz, Saude Coletiva, Recife, Brazil, [2]Universidade Federal do Rio de Janeiro, Departamento de Genética, Rio de Janeiro, Brazil, [3]Secretaria Municipal de Saúde, Laboratório Municipal de Saúde Pública, Recife, Brazil, [4]Secretaria Estadual de Saúde, Laboratório Central de Saúde Pública, Recife, Brazil, [5]Fundação Oswaldo Cruz, Instituto de Comunicação e Informação Científica e Tecnológica em Saúde, Rio de Janeiro, Brazil, [6]Universidade de Pernambuco, Faculdade de Ciências Médicas, Recife, Brazil
Presenting author email: anabrito1009@gmail.com

Background: In the context of expansion of antiretroviral treatment to HIV-infected individuals, and resultant increased survival, the data that best reflect recent changes in patterns of transmission come from studies that consider the number of incident cases in a given period. In this study, we estimated HIV incidence in Recife, Brazil, 2013 through the application of laboratory testing algorithm for detection of recent HIV infections.
Methods: We used the LAg Avidity EIA testing algorithm in the majority of HIV positive tests performed in the public sector for a period of 12 months during 2013-2014 to classify infections as recent or long-standing. This included all HIV tests performed at primary care health units, family health units, HIV testing and counseling centers, mobile units and public hospitals. A sample of HIV positive tests performed in the private sector were also considered in the study. Incidence of HIV in Recife at period was estimated using a statistical approach with adjustment for the probability of an undiagnosed HIV positive person tests in 2013 and the probability that a newly diagnosed person has a LAg -Avidity result. We used a window period of 141 days.
Results: An estimated 538 individuals were diagnosed with HIV in 2013 in Recife. Of the 485 HIV positive specimens tested using the LAg Avidity assay, 48 (9.9%) were classified as recent infections. Based on statistical sample extrapolations from these data, the estimated number of new infections for Recife in 2013 was 553, which represents an estimated incidence rate of 34.6 per 100 000 population.
Conclusions: This study provides the first direct estimates of HIV incidence in a Brazilian city using laboratory assays. Results were corroborated with estimation of HIV incidence, 2013 in Recife based on information of the first CD4 count from the Laboratory Tests Control System (SISCEL).
Therefore, it is a possible approach for monitoring HIV incidence routinely in large Brazilian cities.

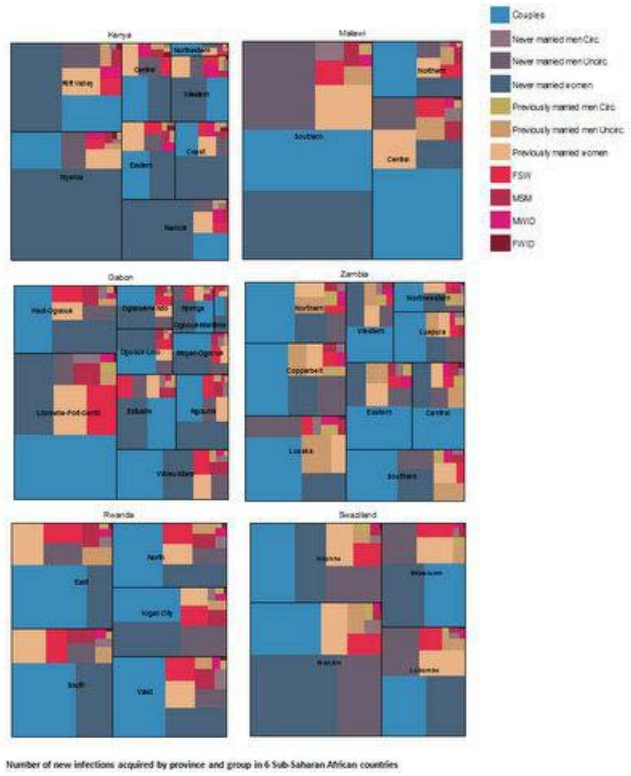
Methods for estimating incidence using cross sectional samples

WEPEC652

Estimating the distribution of new HIV infections by key determinants in generalised epidemics of sub-Saharan Africa using a validated mathematical model

A. Borquez[1], A. Cori[1], E. Pufall[1], K. Jingo[2], E. Slaymaker[3], P. Alison[3], J. Elmes[1], M. Crampin[3], M. Urassa[4], J. Kagaayi[2], T. Lutalo[2], S. Gregson[1], T. Hallett[1]
[1]Imperial College London, Infectious Disease Epidemiology, London, United Kingdom, [2]Rakai Health Sciences Program, Entebbe, Uganda, [3]London School of Hygiene and Tropical Medicine, London, United Kingdom, [4]Mwanza Research Centre, National Institute for Medical Research, Mwanza, Tanzania, United Republic of
Presenting author email: timothy.hallett@imperial.ac.uk

Background: Estimating the distribution of new HIV infections according to identifiable characteristics is a priority for programmatic planning in HIV prevention. We propose a mathematical modelling approach that uses robust data sources to estimate the distribution of new infections acquired in the generalised epidemics of sub-Saharan Africa and validate it against cohort data.
Methods: We developed a predictive model that represents the population according to factors that have been demonstrated to be powerfully associated with risk: gender, marital status, geographic location, key risk behaviours (sex-work, injecting drug use, male-to-male sex), sero-discordancy within couples, circumcision and ART status. Incidence rates obtained from large trials or inference methods are applied to estimate the number of new infections in each group in the next year. The model is applied within a Bayesian framework whereby regional prior information on demographic and epidemiological characteristics is updated, where possible, with national and local data. Uncertainty is propagated to model predictions. We trained and tested the model following an iterative process against cohort data from Manicaland, Zimbabwe. We developed a transmission module which builds on the results from the acquisition model to illustrate likely sources of transmission consistent with the estimated distribution of new infections. The model was applied to six countries in the region to investigate potential differences in incidence patterns.
Results: Without training using the site-specific data, the model was able to predict the pattern of new infections with reasonable accuracy: 95% credible intervals were substantially overlapping and the rank ordering of groups with new infections was consistent. With additional training using site-specific data, and tests on a further round of data from the same site, the accuracy of predictions improved further and credible intervals narrowed. When applied to the six countries in the region the model showed variation in the distribution of infections between and within countries consistent with the data on prevalence (see Fig. 1).



[Figure 1]

Conclusions: It is possible to accurately predict, in broad terms, the distribution of new HIV infections acquired using data routinely available in many countries in the Sub-Saharan African region. This tool can complement additional analyses on programmatic planning and data collection priorities.

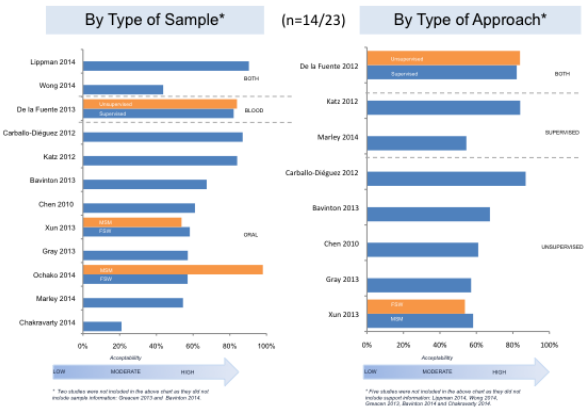
HIV testing and diagnostic strategies

WEPEC653

Attitudes and acceptability on HIV self-testing (HIVST) among key populations: a literature review

C. Figueroa[1,2], C. Johnson[1], A. Verster[1], R. Baggaley[1]
[1]World Health Organization, HIV Department, Geneva, Switzerland, [2]National School of Public Health, Instituto de Salud Carlos III, Madrid, Spain
Presenting author email: johnsonc@who.int

Background: Globally, approximately 40% of new adult HIV infections occur among key populations (KP). Yet, uptake of and access to HIV testing among KP is suboptimal. HIVST has potential to reduce existing disparities in coverage and access to HIV testing, particularly among KP who may be more reluctant to attend services. We examined values and preferences around HIVST among KP.
Methods: We systematically searched electronic databases, including peer-reviewed literature, conference abstracts and gray literature January 1995 to July 2014. Review was restricted to reports on acceptability, values and preferences among KP. Extracted data was analyzed by country income, type of specimen collection (oral fluid-based or blood-based), level of support offered, and other qualitative aspects.
Results: 23 studies met inclusion criteria; 14 reported acceptability (Figure 1). Most studies identified were from high-income countries and were among men who have sex with men (MSM), who found HIVST acceptable. MSM were interested in HIVST because of its convenient and private nature. Several studies identified MSM prefer access to HIVST over-the-counter and via the Internet. Willingness to pay varied across setting. Participants in high-income settings, and for unsupervised HIVST approaches, were willing to pay more (≤ US$ 20 to US$ 50).Concerns, such as lack of counseling accompanying HIVST, possible user error and poor accuracy were identified. No adverse events were identified. Five studies report linkage to care; most participants (range: 81.6%-100%) stated if they received a reactive HIVST result they would seek confirmatory testing and treatment.
Conclusions: Although some concerns remain, HIVST is acceptable among MSM across all settings. Acceptability, values and preferences were similar across studies, regardless of whether HIVST is provided through a supervised or unsupervised approach or using oral fluid or blood-based RTD. Data among other KP groups, particularly in low- or middle-income settings was limited. To more fully understand values and preferences of KP regarding HIVST, future research should include people who inject drugs, transgender people and sex workers.



[Studies evaluating HIV self-testing acceptability]

WEPEC654

Diagnosis of earlier stage disease observed with expanded HIV testing in Vancouver, Canada

E. Demlow[1], R. Gustafson[2], T. Chu[1], L. MacDonald[3], A. Nathoo[2], K. Heath[4], B. Yip[4], W. Chau[4], G. Colley[4], M. Gilbert[3], R. Barrios[2], J. Montaner[4], J. Sandhu[1], P. Daly[2]
[1]Vancouver Coastal Health Authority, Public Health Surveillance Unit, Vancouver, Canada, [2]Vancouver Coastal Health Authority, Vancouver, Canada, [3]BC Centre for Disease Control, Vancouver, Canada, [4]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada
Presenting author email: ellen.demlow@vch.ca

Background: The STOP HIV/AIDS three year pilot program was launched in March 2010 with the goal of improving early diagnosis and timely engagement in HIV care as a model for reducing transmission in British Columbia. Prior to STOP, from 2003-2010, greater than 60% of new HIV diagnoses in Vancouver occurred among individuals with a CD4 count less than 500 cells/mm^3. Here we describe historical, pilot phase and post-pilot temporal trends in disease stage at diagnoses.
Methods: To monitor and evaluate the STOP program, relevant outcome measures, including CD4 at HIV diagnosis as well as patient characteristics, were collected from laboratory testing sources and authorized linkages between public health and clinical databases. Indicators of disease stage from the post-STOP period (July 1, 2013 - June 30, 2014) were compared to the STOP period (July 1, 2010 - June 30, 2013) and a historical period (January 1, 2008-June 30, 2010). Early stage diagnosis was defined as a CD4 count greater than or equal to 500 cells/mm^3 or acute stage disease and late stage diagnosis was defined as a CD4 count less than 200 cells/mm^3.
Results: In the post-STOP period, early stage diagnosis comprised 53% of new diagnoses compared with 45% during STOP and significantly greater than 40% historically. Furthermore, late stage diagnoses declined from 22% historically, to 21% during STOP and 16% post-STOP. During this time, the average regional testing volume increased 53% over the average observed during STOP and 106% over historical averages. Men aged 20-29 had the highest diagnostic yield (1.1%) in the post-STOP period unlike the preceding periods where men aged 40-49 had the greatest diagnostic yield
(0.9% - 1.6%).
Conclusions: Testing promotion activities part of the STOP program, including a city-wide HIV testing strategy in acute and primary care, lead to substantial and sustained increases in HIV testing in the region, and has coincided with the greatest proportion of early stage diagnoses since HIV became reportable in British Columbia in 2003.

Surveillance of HIV (youth and adults)

WEPEC655

Increases in the proportion of HIV among foreign-born individuals in King County, dates of HIV diagnoses and the impact on HIV prevention

S. Buskin[1,2], A. Bennett[1], C. Thibault[1], J. Hood[1,2], R. Kerani[1,2], M. Golden[1,2]
[1]Public Health - Seattle & King County, Seattle, United States, [2]University of Washington, Seattle, United States
Presenting author email: susan.buskin@kingcounty.gov

Background: An estimated 13% of Americans and 16% of U.S. residents diagnosed with HIV are foreign-born. The National HIV Surveillance System (NHSS) collects data on nativity, but defines cases as newly-diagnosed based a first documented HIV positive test, usually one in the U.S. However, many of these people may have been diagnosed prior to immigration.
Methods: We used 2004-2013 King County, WA data from NHSS and supplemental surveillance activities to assess trends in the percentage of people identified as newly diagnosed with HIV infection who were foreign-born and how often these individuals self-reported HIV diagnoses prior to U.S. immigration.
Results: A total of 3,032 KC residents were diagnosed with HIV over the period, including 775 (26%) foreign-born. Foreign-born cases increased nearly 50% over the decade—from 22% in 2004 to 32% in 2013 (p< 0.001). Foreign-born individuals included 39% from Africa, 34% from Mexico or South/Central America, 18% from Asia, 6% from Europe, and 2% from Canada. Foreign-born cases were less likely than U.S.-born cases to be men who have sex with men (40% vs. 83%, p< .0001). Self-reported date of first HIV diagnosis was available for 2,041 (67%). Foreign-born cases were five times as likely as U.S. born cases to self-report HIV diagnosis >1 year prior to NHSS diagnosis date (20% vs 4%, p< 0.0001). We had date of entry to the U.S. for about one-quarter of foreign-born cases; of these, 3% entered the U.S. after their HIV diagnosis in NHSS, however 34% entered the U.S. after a self-reported HIV diagnosis. Misclassification of diagnosis date of foreign-born cases led to an estimated 11% over-estimate of new HIV diagnoses in 2013.
Conclusions: A growing percentage of presumptively newly diagnosed HIV infections - almost one-third of 2013 King County HIV - occur in people born outside of the U.S. Approximately one-third of these cases were likely diagnosed prior to U.S. entry, leading to a substantial overestimate of the number of new diagnoses. These findings highlight the need for data on nativity, HIV testing history, and immigration dates from people with newly diagnosed HIV, and emphasize a growing need for prevention addressing the needs of foreign-born populations.

Surveillance of behaviour

WEPEC656

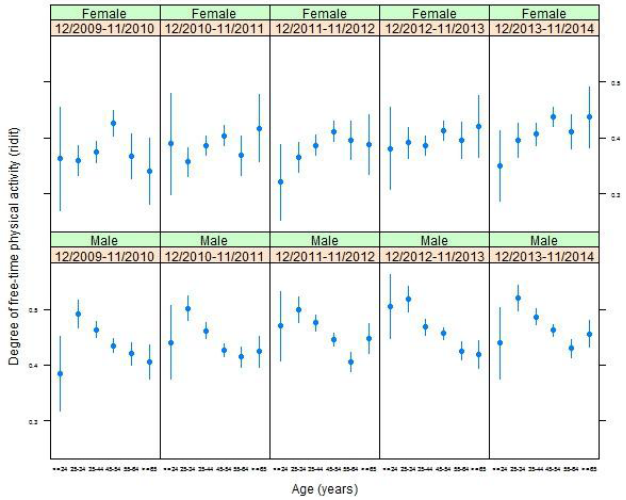
Prevalence of physical activity in patients with HIV over time: the Swiss HIV cohort study (SHCS)

J. Schäfer[1,2], J. Young[1], A. Calmy[3], D. Nicca[4,5], B. Hasse[6], H. Furrer[7], M. Cavassini[8], E. Bernasconi[9], A. Schmidt-Trucksäss[2], H.C. Bucher[1,10], and the Swiss HIV Cohort Study
[1]University Hospital Basel, Basel Institute for Clinical Epidemiology and Biostatistics, Basel, Switzerland, [2]University of Basel, Department of Sport, Exercise and Health, Division Sports and Exercise Medicine, Basel, Switzerland, [3]University Hospital Geneva, Division of Infectious Diseases, Geneva, Switzerland, [4]Cantonal Hospital St Gallen, Division of Infectious Diseases and Hospital Epidemiology, St Gallen, Switzerland, [5]University of Basel, Institute of Nursing Science, Basel, Switzerland, [6]University Hospital Zurich, Division of Infectious Diseases and Hospital Epidemiology, Zurich, Switzerland, [7]Bern University Hospital and University of Bern, Department of Infectious Diseases, Bern, Switzerland, [8]University Hospital Lausanne, Division of Infectious Diseases, Lausanne, Switzerland, [9]Regional Hospital of Lugano, Division of Infectious Diseases, Lugano, Switzerland, [10]University Hospital Basel, Division of Infectious Diseases and Hospital Epidemiology, Basel, Switzerland
Presenting author email: matthias.cavassini@chuv.ch

Background: The prevalence of cardiovascular risk factors is high in patients with HIV. While there is growing evidence that physical activity (PA) is both safe and effective in improving cardiorespiratory fitness, metabolic profile and quality of life in patients with HIV, it is however not certain how physically active patients with HIV are. The aim of this study was to provide population-based estimates of the level of PA in patients with HIV and to see whether this level is changing over time.
Methods: We included all patients from the Swiss HIV Cohort Study (SHCS) who completed at least one report of PA between December 2009 and November 2014 during routine clinical follow-up (scheduled every 6 months). Changes in the level of PA over time were explored with summary statistics and graphs where we divided time since December 2009 into 12-month periods. Data were taken from the first completed report within each period. We used ridit analysis to assess the relationship between the degree of PA and numerous demographic or disease related factors.

	12/2009-11/2010	12/2010-11/2011	12/2011-11/2012	12/2012-11/2013	12/2013-11/2014
Number of patients under follow-up	8104	8394	8635	8947	8888
Patients who answered both questions about physical activity (%)	87	99	99	99	99
Patients who answered at least one question (%)	88	100	100	100	100
Median age (IQR), years	45 (39, 51)	46 (39, 52)	47 (40, 53)	47 (40, 54)	48 (41, 54)
Female sex (%)	30	29	29	29	29
CDC category C (%)	23	23	23	23	23
Median CD4 cell count (IQR), cells/µl	525 (372, 705)	541 (389, 722)	554 (400, 735)	584 (422, 774)	603 (441, 796)
No free-time physical activity at all (%)	48	49	46	45	44
Sedentary activity at work (%)	24	24	25	26	26

[Table. Patient characteristics over time]



[Figure. Average ridits by sex, time period and age]

Results: During the study period, 10417 patients completed at least one report of PA. Except for the first year with a higher non-response rate, the percentage of patients reporting no free-time PA at all gradually declined from 49% to 44% over the four years (Table). At the same time, the percentage of patients reporting sedentary activity at work increased from 24% to 26% over the four years. In contrast, the percentage of individuals reporting no sports activities at all in the "Sport Switzerland" surveys of the general population was estimated to be much lower and seemed relatively stable over time (2008: 27%; 2014: 26%). Average ridits (with 95% confidence intervals) by time period and age suggest no strong trends in free-time PA over time but obvious differences in profiles between women and men, with young men being more active than young women (Figure).
Conclusions: Patients with HIV in Switzerland engage in much less free-time PA than the general population. Thus, increasing PA could be a behavioural change that helps patients with HIV reduce their risk of cardiovascular disease.

WEPEC657

Comparison between the first and the second round of the biological behavioral surveillance survey among male injecting drug users in Cairo

S. Elkamhawi[1], W. Kamal[2], S. Shawky[3], O. Abaza[1], M. Abdel Malak[1], C. Khoury[1], G. Tawakol[1], C. Soliman[1]
[1]FHI 360, Cairo, Egypt, [2]Ministry of Health and Population, Cairo, Egypt, [3]Social Research Center/American University in Cairo, Cairo, Egypt
Presenting author email: csoliman@fhi360.org

Background: FHI 360/Egypt and Ministry of Health and Population conducted two rounds of Biological and Behavioral Surveillance Survey to track trends among Key Population, including Male Injecting Drug Users (IDUs).
Methods: The two rounds were conducted in 2006 and 2010 respectively. Respondent driven sampling was applied to select male IDUs (sample size ranged from 413 in the first round and 275 in the second round). Participants were interviewed by their peers using a standard questionnaire and HIV status was measured by Elisa and Western Blot.
Results: Literacy rate among male IDUs was high, 95.0% in 2006 and 92.3% in 2010 reported attending school. More than half of them reported ever being married to a female (55.5% in 2006 and 56.4% in 2010). More than half of the male IDUs in 2006 (53.0%) and almost one-third of them in 2010 (30.7%) reported injecting drugs with used needles in the past month. Almost one third in 2006 and about one quarter in 2010 reported sharing needles with one or more partners in the past month (32.2% and 22.9% respectively). Almost all the male IDUs reported ever having had sex with a female (96.2% in 2006 and 94.9% in 2010). Having had a commercial sex partner in the last year was reported by 13.3% in 2006 and 13.1% in 2010. Having had a non-regular non-commercial sex partner in the last year was reported by 12.8% in 2006 and 33.8% in 2010. Having had sex with a male was reported by 9.2% of the male IDUs in 2006 and 14.3% in 2010. Condom use was very low among IDUs in the two rounds, 11.8% in 2006 and 12.2% in 2010 reported condom use at least once with commercial sex partners. HIV prevalence among male IDUs was 0.6% in 2006 and 6.8% in 2010.
Conclusions: HIV prevalence among male IDUs increased 10 times between 2006 and 2010. Links with the general population through marriage and an overlap of risk behaviors were common among male IDUs in Cairo. A combined approach including safe sex and safe injection is essential to overcoming the growing HIV epidemic among Male IDUs in Egypt.

WEPEC658

Gay sex-seeking mobile application in China: results from an online survey

W. Tang[1], J. Best[2], Y. Zhang[1], L. Han[3], F. Liu[4], S. Huang[4], B. Yang[4], C. Wei[5], J. Tucker[1]
[1]University of North Carolina, Project-China, Guangzhou, China, [2]University of California, Medicine, San Francisco, United States, [3]University of North Carolina at Chapel Hill, Biostatistics, Chapel Hill, United States, [4]Guangdong Provincial Center for Skin Diseases and STIs Control, Guangzhou, China, [5]University of California, San Francisco, United States
Presenting author email: jdtucker@med.unc.edu

Background: Substantial increases in gay sex-seeking mobile application (gay app) use may facilitate sex partner turnover and HIV transmission. The goal of this study was to compare Chinese MSM demographics and sexual behaviours between gay app users and non-users.
Methods: In October 2014, we recruited individuals (≥16 years old, ever engaged in sex with men, agreed to provide cell phone number and agreed with the inform contents) from three Chinese gay web platforms. Information regarding socio-demographics, sexual behaviours and gay app using history were collected.
Results: Overall, 1723 participants did not meet eligibility criteria and were excluded, while1424 (45.2%) completed the online survey. In the last six months, 800 (56.2%) used gay apps for sex partner-seeking. Most participants were aged < 30 years (77.5%), never married (83.8%), and self identified as gay (72.9%). Among gay app users, 72.8% found two or more sex partners in the last six months, and three quarters (74.9%) met their partners within one week after met on gay app. Among those who found new sex partners through mobile apps, 25.4% did not use a condom during the last anal intercourse with a partner. Gay app users

were more likely to have condomless anal intercourse in the last three months (aOR=1.52, 95% CI 1.19-1.94), and ever experienced intimate partner violence (aOR=1.43, 95% CI 1.15-1.78). Gay app users were less likely to have sex with female (aOR=0.67, 95% CI 0.51-0.89). Among HIV-infected individuals (n=68), gay app users were less likely to receive antiretroviral therapy compare to non-app users (aOR=0.13, 95% CI 0.03-0.56).
Conclusions: Millions of gay men in China meet new sex partners through gay apps. Contrary to other literature, our data suggest gay app users may have risker sex compared to non-gay app users. Further research and programs about the use of social media and unsafe sex are urgently needed.

WEPEC659

Prevalence and correlates of sexual risk behaviours in Cross River State, Nigeria

C. Oyom[1], M. Mbukpa[1], O. Idogho[1], G. Eluwa[2], A. Oginni[2]
[1]Society for Family Health, Abuja, Nigeria, [2]Population Council, Abuja, Nigeria
Presenting author email: oidogho@sfhnigeria.org

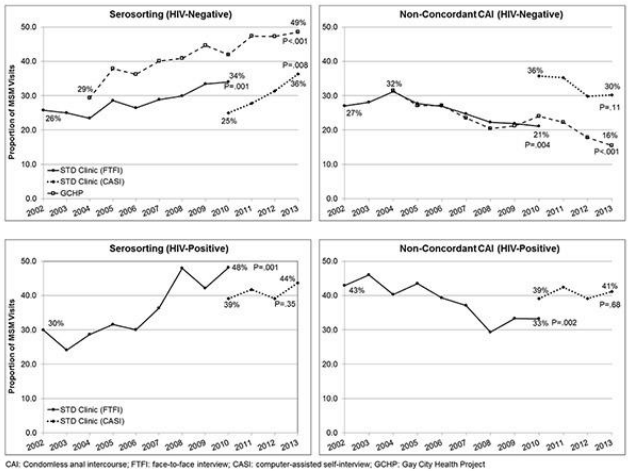
Background: A recent Mode of Transmission (MoT) Survey in Cross River State, Nigeria revealed that 23% of new HIV infections will occur among casual heterosexual groups and that 42% of new infections will come from low risk heterosexuals made up of people in a married or cohabiting relationship. We assessed factors associated with sexual risk behaviour among the general population in Cross River state.
Methods: The survey sampled females aged 15-49 years and males aged 15-64 years in Cross River State using probability sampling. Interviewer administered questionnaires were used to obtain data on sexual risk behaviours and assessed using a cross-sectional analysis. Logistic regression was used to identify factors associated with sexual risk behaviours while controlling for potential confounding factors.
Results: A total of 950 respondents (478 males, 472 females) were surveyed. Median age at first sex among young persons aged 15 to 24 years was reported as 21 for males and 17 for females. More males than females had more than one sex partner (30.5%; 19.2%) and engaged in high risk sex (casual, non-marital partner) (23.2%; 14.2%). More females (17.6%) than males (7.3%) had sex in exchange for gifts/favours. When controlled for age, gender, educational status, marital status and location (urban vs. rural), females (AOR: 0.57; 95% CI:0.41-0.79) and those with at least secondary education (AOR:0.39;95% CI:0.20-0.73) were less likely to engage in multiple sexual partnerships while those with comprehensive knowledge (AOR:1.75; AOR:1.27-2.41) were more likely to engage in multiple sexual partnerships. Age, location and marital status, were not associated with multiple sexual partnerships.
Conclusions: Females were less likely to engage in multiple sexual partnerships indicating that targeted interventions are needed to reduce this risk behaviour among males as a means of mitigating HIV transmission. Those with comprehensive HIV knowledge were more likely to engage in multiple sexual partnerships and suggest a negative feedback in reducing risk behaviour. Knowing how to prevent HIV transmission may have triggered their involvement in risky behaviour as they feel they are well equipped to prevent their acquisition of HIV. Further research is required to understand factors driving the risk behaviour despite having comprehensive knowledge.

WEPEC660

Changes in the prevalence and risk of serosorting among Seattle men who have sex with men (MSM) 2002-2013: is serosorting becoming safer?

C.M. Khosropour[1], J.C. Dombrowski[2,3], D.A. Katz[2,3], R.P. Kerani[2,3], F. Swanson[4], L.A. Barbee[2,3], M.R. Golden[2,3]
[1]University of Washington, Epidemiology, Seattle, United States, [2]University of Washington, Medicine, Seattle, United States, [3]Public Health - Seattle & King County, HIV/STD Program, Seattle, United States, [4]Gay City Health Project, Seattle, United States
Presenting author email: ckhosro@uw.edu

Background: Serosorting among MSM is common but data to describe changes in the prevalence and HIV risk of serosorting in the past decade are limited.
Methods: Data were collected as part of routine care for MSM attending an STD clinic 2002-2013 and a community-based HIV/STD testing center (Gay City Health Project [GCHP]; 2004-2013) in Seattle, Washington. MSM were asked about condom use with HIV-positive, HIV-negative and unknown status partners in the past 12 months. At the STD clinic, data were collected via face-to-face interview (FTFI) until October 2010 and thereafter via computer-assisted self-interview (CASI). All GCHP data were collected via FTFI. We classified behaviors reported at each visit into four mutually exclusive categories: no anal intercourse (AI); consistent condom use (always used condoms for AI); serosorting (condomless anal intercourse [CAI] only with HIV-concordant partners); non-concordant CAI (any CAI with HIV-discordant or unknown status partners; NCCAI). We used linear regression to examine trends and log binomial regression to estimate adjusted relative risks (aRR).
Results: Behavioral data were complete for 49,912 clinic visits by 24,412 unique MSM. The proportion of visits during which MSM reported serosorting increased significantly among both HIV-positive and HIV-negative men over the study period (Figure). NCCAI significantly decreased, though this percentage stabilized among HIV-positive MSM after 2009 (Figure). Among HIV-negative MSM from 2002-2013, consistent condom use was relatively stable (12-year average=32%) as was no AI (12-year average=8%), but these behaviors declined among HIV-positive MSM (20% to 12% and 7% to 4%, respectively). MSM tested for HIV at 38,845 visits. Adjusting for time since last negative HIV test, the risk of testing positive during the study period decreased among MSM who reported NCCAI (7.1% to 2.8%; P=0.02), serosorting (2.4% to 1.3%; P=0.17) and no CAI (1.5% to 0.7%; P=0.01). Serosorting was associated with a 47% lower risk of testing HIV positive compared to NCCAI (aRR= 0.53; 95% CI=0.45-0.62); this aRR did not significantly vary over the study period (P=0.48 for year*behavior interaction).



[Trends in sexual behaviors among MSM 2002-2013]

Conclusions: Serosorting among Seattle MSM increased substantially over the past 12 years. This trend was concurrent with a decline in HIV test positivity among all MSM regardless of reported sexual behavior.

WEPEC661

Sexual behaviour and viral load in MSM HIV-diagnosed at primary infection stage and followed in the French ANRS - PRIMO cohort

K. Champenois[1], R. Seng[1,2,3], A. Essat[1], S. Orr[1], A. Persoz[1], C. Goujard[1,2,4], L. Meyer[1,2,3], ANRS PRIMO Cohort Study Group
[1]Inserm UMR 1018, CESP-4: Epidemiology of HIV and STIs, Le Kremlin Bicêtre, France, [2]South-Paris University, South-Paris Medical School, Le Kremlin Bicêtre, France, [3]AP-HP, Bicêtre Hospital, Epidemiology and Public Health Service, Le Kremlin Bicêtre, France, [4]AP-HP, Bicêtre Hospital, Internal Medicine Department, Le Kremlin Bicêtre, France
Presenting author email: remonie.seng@inserm.fr

Background: From 2008, the diffusion of the concept of treatment as prevention (TasP) in the HIV-infected population may lead to an increase in at-risk sexual behaviour. We aimed to assess the evolution over time of sexual behaviour in HIV-infected MSM followed in the French ANRS-PRIMO cohort.
Methods: In 1996-2014, 1,226 MSM have been enrolled during HIV primary infection. At each visit
(every 6 months), a clinical questionnaire including lab measurements is completed and a self-administered questionnaire collects data on sexual partners, and condom use during the past six months (reasons of inconsistent condom use are available since 2013). The evolution of sexual behaviour in 2000-2014 and the association with the viral load at the preceding visit (undetectable: yes/no) were assessed using GEE models taking into account longitudinal data.
Results: We analyzed 8,395 follow-up visits with completed data on partners and condom use. The proportion of visits where ≥1 casual partner was reported has significantly increased of 3%/year (p=0.03) from 2001 to 2010, and of 11%/year (p< 0.0001) since 2011 to reach 60% of visits in 2013.
In MSM reporting ≥1 casual partner, the frequency of inconsistent condom use with partners of negative or unknown HIV status has risen of 5%/ year (p=0.02) from 18% of visits in 2001 to 23% in 2010, and then of 18%/year (p< 0.0001) up to 36% of visits in 2013. There was no difference in condom use according to the VL (p=0.52).
Since 2013, among the 94 MSM who did not use condom consistently with casual partners despite a detectable VL, 45% thought that they could not transmit HIV because they were treated or thought (wrongly) they had an undetectable VL.
Conclusions: In these MSM, inconsistent condom use has increased since the beginning of 2000s and more dramatically after 2010. We can assume that the concept of TasP is widespread in recent years and assign to it this kind of disinhibition in HIV-infected MSM, but no association was observed with VL. Efforts should be done to inform patients about the impact of treatment on HIV-transmission and the importance to know their VL.

Surveillance of HIV drug resistance (including in PrEP studies)

WEPEC662

Levels of transmitted drug resistance in HIV-1 patients in Cuba

L. Pérez[1], Y. Alemán[1], C. Correa[1], J. Pérez[2], C. Fonseca[2], C. Aragonés[2], J. Campos[2], D. Álvarez[2], Y. Schrooten[3], L. Vinken[3], D. Pérez[2], A. Álvarez[1], Y. Soto[1], C. Limia[1], A.-M. Vandamme[3], K. Van Laethem[3], V. Kourí[1]
[1]Tropical Medicine Institute, Virology, La Habana, Cuba, [2]Tropical Medicine Institute, Hospital, La Habana, Cuba, [3]Rega Institute for Medical Research, Department of Microbiology and Immunology, Leuven, Belgium
Presenting author email: jorge.perez@ipk.sld.cu

Background: Several factors in Cuba might have contributed to high drug resistance levels in the treated HIV-1 population, such as prescription of suboptimal regimens containing non-boosted PI, prolonged exposure to failing therapies due to limited access to laboratory monitoring and limited options for antiviral drug substitutions if required.
This might also result in the subsequent spread of drug resistant strains and therefore, this study aimed to survey the levels and patterns of antiviral drug resistance in therapy-naïve HIV-1 patients in Cuba.
Methods: Demographic, clinical and laboratory data were collected from drug-naïve patients attending a clinical center in Havana from 2008 to 2013. The HIV-1 pol gene was sequenced using Sanger sequencing and drug resistance was interpreted according to the WHO surveillance drug-resistance mutations (SDRM) list, version 2009.
Results: Our study included 323 patients who were HIV-1 diagnosed between 1986 and 2013. The largest number of patients was from Havana City (67.5%). The average time between HIV-1 diagnosis and sampling for HIV-1 genotyping was 2.4 years. The median CD4 count and viral load at sampling was 333 cells /mm^3 and 20,000 RNA copies /ml, respectively. Overall, 45 patients (13.9%) showed any evidence of TDR. Fourty-nine% of patients with evidence of TDR (22/45) displayed a single SDRM. Around half of the patients with evidence of TDR displayed double class resistance against NRTI and NNRTI (22/45, 48.9%), whereas one patient displayed double class resistance against NRTI and PI (0.3%), and two patients triple-class resistance (0.6%). No significant change for the proportion of any TDR was observed over the years. However, when combining the last 3 years (2011-2013) and comparing them with the proportion before (2008-2010), a significant increase in double class resistance TDR against NRTI and NNRTI was observed (OR 5.9, CI 1.3-25.8, p=0.0150).
Conclusions: The prevalence of drug resistance in therapy-naïve HIV-1 patients was 13.9% in our study. Overall TDR remained stable during the investigation period, but double class NRTI and NNRTI resistance increased.

Surveillance systems and methods

WEPEC663

A matter of perspective: comparison of the characteristics of HIV-infected persons in the United States from the HIV outpatient study, the medical monitoring project, and the National HIV Surveillance System

K. Buchacz[1], H.I. Hall[1], E. Frazier[1], D. Franklin[2], R. Hart[2], P. Huang[1,3], X. Hu[1], J.T. Brooks[1], J. Skarbinski[1]
[1]US Centers for Disease Control and Prevention, Division of HIV/AIDS Prevention, Atlanta, United States, [2]Cerner Corporation, Vienna, United States, [3]ICF International, Atlanta, United States
Presenting author email: ixh1@cdc.gov

Background: Owing to dramatic improvements in survival associated with use of cART and a steady rate of incident HIV infections each year, the cumulative number of persons living with HIV infection in the United States is increasing. Longitudinal HIV cohorts and supplemental surveillance projects collect more in-depth data on HIV-infected persons than routine HIV surveillance.
We sought to describe how the characteristics of persons in these enhanced data collections may reflect those of all adults living with diagnosed HIV infection and thus inform HIV care and prevention nationally.
Methods: We compared the characteristics of HIV-infected persons included in three CDC-funded data sources in 2009: the National HIV Surveillance System (NHSS), a comprehensive prospective registry of all HIV-diagnosed persons in the United States whether in or out of HIV care; the Medical Monitoring Project (MMP), a nationally representative surveillance system collecting serial cross-sectional medical chart abstraction and interview data on a probability sample of HIV-infected adults receiving care in the United States; and the HIV Outpatient Study (HOPS), a prospective chart abstraction cohort of persons seen for HIV care at select U.S. specialty clinics.
Results: The median age of persons included was > 45 years across all data sources (Table), with only about one-quarter of persons aged 40 years or younger, and ≤ 3% persons aged 18-24 years. About three-quarters of persons were male. MMP and NHSS populations were more ethnically diverse than the HOPS (Table). Over 50% of persons in each data source were gay, bisexual, and other men who have sex with men (collectively referred to as MSM). The percentage of persons with AIDS diagnosis was 67% in MMP, 64% in HOPS and 58% in NHSS. About 18% of persons in MMP and NHSS were diagnosed with HIV infection in 1996 or later versus 9% in HOPS.

	MMP (N=4217)			HOPS (N=1783)			NHSS (N=806,383)	
Characteristic	**No.**	**(Weighted %)***	**(95% CI)**	**No.**	**(%)**	**(95% CI)**	**No.**	**(%)**
Median age [IQR], years		45.9	[39.2, 52.4]		48.4	[43.0, 54.9]	46.2	[39.1,52.8]
Sex at birth								
Male	3068	72.5	(69.4 – 75.7)	1370	76.8	(74.9 – 78.8)	604,210	74.9
Female	1148	27.4	(24.3 – 30.6)	407	22.8	(20.9 – 24.8)	202,173	25.1
Race/Ethnicity								
White, non-Hispanic	1395	34.6	(28.0 – 41.1)	937	52.6	(50.2 – 54.9)	279,023	34.6
Black, non-Hispanic	1740	41.4	(33.3 – 49.6)	573	32.1	(30.0 – 34.3)	350,977	43.5
Hispanic or Latino	881	19.1	(14.1 – 24.1)	219	12.3	(10.8 – 13.8)	149,897	18.6
Other	201	4.9	(3.8 – 5.9)	54	3.0	(2.2 – 3.8)	26,486	3.3
HIV acquisition risk group								
MSM	2111	51.0	(47.4 – 54.6)	1020	57.2	(55 – 59.5)	398,491	49.4
IDU-male	384	8.6	(7.0 – 10.2)	93	5.2	(4.1 – 6.2)	87,546	10.9
IDU-female	308	7.3	(6.0 – 8.6)	53	3.0	(2.2 – 3.8)	54,268	6.7
MSM-IDU	250	5.6	(4.3 – 6.9)	21	1.2	(0.7 – 1.7)	48,227	6.0
Heterosexual-male	308	6.9	(5.3 – 8.5)	169	9.5	(8.1 – 10.8)	64,782	8.0
Heterosexual-female	817	19.6	(16.8 – 22.4)	322	18.0	(16.3 – 19.8)	143,991	17.9
Other	39	0.9	(0.5 – 1.3)	105	5.9	(4.8 – 7.0)	9,079	1.1

Abbreviations: MMP, Medical Monitoring Project; HOPS, HIV Outpatient Study; NHSS, National HIV Surveillance System; MSM, men who have sex with men; IDU, persons who inject drugs.
* Weighted percentage of HIV-infected adults receiving medical care in the United States in January-April 2009. Data were weighted: 1) based on known probabilities of selection within each state/territory, by facility, and for patients in selected facilities; and 2) to adjust for non-response using predictors of patient-level response (i.e., facility size, race/ethnicity, time since HIV diagnosis, and age group).

[Table. Characteristics of HIV-infected persons in three CDC-funded data sources in the United States]

Conclusions: Persons living with HIV in 2009 captured in three CDC-funded data sources were demographically diverse, and the populations were qualitatively comparable across most characteristics. About three-quarters of persons were aged > 40 years, illustrating the need for HIV care and secondary HIV prevention services for older persons in the United States.

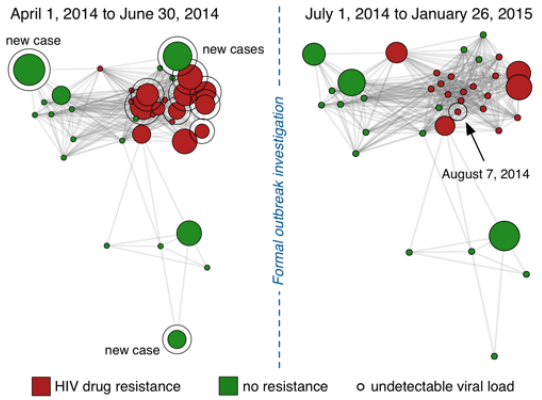
WEPEC664

Near real-time tracking of localized HIV outbreaks using an automated phylogenetic monitoring system: implementation and translation to public health

A. Poon[1,2], C. Woods[1], S. Shurgold[1], G. Colley[1], R. Hogg[1,3], M. Krajden[4,5], D. Moore[1,4], R. Gustafson[6], J. Montaner[1,2], P.R. Harrigan[1,2]
[1]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada, [2]University of British Columbia, Medicine, Vancouver, Canada, [3]Simon Fraser University, Faculty of Health Sciences, Burnaby, Canada, [4]BC Centre for Disease Control, Vancouver, Canada, [5]University of British Columbia, Pathology and Laboratory Medicine, Vancouver, Canada, [6]Vancouver Coastal Health, Vancouver, Canada
Presenting author email: apoon@cfenet.ubc.ca

Background: The rapid evolution of HIV and routine use of genotyping make it possible to use the genetic similarity of new cases to detect newly evolving HIV outbreaks within weeks of diagnosis. We have implemented a monitoring program based on the automated analysis of HIV sequences collected for routine resistance genotyping at the British Columbia (BC) Centre for Excellence in HIV/AIDS (CFE).
Methods: The Drug Treatment Program at the CFE performs all HIV genotyping for BC. De-identified sequences are uploaded to an Oracle database (currently containing over 30,000 genotypes from over 8,000 individuals in BC) and linked to de-identified clinical, demographic, geographic and epidemiological data. The database is queried hourly; when new records are detected, the system retrieves and aligns all sequences, excludes codons associated with drug resistance, and reconstructs phylogenetic trees from 100 bootstrap samples of the alignment. Clusters comprising five or more closely-related infections are assembled from all pairs with a phylogenetic distance below a threshold in the majority of bootstraps. Reports on active transmission clusters are automatically generated and distributed to select CFE directors and individuals at Vancouver Coastal Health and the BC Centre for Disease Control (BCCDC).
Results: About 20-30 genotypes are uploaded to the CFE database every day. Presently, the system requires about two hours to re-process the entire database. While the growth of most HIV clusters has been slowing, our system detected a cluster in June 2014 that had ex-

panded by 11 new cases within 3 months involving individuals with a mean viral load of 4.9 log_{10} copies/mL. Eight of these new cases carried transmitted HIV resistance to NNRTIs (K103N). This report corroborated population-level epidemiological trends monitored at the BCCDC, and prompted a formal outbreak investigation of this sub-population. This transmission cluster since expanded by a single new case in early August, with no other new cases by mid-January 2015.



Each circle represents an HIV-infected individual. Circles sized in proportion to viral load and coloured by resistance. New cases indicated by double outline.

[Cluster triggering outbreak investigation]

Conclusions: The implementation of this monitoring system has resulted in enhanced public health follow-up and engagement into care of individuals involved in a localized HIV transmission cluster. This serves as a model of how the systematic application of molecular phylogenetics can support more effective HIV prevention programming.

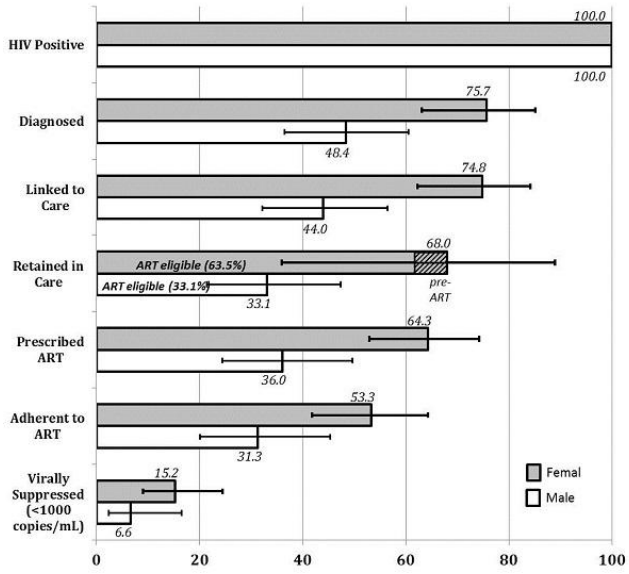
Population-based surveys with HIV testing

WEPEC665

Characterizing the continuum of care in a population-based sample to target programming in North West Province, South Africa

S.A. Lippman[1], S.B. Shade[1], J.M. Gilvydis[2], A.M. El Ayadi[3], E. Naidoo[4], J. Morris[1], L.M. Prach[1], J.S. Grignon[2,4], A. Puren[5,6], T. Liegler[7], S. Barnhart[2]
[1]University of California, Center for AIDS Prevention Studies, Department of Medicine, San Francisco, United States, [2]University of Washington, Department of Global Health, Seattle, United States, [3]University of California, Department of Obstetrics, Gynecology and Reproductive Sciences, San Francisco, United States, [4]University of Washington, International Training and Education Center for Health (ITECH) - South Africa, Pretoria, South Africa, [5]National Institute for Communicable Diseases (NHLS), Johannesburg, South Africa, [6]University of Witwatersrand, Johannesburg, South Africa, [7]University of California, Department of Medicine, HIV/AIDS Division, San Francisco, United States
Presenting author email: jgrignon@uw.edu

Background: Losses along the HIV care continuum will slow potential gains in mitigating the HIV epidemic in South Africa. Determining where losses occur along the continuum will help target intervention strategies; however, population-based data to characterize the continuum is limited.
Methods: We conducted a population-based HIV seroprevalence survey including HIV rapid testing, dried blood spot HIV RNA testing, and point-of-care CD4 testing using a multi-stage cluster sample in two sub-districts of the North West Province between January and March, 2014. We estimated HIV prevalence, undiagnosed infections, linkage to and retention in care, ART adherence, and viral suppression using data from 1044 respondents aged 18-49 years, of whom 745 consented to sample collection. All estimates were weighted to the sub-district population and stratified by gender.
Results: Prevalence was 18.8% (95%CI: 13.7%-25.2%) for men and 26.2% (95%CI: 21.9%-31.1%) for women. Only 48.4% of HIV-positive men and 75.7% of women were aware of their serostatus, with one-third of newly diagnosed infections occurring among those reporting a recent negative result. Among those aware of their status, 90.8% of men and 98.8% of women reported having ever seen a clinician for HIV care (linked). However, because such a large portion of the population was unaware of their status, those linked to care represent only 44.0% and 74.8% of all HIV-positive men and women, respectively. Among those known to be ART-eligible, 85.7% of men and 80.4% of women reported seeing a care provider every 3 months in the past year (retained). Of those prescribed ART, 80% reported taking 90% of their medication in the past month (adherent). Despite reported good retention and adherence, viral suppression was extremely low: 15.2% and 6.6% of infected women and men had a viral load measurement of <1000 copies/ml.
Conclusions: Despite testing campaigns and expansion of treatment in South Africa, the largest number of losses along the HIV care continuum occurs at diagnosis, which will hinder prevention efforts. Improved, early detection of infection must be prioritized, particularly among men. Under treatment is also a concern. While reported retention and adherence to medication is high, viral suppression remains extremely low; this discrepancy merits further investigation.



[Continuum of Care, North West, South Africa]

WEPEC666

Population level adult life expectancy in the era of antiretroviral treatment (ART) in rural Uganda

J. Nakiyingi-Miiro[1,2], G. Reniers[2], G. Asiki[1,3], J. Seeley[1,2], I. Kasamba[1], K. Baisley[2], R. Newton[1,4,5], J. Todd[2], P. Kaleebu[1,2], A. Kamali[1,2]
[1]MRC/UVRI Uganda Research Unit on AIDS, Entebbe, Uganda, [2]London School of Hygiene & Tropical Medicine, London, United Kingdom, [3]Karolinska Institute, Department of Women's and Children's Health, Stockholm, Sweden, [4]University of York, Department of Health Sciences, York, United Kingdom, [5]International Agency for Research on Cancer, Lyon, France
Presenting author email: jessica.nakiyingi-miiro@lshtm.ac.uk

Background: Information on population-level trends in Life Expectancy (LE) is essential for defining policy. Population-level LE in low-income settings has not been evaluated because most sub-Saharan African countries lack population data needed for accurate estimation. We examine LE by HIV-status in a rural Ugandan population cohort that has been under annual HIV and demographic surveillance since 1989.
Methods: We measured changes in adult LE from 1991 to 2012 using annual census, medical survey, and monthly vital registration from a general population cohort in Southwest Uganda. Life-table methods were used to quantify
(a) population-wide changes in adult LE at 15 years, calculated as number of life-years gained since LE reached its lowest (observed) level,
(b) LE trends by HIV status, and
(c) trends in LE deficit due to HIV; that is, the difference in LE of known HIV-negatives and the whole population.
All estimates are disaggregated by sex.
Results: From 1991-93 to 2009-12, overall female LE rose from 39.3 [95%CI=35.9-42.8] to 56.1 [54.0-58.5] years and male LE rose from 38.6 [35.4-42.1] to 51.4 [49.2-53.7] years. LE among HIV-positive individuals rose substantially between 2000-02 and 2009-12 (females: 13.0 [10.9-15.4] to 36.0 [30.8-46.0] years and males: 14.3 [6.6-20.6] to 34.3 [18.3-47.3] years), especially after 2004, coinciding with ART introduction. Among HIV-negative individuals there was no change in LE. Years-lost due to HIV decreased 3-fold among females (16.1 [12.7-19.8] to 6 [4.1-7.8] years) and 5-fold (16.0 [12.1-19.9] to 2.8 [1.2-4.6] years) among males. Contributions to adult LE gains by age-group between 1991-2003 and 2009-12 show that most of the 13.2 years gained in women and 8.8 years in men were in those of reproductive age, for women this occurred at younger ages than men.
Conclusions: Adult LE increased substantially in this population but not among HIV-negative individuals. This is attributed to ART introduction reducing mortality among HIV-infected adults. Despite the important recent gains in, the adult LE deficit remains substantial (particularly among women), implying that HIV/AIDS service provision and uptake needs further improvement. Interventions for: causes of most deaths in HIV-negatives; increasing the age of HIV infection among women; and reduction in HIV-incidence are needed to improve LE.

Surveillance of Hepatitis C (HCV) and HIV co-infection

WEPEC667

Inferring the transmission dynamics of acute hepatitis C virus infection in HIV-positive MSM in Hong Kong

D.P.C. Chan[1], A.W.C. Lin[2], K.H. Wong[2], N.S. Wong[1], S.S. Lee[1]
[1]Chinese University of Hong Kong, Stanely Ho Centre for Emerging Infectious Diseases, Shatin, Hong Kong, [2]Special Preventive Programme, Department of Health, Hong Kong, Hong Kong
Presenting author email: chandenise@gmail.com

Background: Sexual transmission of hepatitis C virus (HCV) infection has been increasingly recognized among men who have sex with men (MSM) in Western countries. Recently, there has been a marked rise of acute HCV infection in HIV-positive MSM in Hong Kong. The aim of our study was to characterize the transmission dynamic and genetic diversity of acute HCV infection in HIV-positive MSM in Hong Kong.
Methods: A retrospective analysis was carried out on HIV-positive MSM diagnosed with acute HCV infection between 2009 and 2014. Additional HCV RNA detection and genotyping were performed for all HCV seroconverters. Phylogenetic analysis of the HCV-NS5B region was conducted by neighbor-joining method to examine the local molecular epidemiology of HCV co-infection.
Results: Of 24 HIV/HCV co-infected MSM, the median age at HCV infection was 32 years (IQR 27-41), and the median time from HIV to HCV diagnosis was 3.1 years (IQR 1.2-6.5). The majority of patients (87.5%) were Chinese, and 23 (95.8%) were on antiretroviral treatment. None of them reported history of injection drug use. Among 22 (91.7%) HIV-positive MSM with detectable HCV RNA, infection with HCV genotype 3a (63.6%) was the most common, followed by genotypes 1a (18.2%), 6a (9.1%), 1b (4.5%) and 2a (4.5%). Acute HCV infection identified before 2012 were mostly of genotypes 1a and 6a, whereas genotype 3a predominated in the majority of acute HCV cases diagnosed between 2013 and 2014. Phylogenetic analyses revealed a monophyletic cluster of HCV-3a lineage from 2013 onwards, and a homologous pair of MSM-specific HCV-6a strain that were separate from those circulating in local injection drug users.
Conclusions: Our study indicates the existence of MSM-specific networks that has contributed to the sexual transmission of HCV in HIV-positive MSM in Hong Kong. Recent finding of the emergence of an independent and non-injecting HCV-3a cluster further implicates the rapid spread and increasing burden of sexually acquired HCV infection within our local HIV-positive MSM community.

Innovations in the measurement of sensitive behaviours and adherence

WEPEC668

Behavior change, a critical step in HIV prevention: utilizing LQAS to monitor behavior change among youth age 15-24 years in East Central Uganda

F. Ajok Odoch[1], F. Kazibwe[1], T. Odong[2], D. Businge[2], A. Mugume[1], J. Mukokha[3]
[1]JSI Research & Training Institute, Inc.(JSI)/Strengthening TB and HIV&AIDS Responses in East Central Uganda (STAR-EC), Technical Department, Kampala, Uganda, [2]JSI Research & Training Institute, Inc.(JSI)/Strengthening TB and HIV&AIDS Responses in East Central Uganda (STAR-EC), Strategic Information, Kampala, Uganda, [3]Namayingo District, Health Department, Kampala, Uganda
Presenting author email: fajok@starecuganda.org

Background: In many regions of the world, new HIV infections are heavily concentrated among young people aged 15-24 years. It accounts for close to 40% of all new HIV infections globally.it is believed that the majority do not know that they are infected. Young people exhibit risky behaviours that expose them to HIV infections including: early sexual debut, none condom use, multiple and concurrent partnerships, lack of comprehensive knowledge on HIV prevention.
Methods: Lot Quality Assurance Survey (LQAS) were conducted annually from 2009 - 2014. A total of 63 research teams were trained application of the LQAS survey methodology. Basing on key indicators developed, data was collected from over 3,000 households.
Results: The Lot Quality Assurance Survey results shows positive behaviour change among young people from baseline period upward to 2014 as summaries below:
· Percentage of young people 15-24 who had sexual intercourse with a non marital or non cohabiting sexual partner in last 12 months and used a condom at last higher risk sex improved from 64.9% in 2013 to 71.2% in 2014
· Percentage of Youth 15-24 years who have had sexual intercourse before the age of 15 decreased from 12.5% in 2009 to 11.4% in 2014
· Percentage of Youth 15-24 years who perceive low or no risk of getting HIV&AIDS infection improved from 30.1% in 2011 to 17.3% in 2014
Percentage of adults (15+) who can mention the 3 major ways of HIV&AIDS prevention improved from 58.7% in 2009 to 72.8% in 2014
· Percentage of adults (15+) able to reject three of the major HIV&AIDS misconceptions (witchcraft, mosquito bites and sharing food) improved from 48.3% in 2009 to 68% in 2014.
Conclusions: Measurement of risky behaviors among young people using LQAS has shown positive behavior change among young people aged 15-24 years in East Central Uganda.

HIV testing

WEPEC669

Making it available is not enough: a qualitative study on MSM's views towards HIV self-testing

H.T.H. Wong[1], S.S. Lee[1], D.P.C. Chan[1], C.M. Poon[2]
[1]Chinese University of Hong Kong, Stanley Ho Centre for Emerging Infectious Diseases, Hong Kong, Hong Kong, [2]Chinese University of Hong Kong, Jockey Club School of Public Health and Primary Care, Hong Kong, Hong Kong
Presenting author email: steven_poon@cuhk.edu.hk

Background: Despite controversies, HIV self-testing (HIVST) is a potentially useful approach to increase uptake of HIV testing among men having sex with men (MSM). Self-test kits are now available in many countries. This study aimed to explore the views on HIVST among MSM in Hong Kong where self-test kits can be accessible through purchases.
Methods: Email invitations to qualitative interviews were sent to 606 participants of an online survey. Two focus group interviews were successfully conducted with 15 HIVST-naïve MSM; and key informant interviews were organised with 5 ever self-testers. Verbatim transcripts were analysed using a thematic analysis approach to identify a number of recurring themes related to views on HIVST and reasons for (not) choosing self-testing.
Results: In the focus groups, very few participants reported having heard about HIVST and most were skeptical about the accuracy of self-test kits. HIV was commonly described in terms of "social discrimination" and "death". Therefore, privacy and the availability of support services were key considerations for participants when choosing an HIV test. Although most participants acknowledged the privacy provided by HIVST, this advantage was outweighed by their intense fear of facing test results alone and the uncertainties regarding HIV treatments and supports ("what if I test positive?"). Most participants were not interested in HIVST but felt that more formal information should be available to enable the community to make informed choices. For the self-testers, two distinct reasons for self-testing could be identified. Some self-testers were not satisfied with the current testing and counselling services; while others saw self-testing not as a health check, but as a convenient way to provide psychological comfort (to "prove one's HIV negativity"). Even if they had doubts about the accuracy of the test, they would not go for another HIV test after a negative result.
Conclusions: Market availability of self-test kits alone is not enough to attract more MSM to receive HIV test and may even induce harm. Policy goals to increase uptake of HIV test by HIVST may benefit from taking account of fears of HIV and social discrimination, and concerns over the accuracy of HIVST held by the MSM community.

WEPEC670

Personal risk factors and HIV positivity among female sex partners of people who inject drugs (PWID) at voluntary HIV counseling and testing (VCT) sites in Vietnam, 2011-2013

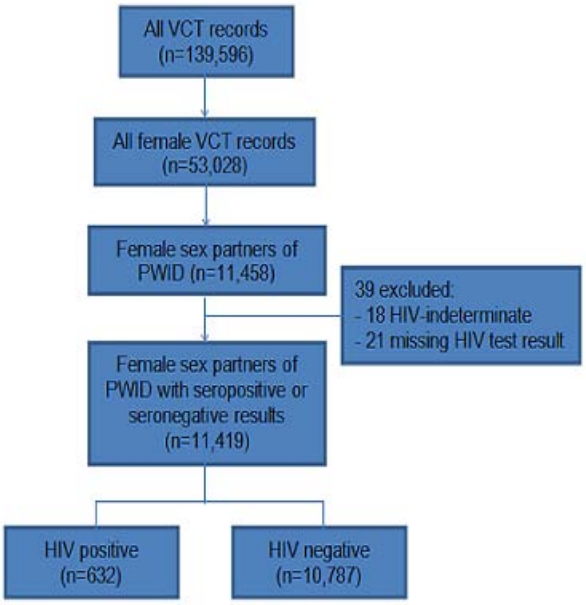
V. Dao[1], H. Nguyen[1], A. Vu[2], H. Duong[1], T. Nguyen[2], H. Nguyen[1], S. Lyss[1], T. Bingham[3], H. Vo[4]
[1]United States Centers for Disease Control and Prevention (CDC), U.S. Embassy, Hanoi, Vietnam, [2]Vietnam Administration of AIDS Control (VAAC), Ministry of Health, Hanoi, Vietnam, [3]United States Centers for Disease Control and Prevention (CDC), Atlanta, United States, [4]Ho Chi Minh Provincial AIDS Committee, HIV Testing and Counseling, Ho Chi Minh City, Vietnam

Background: People who inject drugs (PWID) account for the largest proportion of HIV infections in Vietnam; 42% of cases reported in 2013 were among PWID, 95% of whom were male. Forty percent of male PWID report unprotected sex with regular partners in the last 12 months, suggesting that sex partners of PWID are at high risk for HIV. We assessed personal risk factors associated with HIV positivity among female sex partners of PWID.
Methods: We examined all records routinely collected during 2011-2013 from all 47 CDC-funded voluntary counseling and testing (VCT) sites throughout Vietnam. We analyzed records

of female VCT clients who self-reported being sex partners of PWID. We used bivariate analysis to estimate associations between HIV positivity and clients' personal behaviors (including those with multiple risks) according to highest HIV transmission risk category (personal injection>sex work>having multiple sex partners>none of these).

Results: Of 11,419 female sex partners of PWID (figure), mean age was 29 years, 7,556 (66.5%) were married, and most had attended some high school; 10,143 (88.8%) reported not having previously tested for HIV. Regarding personal risk behaviors, 547 (4.8%) reported drug injection; 1,749 (15.3%) sex work; 1,006 (8.8%) having multiple partners; and 8,117 (71.1%), none of these (table).

Overall, 632 (5.5%; 95% confidence interval [CI]=5.1-6.0) tested HIV-seropositive. HIV positivity was 16.8% (95% CI=13.8-20.2) among those reporting personal drug injection, 3.7% (95% CI=2.9-4.7) among those reporting sex work, 7.1% (95% CI=5.6-8.8) among those reporting multiple partners, and 5.0% (95% CI=4.5-5.5) among those reporting none of these. Compared with sex partners of PWID reporting no personal behavioral risks, HIV positivity was greater among those reporting drug injection (prevalence ratio [PR]=3.4, 95% CI=2.8-4.2) and multiple sex partners (PR=1.4, 95% CI=1.1-1.8).



[Figure: Selection of female sex partners of PWID]

Characteristics	Total N (%)	HIV positivity N (%)	Prevalence ratio (95% CI)	Characteristics	Total N (%)	HIV positivity N (%)	Prevalence ratio (95% CI)
Overall	11,419	632 (5.5)	n/a	Previous HIV testing: Never tested	10,143 (88.8)	515 (5.1)	**Reference**
Residency: Urban*	6,202 (54.3)	341 (5.5)	**Reference**	Previous HIV testing: Yes, HIV negative	1,151 (10.1)	32 (2.8)	0.55 (0.39-0.78)
Residency: Rural*	4,384 (38.4)	216 (4.9)	0.90 (0.76-1.06)	Previous HIV testing: Yes, HIV positive	39 (0.3)	38 (97.4)	n/a
Residency: Other province	828 (7.3)	74 (8.9)	1.63 (1.28-2.07)	Previous HIV testing: Yes, indeterminate	54 (0.5)	32 (59.3)	11.67 (9.21-14.79)
Marital status: Never married	2,752 (24.1)	118 (4.3)	**Reference**	Previous HIV testing: Yes, but not received or lost	25 (0.3)	15 (60.0)	n/a
Marital status: Married/living with sex partners	7,556 (66.5)	382 (5.1)	1.18 (0.96-1.44)	Personal risk: Drug injection	547 (4.8)	92 (16.8)	3.38 (2.74-4.17)
Marital status: Divorced/ separated	749 (6.6)	66 (8.8)	2.06 (1.54-2.75)	Personal risk: Sex work	1,749 (15.3)	65 (3.7)	0.75 (0.58-0.97)
Marital status: Widowed	358 (3.1)	66 (18.4)	4.30 (3.25-5.69)	Personal risk: Having multiple sex partners	1,006 (8.8)	71 (7.1)	1.42 (1.11-1.81)
*- Client lives in urban or rural district within the province where the VCT was located				Personal risk: None of above	8,117 (71.1)	404 (5.0%)	**Reference**

[Table: Characteristics and positivity association]

Conclusions: Although HIV positivity was highest among the few female sex partners of PWID who reported injecting drugs themselves, it was also high among those without reported high-risk behaviors. Few sex partners of PWID have tested for HIV. Traditional outreach targeting PWID and sex workers might not reach sex partners of PWID. Safe sex messages and promotion of VCT should be expanded to target sex partners of PWID through new approaches delivered by PWID.

WEPEC671

'Going Viral': a universal blood-borne virus (BBV) testing campaign for HIV, hepatitis B and C in ten UK Emergency Departments

C. Orkin[1], S. Flanagan[1], E. Wallis[1], R. O'Connell[1], R. Dhairyawan[2], J. Fox[3], R. Nandwani[4], G.R. Foster[5], I. Reeves[6], M. Lascar[1], J. Bulman[7], A. Palfreeman[8], C.J.W. Tong[1], J. Anderson[9], G. Ireland[9], S. Lattimore[9]

[1]Barts Health NHS Trust, Infection and Immunity, London, United Kingdom, [2]Barking, Havering & Redbridge University Hospitals NHS Trust, London, United Kingdom, [3]Guys and St Thomas' NHS Trust, London, United Kingdom, [4]Greater Glasgow and Clyde NHS Trust, Glasgow, United Kingdom, [5]Queen Mary University London, London, United Kingdom, [6]Homerton University Hospital, London, United Kingdom, [7]Leeds Teaching Hospital NHS Trust, Leeds, United Kingdom, [8]University Hospitals of Leicester NHS Trust, Leicester, United Kingdom, [9]Public Health England, London, United Kingdom

Presenting author email: chloe.orkin@bartshealth.nhs.uk

Background: The CDC recommends universal HIV testing in 15-65's and targeted screening for Hepatitis C (HCV) and B (HBV). UK guidelines recommend HIV testing where the diagnosed prevalence is >2/1000, and targeted screening for HBV/HCV. 1 in 4 people attend ED in England annually (18 million in 2012), of whom 13% have bloods taken- a significant testing opportunity. Few hospital-based universal BBV screening initiatives have been described. 'Going Viral' is a multi-ED universal BBV testing campaign.

Methods: During 13th- 20th October 2014, 10 UK ED departments serving populations with a diagnosed HIV prevalence of >2/1000 took part in an opt-out BBV screening programme; 9 provided data. ED staff offered BBV tests to patients >16 years having bloods as part of routine care. HIV Ab, HBV Surface Ag & HCV Ab were tested by local labs. Uptake was defined as those ED attendees having bloods who were also tested for BBV's. Demographic data were extracted from electronic records, analysed with R (CRAN).New and known positives were contacted and linked to care.

Results: 2124 individuals had the BBV test and 69 infections were diagnosed (3.25%), 31 new: HCV+ 37
(14 new), HIV+ 17 (6 new), HBV+ 15 (11 new). Those aged 25-54 had the highest prevalence: HCV 2.45%, HIV 1.36%, HBV 1.09%. Testing uptake 2124/7961 (27%)) range 17.4%- 60.5%. Uptake was 1/3 higher in hospitals with high diagnosed HIV+ prevalence (>6/1000 population), 29.4% cf 20.8}. Women had lower odds of accepting testing than men (OR 0.86) and the odds of accepting testing decreased with each successive 10 year increase in age (OR 0.91). Assuming the cost per test as £7 for each virus, the cost per new case detected is £1,062 for HCV, £1,351 for HBV and £2,478 for HIV.

		HIV		HBV		HCV	
Age groups	All tested	All Positive (rate)	New Positive (rate)	All Positive (rate)	New Positive (rate)	All Positive (rate)	New Positive (rate)
16-24	256	0 (0%)	0 (0%)	1 (0.39%)	1 (0.39%)	1 (0.39%)	1 (0.39%)
25-34	424	7 (1.65%)	4 (0.94%)	6 (1.42%)	5 (1.18%)	8 (1.89%)	2 (0.47%)
35-44	338	4 (1.18%)	2 (0.59%)	4 (1.18%)	3 (0.89%)	10 (2.96%)	5 (1.48%)
45-54	338	4 (1.18%)	0 (0%)	2 (0.59%)	0 (0%)	10 (2.66%)	5 (1.48%)
55-64	281	1 (0.36%)	0 (0%)	1 (0.36%)	1 (0.36%)	6 (2.14%)	0 (0%)
65 plus	482	1 (0.21%)	0 (0%)	1 (0.21%)	1 (0.21%)	2 (0.41%)	1 (0.21%)
Total	2,119	17 (0.80%)	6 (0.28%)	15 (0.71%)	11 (0.52%)	37 (1.74%)	14 (0.66%)
25-54	1,100	15 (1.36%)	6 (0.55%)	12 (1.09%)	8 (0.73%)	27 (2.45%)	12 (1.09%)

[Age specific prevalence for HIV, HBV, HCV]

Conclusions: Universal testing in the ED identified 31 new infections in 7 days, 4.4 per day, with an uptake rate of 17-60.5%. Testing for HIV only, as per the current UK recommendations, would have missed 52 viral hepatitis diagnoses, 25 of them new. This week-long campaign calls strongly for BBV testing to be considered.

WEPEC672

Community-based HIV rapid testing and linkage to care. Efficacy of multi-country testing initiatives during European testing week 2014

A.M. Zakowicz[1], O. Lozytska[1], K. Bidzinashvili[2], B. Billie[3], Z. Dominković[4], S. Golovko[5], M. Jacovleva[6], R. Kaupe[7], S. Kostenko[8], L. Aleksanyan[9], A. Slominskaya[10], N. Voudouri[11], D. Raben[12], M. Donoghoe[13], T. Noori[14], Z. Shabarova[1]
[1]AHF Europe, Amsterdam, Netherlands, [2]Step to the Future, Tblilisi, Georgia, [3]GOSHH, Limerick, Ireland, [4]Iskorak, Sexual and Gender Minorities Rights Center, Zagreb, Croatia, [5]PLWH 'From Heart to Heart', Cherkassy, Ukraine, [6]'Svecha' (Candle), St. Petersburg, Russian Federation, [7]DIA+LOGS NGO, Riga, Latvia, [8]Public Fund Gender-Vector, Bishkek, Kyrgyzstan, [9]'Real World, Real People', Yerevan, Armenia, [10]'Vertical' NGO, Kiev, Ukraine, [11]Praksis, Athens, Greece, [12]CHIP, Rigshospitalet, Copenhagen, Denmark, [13]WHO Regional Office for Europe, Copenhagen, Denmark, [14]European Centre for Disease Prevention and Control, Stockholm, Sweden
Presenting author email: anza1@wp.pl

Background: HIV testing and early detection remains a challenge in Europe. Of the estimated 2.3 million PLHIV in Europe, approximately 30% are unaware of their status. As a consequence, almost half (49%) of all newly reported cases in Europe in 2013 were late presenters (CD4 cell count < 350/mm3). Increasing uptake of testing will require innovative and community-based approaches to ensure that HIV testing services are targeted at, accessible to and used by those people who are most at risk of infection.
Methods: During the European HIV Testing Week, 21-28 November 2014, AHF Europe selected 12 community-based organisations in 11 countries (6 EU and 5 non-EU) to conduct testing using AHF Rapid Testing Model. They received small grants to cover direct and indirect costs to conduct rapid testing for key populations. The organisations received technical assistance on unified data collection, reporting and key elements of the model. They provided rapid testing, counselling and referral with linkage to care. Full linkage and late presentation data will be available in March 2015.
Results: 4208 people were screened for HIV at on-site and off-site events (median age 34; 68% male; 18% MSM, 17% PUD, 13% SW). 56% had never tested for HIV before. 167 received reactive results; including 107 (2.5% (0%-9.3%)) self-reported new cases. 70% of new cases were among men. Overall, the results in different populations were: MSM-3.6% (29), PUD-15.7% (113) and SW-1.8% (8). New cases across different populations included: MSM-3.5% (27) PUD-7.4% (57) and SW-1.5% (8). 91% (152) of all positive cases referred to care attended their appointment. The average AHF Europe investment per test performed including direct and indirect costs was USD9.67 (USD6.05-86.94) with the average cost per new reactive case USD380.39 (USD138.33-3540).
Conclusions: There is a pressing need to increase uptake of HIV testing among key populations and promote earlier diagnosis and linkage to care. Community-based HIV rapid testing interventions demonstrate a potential to reach people who have never been tested or those who know their status but are not in care, ensure efficacy and effective linkage to care.

WEPEC673

Expanding HIV testing and counselling (HTC) coverage through integration of community and facility strategies in an informal settlement in Kenya

S. Muhula[1], P. Kisia[2], B. Baker[2], G. Ikiara[3], M. Ndirangu[4], B. Abunah[5]
[1]Amref Health Africa, Monitoring, Evaluation and Research, Nairobi, Kenya, [2]Amref Health Africa, Kibera Care and Treatment Project, Nairobi, Kenya, [3]Amref Health Africa, Kibera Care and Treatment Project - M&E, Nairobi, Kenya, [4]Amref Health Africa, Head of Programmes, Nairobi, Kenya, [5]AMREF Kenya, Nairobi, Kenya
Presenting author email: samuel.muhula@amref.org

Background: Knowledge of HIV status is often the first step in the management of HIV/AIDS. People living in informal settlements, often low income earners are unique and require innovative approaches to spur their interest in HIV testing. AMREF has integrated community and facility strategies to expand coverage of HTC services. We hereby share our experiences, key challenges and successes.
Methods: The project is implemented at four Health Centers situated within Kibera Informal settlement, which is the largest urban slum in Africa. We analyzed data on testing strategies employed both at clinics (Facility based testing) and community level strategies, for cohort starting October 2013 and September 2014. Facility based testing strategies include Provider Initiated testing and counselling (PITC) and Client Initiated Testing and Counselling (CITC), while the community approaches are mainly Home Based Counselling and Testing (HBTC). We used univariate and multivariate analysis to compare the outcomes of both approaches and determine the predictors of positivity and hereby present results of both testing strategies.
Results: A total of 18,591 patients were tested during the cohort period. About 73% (13,485) were tested at the 4 facilities with the remainder tested in the community. Within the facilities, PITC accounted for 80% (11,015) of the clients with the remaining 20% tested through CITC. Individuals at the outpatient unit were provided with health education and appropriately referred for testing. HBTC contributed 5,106 (27%) clients and was mainly through door to door campaigns, community mobilization and referrals. Positivity for those tested at the facilities was 7% versus 1% among those tested in the community. Couple testing was better done in facility based testing and counselling centers. Major challenges with HBTC were difficulties linking HIV positive individuals to care, difficulties getting couples at home, couples refusing testing, high costs incurred, yet few positive clients identified and dispute of results among clients.
Conclusions: Though facility based testing and counselling is better in identifying HIV positive individuals, integration of both community and facility testing model, helps in capturing otherwise healthy HIV infected patients and expands testing coverage.

WEPEC675

Confidence in HIV testing ability is associated with higher HIV testing frequency and likelihood to self-test among gay and bisexual men

M.S. Jamil[1], B. Bavinton[1], R. Guy[1], C. Fairley[2,3], A. Grulich[1], M. Holt[4], K. Smith[1], M. Chen[2,3], A. McNulty[5], D. Conway[1], P. Keen[1], J. Bradley[1], D. Russell[6,7,8], J. Kaldor[1], G. Prestage[1,9], FORTH Study Group
[1]The Kirby Institute, UNSW Australia, Sydney, Australia, [2]Monash University, Melbourne, Australia, [3]Melbourne Sexual Health Centre, Melbourne, Australia, [4]Centre for Social Research in Health, UNSW Australia, Sydney, Australia, [5]Sydney Sexual Health Centre, Sydney Hospital, Sydney, Australia, [6]James Cook University, Townsville, Australia, [7]University of Melbourne, Melbourne, Australia, [8]Cairns Sexual Health Service, Cairns, Australia, [9]Australian Research Centre in Sex Health and Society, La Trobe University, Melbourne, Australia
Presenting author email: mjamil@kirby.unsw.edu.au

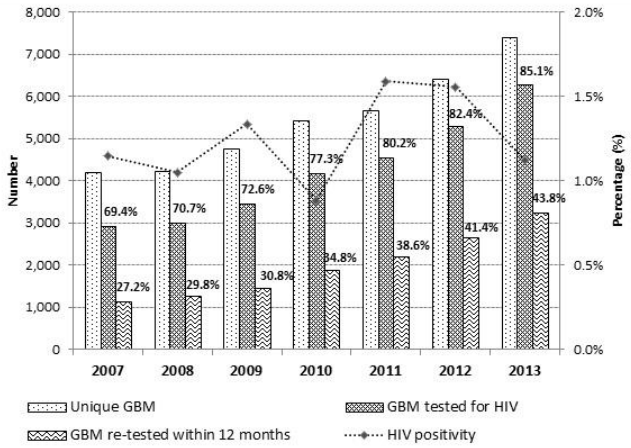
Background: Regular testing of high-risk individuals is central to biomedical and behavioural prevention strategies, and specifically crucial to decrease time between infection and diagnosis. Little research has been conducted on 'self-efficacy' in relation to perceived ability to undertake HIV testing among gay and bisexual men (GBM). We examined self-efficacy in relation to HIV testing frequency and likelihood to self-test among GBM.
Methods: Participants were HIV-negative Australian GBM at increased risk of HIV (>5 partners or unprotected anal intercourse in previous 3 months) in a randomised controlled trial of HIV self-testing (FORTH). We constructed a HIV Testing 'Self-Efficacy' scale (HTSE) measuring confidence in one's perceived ability to undertake HIV testing comprising 8 items (responses: 'not at all confident'=0 to 'completely confident'=4; Cronbach's α=0.81). Total HTSE score consisted of the sum of scores for all items. Prior to the trial (and self-testing) commencing, a cross-sectional analysis was conducted including surveys with complete responses to HTSE items. Factors associated with past HIV testing frequency and perceived likelihood to self-test in the future were determined using logistic regression.
Results: A total of 352 GBM were included. Median age was 33 years (inter-quartile range [IQR]=26-41), and 63% were Australian-born (n=227). Overall, 95.4% reported having previously tested for HIV (n=336): 65.3% in the last 12 months (n=230) and 64.2% reported being 'very likely' to self-test for HIV (n=231). The median HTSE score was 26 (IQR=23-29, range=8-32). In multivariate analysis, independent factors associated with ≥3 HIV tests in last 12 months were: higher HTSE score (adjusted odds ratio [AOR]=1.1 for increase in score by 1, 95%CI=1.02-1.13,p=0.006); and >5 partners in last 6 months (6-10 partners AOR=2.7, 95%CI=1.30-5.80,p=0.008; 11-20 partners AOR=3.0, 95%CI=1.48-6.22,p=0.002; ≥21 partners AOR=6.5, 95%CI=3.03-13.73,p< 0.001). Only HTSE score was associated with high perceived likelihood to self-test (odds ratio=1.1,95%CI=1.03-1.13,p=0.001).
Conclusions: Self-efficacy in relation to HIV testing is independently associated with HIV testing frequency and likelihood to self-test. Improving GBM's confidence in HIV testing such as by improved knowledge and greater experience may lead to higher testing frequency. Future longitudinal analysis will provide information about the causal pathway direction between HTSE, testing frequency and actual self-testing measured in the FORTH trial.

WEPEC676

Increasing HIV testing and re-testing without declining HIV positivity among gay and bisexual men attending public sexual health clinics

M.S. Jamil[1], D. Callander[1,2], H. Ali[1], G. Prestage[1,3], V. Knight[1,4], T. Duck[5], C. O'Connor[1,6], M. Chen[7,8], M. Hellard[9], A. Grulich[1], D. Wilson[1], J. Kaldor[1], C. Fairley[7,8], B. Donovan[1,4], R. Guy[1]
[1]The Kirby Institute, UNSW Australia, Sydney, Australia, [2]Centre for Social Research in Health, UNSW Australia, Sydney, Australia, [3]Australian Research Centre in Sex Health and Society, La Trobe University, Melbourne, Australia, [4]Sydney Sexual Health Centre, Sydney Hospital, Sydney, Australia, [5]NSW Ministry of Health, Sydney, Australia, [6]Royal Prince Alfred Hospital Sexual Health Service, Sydney, Australia, [7]Monash University, Melbourne, Australia, [8]Melbourne Sexual Health Centre, Melbourne, Australia, [9]Centre for Population Health, Burnet Institute, Melbourne, Australia
Presenting author email: mjamil@kirby.unsw.edu.au

Background: Gay, bisexual and other men who have sex with men (GBM) are a risk group most affected by HIV in Australia. Mathematical modelling suggests that reducing the time between infection and diagnosis can lead to reductions in population incidence. Public sexual health clinics (SHCs) implemented a range of initiatives to increase HIV testing including express clinics, after-hours and drop-in services, online booking, rapid testing, and reminders. We measured the impact of these strategies on HIV testing among GBM attending SHCs in the state of New South Wales (NSW).
Methods: We utilised routinely collected data from 33 large SHCs in NSW. The analysis was restricted to HIV-negative GBM from 2007-2013. We calculated the following indicators: unique GBM attending; proportion of attendees tested at least once in a year (tested/attended); proportion of attendees re-tested within 1-12 months (re-tested/attended). We also calculated annual HIV positivity defined as the proportion of attendees testing positive for HIV (positive/attended). Analyses were for all GBM and (2) higher-risk GBM (>5 partners in last 3 months or previous diagnosis of a sexually transmissible infection).
Results: From 2007-2013, 20,542 unique HIV-negative GBM had 117,796 visits and 42,360 HIV tests. The median age at first visit was 31 years (inter-quartile range:25-40). In 2007, 4,202 unique GBM attended, 69.4% had an HIV test and 27.2% were re-tested within 12 months (see Figure). In 2013, 7,387 unique GBM attended (76% relative increase from 2007), 85.1% had an HIV test (23% increase) and 44% were re-tested within 12 months (61% increase) with a significant increasing trend in all indicators over time (p< 0.001). Testing uptake was greatest in higher-risk GBM and increased from 79.6% in 2007 to 93% in 2013. Overall, HIV positivity fluctuated (0.9%-1.6%) with no significant trend over time (p=0.264).



[HIV testing, re-testing and positivity rate in GBM]

Conclusions: Public SHCs in NSW have successfully increased attendance and HIV testing among GBM, and prioritised testing in higher-risk men. The HIV positivity data suggest that the increase in testing has remained well targeted, and not extended into a group at lower risk of HIV. There is potential to further improve testing uptake and re-testing to decrease the time between infection and diagnosis.

WEPEC677

Clinic-based supervised oral self-testing for HIV is feasible and accurate in rural KwaZulu Natal, South Africa

A. Mkwamba, A. Shroufi, E. Venables, T. Ellman, G. Martínez Pérez, B. Mazibuko, R. Giuliani, G. van Cutsem, B. Hwang
Medecins Sans Frontieres, Eshowe, South Africa
Presenting author email: msfocb-capetown-deputymed@brussels.msf.org

Background: Key to decreasing HIV incidence is promoting people's awareness of their HIV status and initiating eligible people on ART. This study examines the feasibility of oral self-testing (OST) in a primary healthcare environment as a step towards wider access to HIV counseling and testing (HCT). Confirmatory testing and linkage to care are key elements to be implemented as per Médecins Sans Frontières/UNAIDS recommendations on OST, and are ensured in our study setting.
Methods: Recruitment took place in two clinics in uThungulu district, KwaZulu Natal, from June 2014 to January 2015. Potential participants were approached at the waiting areas, performed OST under the supervision of a counselor, and read their results. Confirmatory blood-based rapid-tests were done for all participants.
Results: 1001 (26%) among the 3955 clinic attendants sensitized accepted to enroll in the study. Median age of the 259 (25.8%) men and 742 (74.1%) women participants was 28.7 (IQR 22.5-36.0) and 25.0 (IQR 21.0-32.6) respectively. 933 (93%) had a HIV test before, but only 53 (5.3%) had ever heard of OST. Counselor-participant concordance in results interpretation was 99.7%. A sensitivity-specificity of 99.55% and 99.87% was observed, with positive and negative predictive values having the same values. A total of 222 (22.2%) participants were confirmed as HIV-positive by the finger-prick rapid-test.
Conclusions: The use of supervised OST is feasible in rural clinics in KwaZulu Natal and with diagnostic performance observed in this setting being very similar to that of the rapid test. OST can be a feasible option to improve uptake of HCT at clinic level, and rural clinics in KwaZulu Natal need support to roll-out OST in their HIV testing services to increase awareness of HIV status among population who regularly do not access conventional HCT. Further research is needed to assess feasibility of unsupervised self-testing in settings outside of health facilities.

WEPEC678

Gay men's awareness of pooled nucleic acid amplification testing (pNAAT): examining diffusion among networks and influence on testing following implementation and promotion in Vancouver, Canada

J. Wilton[1], M. Kwag[2], D. Grace[1], J. Jollimore[2], T. Trussler[3], R. Marchand[3], O. Ferlatte[3,4], D. Taylor[5], M. Steinberg[4], M. Gilbert[5,6]
[1]University of Toronto, Dalla Lana School of Public Health, Toronto, Canada, [2]Health Initiative for Men, Vancouver, Canada, [3]Community-Based Research Centre for Gay Men's Health, Vancouver, Canada, [4]Simon Fraser University, Vancouver, Canada, [5]British Columbia Centre for Disease Control, Vancouver, Canada, [6]Ontario HIV Treatment Network, Toronto, Canada
Presenting author email: wiltonjames@gmail.com

Background: In 2009, pNAAT was implemented at 6 clinics accessed by gay men in Vancouver, Canada. This introduction was accompanied by social marketing campaigns and led to the increased detection of acute HIV infection (AHI) over time. We aimed to understand if (and how) awareness of pNAAT testing diffused among gay men following implementation, and whether this awareness influenced testing patterns.
Methods: Men identifying as having sex with men and testing HIV-negative at 1 of the 6 clinics were enrolled into a prospective cohort between June 2011 and March 2012. Participants self-completed questionnaires at 7, 30, 180, and 360 days that spanned domains including personal/social background, HIV testing and sex life. We used baseline data to explore outcomes related to awareness of pNAAT, diffusion of knowledge, and influence on testing behavior. Chi-squared analyses were used to identify variables associated with these outcomes.
Results: 166 men completed the baseline questionnaire. The mean age was 32 years and the majority self-identified as gay (89%), were Caucasian (67%), and resided in Vancouver (84%). Awareness of pNAAT was high (72%) across all sociodemographic groups. Most men reported telling sex partners (53%) or gay friends (66%) about the test but fewer heard about the test from these sources (8% and 35%, respectively). Men who talked to sex partners about the early test were more likely to report looking for sex among friends of friends, friends, and ex-boyfriends (34.5% vs. 14.6%, p=0.02) and discuss HIV status with their sex partners (74.5% vs. 47.9%, p=0.005). Almost half (41%) of participants reported that awareness of pNAAT availability influenced them to test earlier than normal. Of reasons given for testing, men who reported they wanted pNAAT were also likely to report testing due to a sexual event that risked HIV transmission (p=< 0.001), suggesting awareness was correlated with earlier testing after a risk event.
Conclusions: Awareness of pooled NAAT was high among this sample of gay men in Vancouver, discussion of pNAAT in sexual and social networks was common, and awareness appeared to contribute to earlier testing. Efforts to promote AHI testing are an important component of increasing AHI diagnosis capacity.

WEPEC679

Self-reported satisfaction and intent to retest among adolescents tested for HIV in a pediatric emergency department

N. Ellenberger[1], K. Ganesan[1], S. Morrison[1,2], J. Payne[1], N. Rakhmanina[1,2]
[1]*Children's National Health System, Washington, United States,* [2]*George Washington University, School of Medicine and Health Sciences, Washington, United States*
Presenting author email: nellenbe@childrensnational.org

Background: Routine HIV screening of youth starting 13-15 years of age has been recommended in healthcare settings including Emergency Departments (EDs). Children's National Health System's (CNHS) ED provides universal, opt-out HIV screening for adolescents ≥ 13 years. Few studies have assessed the satisfaction and experience of young people approached and screened for HIV in a pediatric ED setting. This study was conducted to evaluate patient satisfaction and perceived impact on patients' future HIV testing following HIV screening at the CNHS United Medical Center (UMC) community hospital pediatric ED.
Methods: A voluntary, anonymous survey with multiple choice questions assessing patient satisfaction and experience with HIV testing was administered from March 2013 to August 2014 to adolescents who tested negative for HIV after they received their results. Adolescents with positive HIV test results were excluded from participating in the survey. Descriptive statistics were used to assess patient perception and satisfaction of ED HIV screening.
Results: A total of 405 adolescents (median age=16 years) completed the survey. The majority were female (70%; n=285) and Black (95%; n=385). The large majority of adolescents were "*satisfied"* or
"very satisfied" with their HIV testing experience (86%; n=349) and with the way the test results were presented to them (97%; n=395). The majority of adolescents (66%; n=266) were also *"satisfied"* or
"very satisfied" with the time spent on HIV education and reported increased awareness (72%; n=293) about the risk factors for acquiring HIV. Approximately half (56%; n=225) of adolescents reported that they would encourage their partners to get an HIV test and would retest themselves in 3 months (47%; n=191) or 6 months (27%; n=110).
Conclusions: In addition to identification of an infection, HIV screening provides an opportunity for adolescents to increase their awareness about HIV. High levels of patient satisfaction have been observed among adolescents tested for HIV in the UMC ED. Most importantly, testing for HIV appears to have motivated almost half of adolescents to consider encouraging their partners to test for HIV and to retest themselves for HIV within 3 months although the intent to retest for HIV appeared to decrease at 6 months.

WEPEC680

The impact of HIV counseling and testing on HIV acquisition: a systematic review

B.M. Hauser[1,2], J. Ryan[2,3], W.C. Miller[4,5], N.E. Rosenberg[2,4,5]
[1]*University of North Carolina at Chapel Hill, Environmental Sciences and Engineering, Chapel Hill, United States,* [2]*University of North Carolina Project, Lilongwe, Malawi,* [3]*London School of Hygiene and Tropical Medicine, London, United Kingdom,* [4]*University of North Carolina at Chapel Hill, Epidemiology, Chapel Hill, United States,* [5]*University of North Carolina at Chapel Hill, Medicine, Chapel Hill, United States*
Presenting author email: bmhauser@live.unc.edu

Background: Each year, millions of people in sub-Saharan Africa receive HIV counseling and testing (HCT), a service designed to inform persons of their HIV status and, if HIV-uninfected, reduce HIV acquisition risk. However, the impact of HCT on HIV acquisition has not been systematically evaluated. We conducted a systematic review to assess whether HCT was associated with reduced HIV acquisition in sub-Saharan Africa.
Methods: In August 2013, we searched PubMed for articles from sub-Saharan Africa meeting the following criteria: an HIV-uninfected population, HCT as an exposure, longitudinal design, and an HIV acquisition endpoint. Quality indicators and effect estimates were abstracted by two independent coders and reconciled by an epidemiologist. Three sets of comparisons were abstracted:
A) sites receiving HCT versus sites not receiving HCT,
B) persons receiving HCT versus persons not receiving HCT, and
C) persons receiving HCT alone versus persons receiving HCT as a couple.
Results: The search yielded 1622 abstracts with nine meeting inclusion criteria; one was omitted due to duplicate reporting. All studies had at least one limitation: insufficient sample size, failure to randomize or account for confounding factors, or substantial loss to follow-up. Comparison A consisted of one cluster randomized trial with an imprecise trend towards HCT being harmful: incidence rate ratio (IRR): 1.5, 95% confidence interval (CI): 0.8, 2.8. Comparison B consisted of six observational studies. All reported estimates that did not adjust for sexual behavior and were not statistically significant, with IRRs ranging from 0.6 to 1.3. One also reported that HCT was protective adjusting for sexual behavior (0.6, 95% CI: 0.5, 0.9). Comparison C consisted of two studies reporting two unadjusted estimates for women, one adjusted estimate for women, and one unadjusted estimate for men. All estimates showed that couple HCT was more protective than individual HCT (IRRs: 0.4 to 0.5) with all being statistically significant or nearly so.
Conclusions: In spite of intensive scale-up of HCT in the region, few well-designed studies assess the prevention impacts of HCT. HCT is not consistently protective, although couple HCT is more protective than individual HCT. Strategies enhancing HCT prevention impacts, including couple-based approaches, are urgently needed.

Provider and facility determinants of outcomes

WEPED841

The challenges with management of HIV infection where the law criminalizes MSM: a case study of MSM population in Abuja, Nigeria

I.K. Orazulike[1], J. Adeniyi[2], E. Nnolum[3], B. Ibe[2]
[1]*International Center for Advocacy on Right to Health, Executive Director, Abuja, Nigeria,* [2]*International Center for Advocacy on Rights to Health, Human Rights, FCT, Nigeria,* [3]*International Center for Advocacy on Right to Health, M&E, FCT, Nigeria*
Presenting author email: natcoor.smaan@gmail.com

Background: The 2013 Same sex prohibition Act in Nigeria has severe impact on the HIV response in Nigeria. Prior reports have shown how this law has resulted in significant reduction (73.0%) in access of MSM in Abuja to HIV prevention services at a MSM friendly service outlet in Abuja.
This report highlights the impact of the law on access of MSM to HIV treatment and the implication of this for the health and well-being of MSM in Nigeria.
Methods: The International Centre for Advocacy on Rights to Health - ICARH, documented the medical history of 899 MSM who access HIV services at the clinic between 2011 and 2014. Of these, 359 clients are HIV positive and 129 (35.9%) are on ARV. We specifically reviewed the profile of MSM who access treatment services in the Clinic for year 2014 following the promulgation of the same sex marriage prohibition Act in Nigeria
Results: In 2014, 260 MSM enrolled into ICARH MSM HIV prevention, care and support programmer. Of these 86(33.1%) tested HIV positive of which 84 were placed on first line ARV and two were on placed on second line ARV. One of the two MSM on second line ARV commenced second-line drugs directly as initial treatment, having had a positive drug resistance test. The second MSM on second line ARV was due to default of treatment resulting from fear of violence when he shows up at the clinic for treatment access.
Also, eight other HIV positive MSM in care of ICARH died in 2014 due to their drop out of HIV care due to concerns about violence that could result from public reactions to the promulgated law.
Conclusions: The impact of the promulgated same sex prohibition Act in Nigeria has significant impact on the health and well-being of MSM in Nigeria. The law drives MSM from access to ARV currently largely placed within the previse of public health centers. With low national investment in MSM programmes in Nigeria, the long-term welfare of MSM living with HIV would be a challenge.

WEPED842

Decentralizing HIV care and treatment to primary health centers as a strategy to improve retention on treatment

A. Tiam[1], A. Isavwa[2], A. Thompson[3], M. Letsie[4], M. Foso[5], M. Putsoane[5], M. Mokone[5], O. Akintade[5], I. Oluwatimilehin[5], T. Koppenhaver[6], F. Ndagije[5]
[1]Elizabeth Glaser Pediatric AIDS Foundation, Research and Program Management, Maseru, Lesotho, [2]Elizabeth Glaser Pediatric AIDS Foundation, Strategic Information and Evaluation, Maseru, Lesotho, [3]Elizabeth Glaser Pediatric AIDS Foundation, Medical and Scientific Affairs, Seattle, United States, [4]Ministry of Health, Disease Control, Maseru, Lesotho, [5]Elizabeth Glaser Pediatric AIDS Foundation, Program, Maseru, Lesotho, [6]United States Agency for International Development, SI&E, Pretoria, South Africa
Presenting author email: aptiam@yahoo.com

Background: The use of antiretroviral treatment (ART) has substantially decreased morbidity and mortality in people living with HIV/AIDS. In order to reach patients across countries with high disease burden, task shifting from physicians to nurses and decentralization of HIV treatment services are needed to support growing ART programs. Retention of HIV-positive patients in treatment programs remains central to the success of treatment outcomes. However, there is paucity of data on whether retention was dependent on health facility level (hospitals or lower-volume health centers). In Lesotho, the Elizabeth Glaser Pediatric AIDS Foundation conducted a patient care audit to assess the difference in retention between hospital clinics and primary health centers (HC).
Methods: We carried out a cross-sectional descriptive review of patient clinical cards of patients ever enrolled in HIV care and treatment in Lesotho in the last ten years (2004-2014). We compared patient outcomes between patients attending ART clinics based in hospitals and those attending in HC in Lesotho.
Results: Overall 88,768 clinical cards were reviewed; 49.3% (43,729/88,768) patients enrolled into ART in hospitals and 50.7% (45,039/88,768) in HC. Retention was better in HC than hospitals: 68% (30,626) patients starting ART at HC were still active at the time of the review compared to 59% (25,896) in hospitals (p<0.001) Baseline CD4 availability at enrolment was similar in hospitals and HC, 91% and 88%, respectively; baseline median CD4 was 218 and 180 in hospital and health center respectively. Availability of a recent CD4 was 56% and 80% of patients in health center and hospital respectively for those with CD4 available, most recent median CD4 was 449 for hospitals vs 445 for HC. . Mortality was higher in HC, 11% (5,096/45,039) compared to 7% (3,191/43,729) in hospitals (P<0.001).
Conclusions: Decentralization of HIV treatment to primary HC can improve retention in active care, likely due to easier clinic access in settings closer to the patient. It may be necessary to scale up point-of-care CD4 at HC to improve treatment monitoring. Further research is necessary to identify causes of higher mortality in ART clinics at decentralized HC compared to hospitals in resource-limited settings.

WEPED843

Clinical outcomes of patients in 10 years of national antiretroviral therapy scale up in Lesotho: results from a national patient file audit

A. Tiam[1], F. Ndagije[2], A. Thompson[3], M. Letsie[4], A. Isavwa[5], I. Oluwatimilehin[2], M. Tsoeu[5], M. Khang[5], O. Akintade[2], M. Putsoane[2], M. Foso[2], T. Koppenhaver[6]
[1]Elizabeth Glaser Pediatric AIDS Foundation, Clinical Services, Maseru, Lesotho, [2]Elizabeth Glaser Pediatric Aids Foundation, Program, Maseru, Lesotho, [3]Elizabeth Glaser Pediatric AIDS Foundation, Medical and Scientific Affairs, Seattle, United States, [4]Ministry of Health, Disease Control, Maseru, Lesotho, [5]Elizabeth Glaser Pediatric AIDS Foundation, Strategic Information and Evaluation, Maseru, Lesotho, [6]United States Agency for International Development, SI&E, Pretoria, South Africa
Presenting author email: aptiam@yahoo.com

Background: Lesotho introduced ART in public facilities in 2004 and country has significantly scaled-up the HIV treatment program. By August 2014, nearly 150,000 HIV-positive people initiated ART at 190 clinics. Yet, patient health outcomes have remained somewhat unknown over the years.
Methods: EGPAF conducted a cross-sectional review of patient clinical cards of all patients enrolled in HIV care and treatment in 21 public hospitals and 103 health centers across Lesotho, from August 2013 through August 2014. The aim of was to use cumulative data from the patient care audit to improve program quality and patient outcomes. Age at enrolment, gender, CD4 at various points, drug regimen, treatment failure, clinical outcomes (active on treatment, transferred out, defaulter and loss to follow-up) were extracted. Data were entered into MS Access, cleaned and transferred into Stata 11.0 for analysis to generate frequency and cross tabulation. Chi square test of significance was done.
Results: 114,854 records were reviewed and analyzed: 64% were female; 95% were adults with a mean age at enrolment of 37.5 years; and 5% were children with a mean age at enrolment of 5.6 years. The mean duration on treatment for all patients enrolled on treatment was 3.8 years. Overall, 63% of patients enrolled on ART were still active at the time of the review, 28% were lost to follow-up, and 9% were dead. The overall retention was higher in children (69% compared to adults at 63% (p<0.001)). Of patients enrolled on ART, 86% were still active within one year, declining to 75% for those enrolled for 2 years; 61% for those were enrolled for 5 years and 43% of patients stayed active on ART for 10 years. Baseline CD4 was preformed among 90% of patients.
Conclusions: Lesotho's national ART program achieved good retention at one year which gradually declined over the years. The results of this audit can and should be used as baseline to define clear targets as Lesotho develops strategies to achieve the global call for " 90-90-90" that is 90% of PLHIV know their status, of whom 90% are initiated on treatment and out of whom 90% are virally suppressed.

WEPED844

Evaluation of ART program outcomes: a comparison of public and private ART facilities in Maseru District

A. Isavwa[1], A. Tiam[2], A. Thompson[3], M. Letsie[4], I. Oluwatimilehin[5], M. Makhohlisa[1], M. Mokone[5], O. Akintade[5], M. Foso[5], M. Putsoane[5], M. Tsoeu[1], T. Koppenhaver[5], F. Ndagije[5]
[1]Elizabeth Glaser Pediatric AIDS Foundation, Strategic Information and Evaluation, Maseru, Lesotho, [2]Elizabeth Glaser Pediatric AIDS Foundation, Research and Program Management, Maseru, Lesotho, [3]Elizabeth Glaser Pediatric AIDS Foundation, Medical and Scientific Affairs, Seattle, United States, [4]Ministry of Health, Disease Control, Maseru, Lesotho, [5]Elizabeth Glaser Pediatric Aids Foundation, Program, Maseru, Lesotho
Presenting author email: tisavwa@pedaids.org

Background: A number of evaluations have been conducted on national antiretroviral therapy (ART) programs in Africa to assess clinical outcomes or discern lessons learned, but few have evaluated outcomes in private ART clinics. Private health facilities usually offer services to more privileged populations; they have a smaller population reach and care is generally tailored toward patients' convenience. Many private sector providers pioneered the provision of HIV-related care in developing countries, but they have largely been overlooked in program implementation science. In Lesotho, the Ministry of Health mandated that private care providers should receive free antiretrovirals from the national system, to distribute free ART to their patients. The Elizabeth Glaser Pediatric AIDS Foundation Lesotho Program compared key clinical and program outcomes in private versus public facilities in Maseru district.
Methods: EGPAF-Lesotho carried out a national, cross-sectional review of clinical cards of all patients enrolled in HIV care and treatment in Lesotho over a period of ten years (2004-2014). Clinical and program outcomes from private and public health facilities in Maseru were compared for clinical outcomes including mortality, retention on treatment, and CD4 counts.
Results: Overall, 88,768 patients were enrolled in ART at public facilities compared to 1,895 at private facilities. Retention on ART was better at private than public health facilities: 74% (1,340) patients starting ART were still active at the time of the review vs 64% (56,522) in public health facilities (p<0.001). While baseline median CD4 count was higher in patients seen at public health than private facilities (225 vs 192, respectively), the most recent CD4 was similar at both facility types (411 in public health vs 406 in private facilities). Mortality was higher in public health facilities, 11% (8,287/88,768) compared to 5% (91/1,895) in private facilities (P<0.001).
Conclusions: In high burden countries like Lesotho, innovative strategies to provide free ARV to accredited private sector providers who provide ART to clients at no cost are useful in complementing public ART services. Although patient numbers in private sector facilities were low, the public sector could benefit from an exploration of approaches employed by private facilities to attain better outcomes.

WEPED845

Antiretroviral (ARVs) prescribing outcomes among physicians: a rural-urban comparison in British Columbia (B.C.) Canada in 2013

M. Matsukura[1], H. Kang[1], D. Shopin[1], G. Colley[1], D. Moore[1], R. Hogg[1,2], S. Guillemi[1], R. Barrios[1,3]
[1]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada, [2]Simon Fraser University, Faculty of Health Science, Burnaby, Canada, [3]Vancouver Coastal Health, Vancouver, Canada
Presenting author email: rbarrios@cfenet.ubc.ca

Background: Disparities in HIV care between rural and urban settings, including access to physicians who prescribe ARVs (hereon ARV Physicians), have been recognized globally. The profile and prescribing patterns of ARV Physicians can provide a better understanding of educational and programmatic needs of each geographic area and address the disparities in the care and treatment of HIV-positive patients.
Methods: We analyzed data from the B.C. HIV/AIDS Drug Treatment Program (DTP) collected between January 1, 2013 and December 31, 2013. The DTP is a centralized program that provides access to ARVs free-of-charge to all HIV-positive individuals residing in B.C. We compared characteristics of ARV Physicians in rural and urban areas using Pearson's chi-squared test. Experience in ARV prescribing was defined as have treated more than 6 HIV-positive patients in the past since DTP was initiated in 1996.

Results: In 2013, 894 physicians completed at least one ARV prescription (7.9% of the total general practitioners [GPs] and specialists in B.C.), and among them 749 (83.8%) only completed ARV refill prescriptions but did not initiate or change any ARV regimen, 8 (0.9%) only initiated or changed ARV and 137 (15.3%) performed both initiation/change and refill prescriptions. 93.4% of the ARV Physicians were GPs, 2.8% were infectious disease specialists, 1.9% were internal medicine specialists and 1.9% were other specialists. Physicians prescribed ARVs for a mean of 11.4 and median of 1 (interquartile range=1-3) patients each. There were 105 (11.7%) ARV Physicians practicing in rural areas and 789 (88.3%) in urban areas. In rural areas, significantly fewer ARV Physicians were specialists when compared to urban areas (1.0% vs. 7.4%, p=0.023), and a larger proportion of ARV Physicians only refilled ARVs in rural areas (93.3% vs. 82.5%, p=0.007). Also, a significantly larger proportion of urban ARV Physicians were experienced in HIV care compared to their rural counterparts (30.9% vs. 9.5%, p< 0.001).
Conclusions: A smaller proportion of ARV Physicians in rural areas were experienced in HIV care and fewer of them initiate and/or change medication compared to their urban counterparts. These results suggest the need to support and train GPs in HIV care and treatment, particularly in rural areas.

WEPED846

The roles of implementation leadership and implementation climate in provider attitudes toward HIV prevention EBP in Mexico

G. Aarons[1], E. Torres[1], C. Chavarin[1], D. Mendoza[2], T. Patterson[1]
[1]UC San Diego, Psychiatry, La Jolla, United States, [2]MexFam, Mexico City, Mexico
Presenting author email: gaarons@ucsd.edu

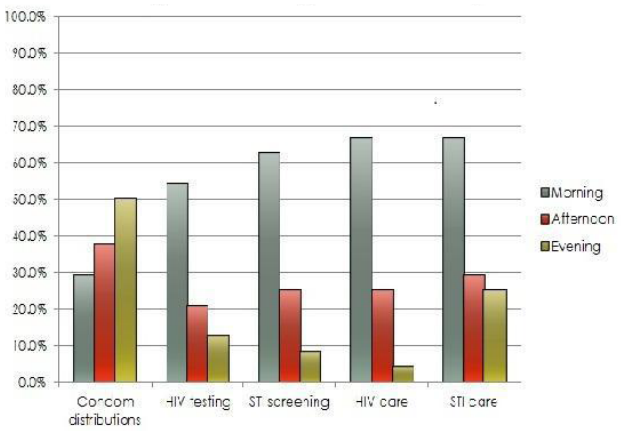
Background: The use of evidence-based practices (EBPs) for HIV prevention and intervention is associated with more favorable patient outcomes. Service provider attitudes toward EBPs is associated with increased use of EBPs in health, mental health, and substance abuse treatment. However, service provider attitudes can be impacted by the organizational context in which they work. Specifically, leadership and organizational climate are associated with provider attitudes to EBP. We examined the extent to which implementation leadership affected HIV prevention worker attitudes to EBP as mediated by implementation climate.
We hypothesized that stronger implementation leadership and implementation climate would be associated with stronger provider attitudes toward EBP and that climate would partially mediate these effects.
Methods: The Mujer Segura HIV prevention study is a Hybrid Type 1 effectiveness/implementation trial taking place in 13 women's reproductive health clinics in eight states in Mexico. Participants were N=59 clinic employees including outreach workers and counselors. Measures included the Implementation Leadership Scale, Implementation Climate Scale, and Evidence-Based Practice Attitude Scale. All measures were completed by clinic employees and data were nested at the clinic level. We utilized Mplus to conduct a multilevel path analyses examining the impact of implementation leadership on implementation climate and their associations with provider attitudes to EBP while controlling for the nested data structure.
Results: Results indicated a significant positive path between implementation leadership and implementation climate (b=0.51; p< .001). The path from implementation climate to attitudes to EBP was also significant (b=0.30; p< .01). The direct path from implementation leadership to provider attitudes to EBP was also significant (b=0.19; p< .05). We conducted a Sobel test for mediation which was significant (s=2.17; p< .05) indicating significant partial mediation.
Conclusions: This is the first test of the new constructs of implementation leadership and implementation climate in an HIV prevention study.
Findings suggest that clinics should consider improving leadership and climate as avenues for improving provider attitudes to EBPs and this is consistent with emerging work in other public health and allied health settings that have shown that provider attitudes predict increased adoption and use of EBPs.

WEPED847

Addressing HIV care in vulnerable populations: barriers and accessibility to care for truck drivers and commercial sex workers in rural Malawi

C. Kachimanga[1], R. Msiska[1], O. Pasulani[2], B. Kalombo[3], I. Musisi[4], S. Njolomole[1], B. Dunbar[1], F. Zuccaro[2], G. Bronson[1], L. Dullie[1], E. Wroe[1]
[1]Partners In Health, Neno, Malawi, [2]Médecins Sans Frontières, Neno, Malawi, [3]Ministry of Health, Neno, Malawi, [4]Partners in Health, Community Health Department, Neno, Malawi
Presenting author email: imusisi@pih.org

Background: HIV disproportionately affects mobile populations in Malawi. While Malawi's HIV prevalence is 11%, prevalence among truck drivers and commercial sex workers is 14% and 70%, respectively.[1] Their mobility can lead to barriers in access to effective health services in an already vulnerable population.
We conducted a needs assessment with truck drivers (TDs) and commercial sex workers (CSWs) utilizing a trading center in rural Malawi, which is centered on a highway connecting to Mozambique, South Africa, Tanzania and Zambia.
Methods: Fifty TDs and twenty-four CSWs were interviewed using semi-structured questionnaires. Data were recorded, cleaned and analyzed using Excel.
Results: The mean age of TDs was 40 years (range: 24-64). Most were married (96%) and of Malawian nationality (84%). The mean age of CSWs was 25 years, all were local residents, and only 25% were married. Over 66% of CSWs were HIV+, and 52% reported work-related travel outside the trading center in the previous 6 months.
Fifty-two percent of TDs accessed care in countries other than Malawi, and only two reported utilizing the local health center. Only 21 (42%) reported receiving an HIV test while on a work trip. Nearly all (95%) of TDs reported they would prefer 24-hour health service availability.
Only 64% of CSWs had an HIV test in the preceding 3 months, 60% reported not using condoms at least once during the previous week, and only 50% sought care after abuse. CSWs also reported that confidentiality concerns would dissuade them from attending a clinic that also targeted their clients. CSWs preferred daytime facilities, although time of day preference varied by service type. (Figure 1)



[Figure1:Time of day at which CSWs prefers to access key services]

Both TDs and CSWs reported substantial barriers to care. CSWs reported condom stock outs, inconvenient time of services, lack of confidentiality, and poor staff support as the most common barriers while TDs most commonly cited lack of time (table 1).

Primary barrier to care	TOTAL
No time, always on road	34 (68%)
Services not convenient times	7 (14%)
TD attitude not seek services	3 (6%)
Unfriendly providers	2 (4%)
Unsure where to access care	2 (4%)
Services not available	2 (4%)

[Table 1: Barriers to Care for Truck drivers]

Conclusions: Mobile populations face significant barriers to HIV care in rural Malawi. This study provides the foundation for designing effective and accessible services to prevent and treat HIV among this vulnerable population.

Strategies to increase adherence

WEPED848

Examining the impact of a health-equity-oriented approach on treatment adherence in an integrated HIV care facility in Vancouver, Canada

S. Parashar[1], Z. Cui[2], N. Oliveira[1], B. Pauly[3], C. Worthington[3], S. Kirkland[4], K. Salters[1,5], S. Fernando[1], S. Guillemi[1], P. McDougall[6], R. Baltzer-Turje[6], R. Barrios[1], B. Hogg[1,5]
[1]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada, [2]BC - Centre for Excellence in HIV/AIDS, Vancouver, Canada, [3]University of Victoria, Victoria, Canada, [4]Dalhousie University, Halifax, Canada, [5]Simon Fraser University, Burnaby, Canada, [6]Dr. Peter AIDS Foundation, Vancouver, Canada
Presenting author email: sparashar@cfenet.ubc.ca

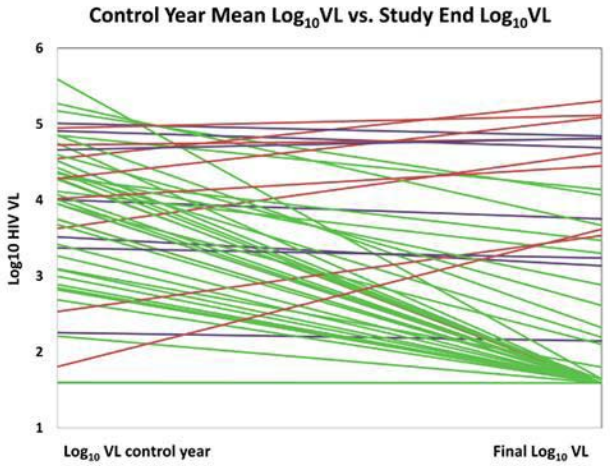
Background: The Dr. Peter Centre (DPC) is a low-threshold care facility for People Living with HIV in Vancouver, Canada who experience concurrent barriers to achieving optimal therapeutic outcomes. There is no documented evidence of the impact of the DPC's health-equity approach on the health outcomes of clients. Here we report on the relationship with adherence to antiretroviral treatment (ART).
Methods: A longitudinal cohort of recently enrolled DPC clients provides the data frame for this analysis. Socio-demographic, relevant social determinants of health, and health and social service utilization data are ascertained through an interviewer-administered survey. Clinical variables are obtained through longitudinal linkages with the provincial Drug Treatment Program. The survey adapts a set of eight health-equity indicators (HEI) designed to measure clients' perception of the DPC based on a Likert response scale, which were then trichotomized as positive (always/most of the time), neutral (sometimes) and negative (not usually/never). Univariate analyses were conducted to measure the association between optimal ART adherence (≥95%) in the 12 months prior to interview date and salient explanatory variables, including positive responses to the HEI.
Results: This analysis is based on the 74 out of 99 participants who completed the baseline interview between February 2012 and December 2014, and for whom we have an up-to-date clinical linkage. Median age was 46.5 (IQR 41-51), 18.9% were female, 31.1% identified as Aboriginal and 45.9% were optimally adherent to ART. The three HEI that were most frequently ranked positively were feeling: welcomed by staff (95.9%), respected by staff (95.9%), and cared for by staff (89.2%).
In univariate analyses, only higher income was associated with optimal adherence (p=0.031). None of the HEI attained statistical significance.
Conclusions: As organizations adapt an equity-oriented approach to ameliorate health inequities, researchers are tasked with developing tools to measure their efficacy. The HEI fell short in explaining the disparity in ART adherence, potentially a reflection of the adherence measure being taken during a time period when the client was not engaged in DPC services. More in-depth consultation with clients is underway to refine the indicators and isolate the impact of a health-equity oriented approach to care.

WEPED849

mHealth to improve health: effectiveness of a weekly text messaging intervention to improve ART adherence and HIV viral load in a Canadian context: WelTel OAKTREE

M.C.M. Murray[1,2,3], K. Friesen[2], O. Sara[2], A. Albert[3], E.J. Maan[2], N. Pick[2,3,4], A. Alimenti[2,5], M. Kestler[1,2], K. Smillie[6], D. Money[2,3,7], R. Lester[1], WelTel OAKTREE Study Team
[1]University of British Columbia, Medicine, Division of Infectious Diseases, Vancouver, Canada, [2]Oak Tree Clinic, British Columbia Women's Hospital, Vancouver, Canada, [3]Women's Health Research Institute, Vancouver, Canada, [4]University of British Columbia, Medicine, Vancouver, Canada, [5]University of British Columbia, Department of Pediatrics, Vancouver, Canada, [6]British Columbia Centre for Disease Control, Vancouver, Canada, [7]University of British Columbia, Department of Obstetrics and Gynecology, Vancouver, Canada
Presenting author email: melanie.murray@cw.bc.ca

Background: Antiretroviral therapy (ART) improves health and survival of HIV-positive individuals. However, engagement in care and medication adherence are essential to prevent resistance, morbidity and mortality. In a randomized control trial in Kenya, WelTelKenya1, a weekly mHealth (mobile phone technology for health care) intervention improved ART adherence and HIV viral load (VL) suppression.
We conducted a repeated measures study of weekly interactive text-messaging intervention effectiveness using the WelTel model with 85 participants on ART in Canada.
Methods: Between April 2013 and May 2014, 85 participants were recruited from the Oak Tree Clinic in Vancouver, Canada. Inclusion criteria included age ≥14 years old, qualify for ART, detectable HIV VL (>200 copies/mL), and "vulnerable" (i.e. ≥1 of: unstable housing, active addiction, domestic violence, poor care engagement or adherence, advanced HIV infection/AIDS, or mental health factors). Participants who did not have a cell phone were given one with unlimited texting capability. Participants received a weekly interactive SMS/text message check-in on their health status for one year. A clinic nurse triaged responses. Demographic and clinical data were collected for pre-intervention and intervention years. Adherence data was obtained from pharmacy refill records and patient report. Repeated measures mixed-effects linear regression was used to take into account repeated measures on the same subject from pre-study to intervention years.
Linear regression was used for CD4 count and VL (log_{10} transformed), while logistic regression was used for ART adherence and appointment attendance.
Results: Preliminary analysis of the first 62 individuals to reach study completion are included here. Demographics included median age 39 years (range 15-60), 90.3% female, 3.2% trans-gendered, 6.5% male. Participant ethnicity was 37% Caucasian, 34% Aboriginal, 21% Black and 8% South Asian. Mean ART adherence improved from 61.7% to 68.3% (p< 0.00001), and mean population HIV log_{10}VL declined by 0.36 log (p=0.0002) from the pre-intervention to intervention year. 28/62 individuals had HIV VL < 50 at study end (Figure). Mean CD4 count and appointment attendance did not change.



[Figure: HIV Viral Load Change]

Conclusions: Preliminary results suggest the WelTel intervention is an effective tool for reducing HIV VLs and improving ART adherence in poorly engaged, vulnerable Canadian HIV+ populations.

WEPED850

A text message (SMS) based active defaulter tracing system in Lesotho, a high HIV prevalence country

B. Hwang[1], A. Shroufi[2], M. Motsami[3], H. Duvuvier[3]
[1]Medecins Sans Frontieres, Johannesburg, South Africa, [2]Medecins Sans Frontieres, Cape Town, South Africa, [3]Medecins Sans Frontieres, Roma, Lesotho
Presenting author email: msfocb-capetown-deputymed@brussels.msf.org

Background: For ART programs in Southern Africa patient retention is a persistent challenge. In Lesotho where MSF provides HIV and TB support, we observe retention of around 80% at 12 months. Defaulter tracing in Lesotho utilizes home visits by Village Health Workers (VHWs), preferred over direct patient contact. Mobile networks cover only 59% of geographical locations, with patient phone ownership at 62.9% and 62.3% of those able to receive calls inside their home. Defaulter tracing occurs sporadically and outcomes are hard to establish. In an effort to strengthen this system, MSF piloted a text messaging (SMS) based active defaulter tracing system in 3 clinics over a 5 month period.
Methods: Missed appointments were identified using appointment books (by ≥ 1 week for ART patients or 1 day for PMTCT patients) leading to a coded SMS being sent to the responsible VHW, who were provided with phones ($14USD). VHWs are prompted to carry out tracing and return a code corresponding to the outcome within one week. Where patients promise to return to care, facilities verify whether this occurs. Facility referrals and VHW responses are logged on a SMS messaging database (Telerivet) and reviewed by managers.
Results: Between 1 July to 30 November 2014, 235 SMS referrals were sent to fifteen VHWs. VHWs completed tracing activities in 74% of cases (174/235). For all those who a tracing attempt was made 36% (72/174) were referred back to the facility; with 86% (62/72) confirmed to have arrived within two weeks. Of the other patients traced, 7% (13/174) refused to return; 3% (5/174) died; 1% (2/174) moved; 3% (6/174) transferred; 1% (2/174) referred to another VHW; 3% (6/174) not locatable; 27% (47/174) already arrived to clinic prior to tracing; and 12% (21/174) had other outcomes.
Conclusions: Under this system over a third of defaulters were confirmed as having returned to clinics. Implemented at scale this low resource intervention has great potential to reduce loss to follow up. Additionally, activity of VHWs can be closely monitored, aiding in performance management. Outcomes of activity are also easily available, increasing understanding of the reasons for default and aiding efforts to address this.

WEPED851

Dose-response relationship between methadone dose and adherence to antiretroviral therapy among HIV-positive persons who use illicit drugs

L. Lappalainen[1,2], S. Nolan[1,3], S. Dobrer[1], C. Pucas[1,4], J. Montaner[1,3], K. Ahamad[1,2], H. Dong[1], T. Kerr[1,3], E. Wood[1,3], M.J. Milloy[1,3]
[1]British Columbia Centre for Excellence in HIV/AIDS, Vancouver, Canada, [2]University of British Columbia, Department of Family Medicine, Vancouver, Canada, [3]University of British Columbia, Department of Medicine, Vancouver, Canada, [4]Faculty of Health Sciences, Simon Fraser University, Burnaby, Canada
Presenting author email: leslie.lappalainen@medportal.ca

Background: For HIV-positive individuals who use illicit drugs, engagement in methadone maintenance therapy (MMT) can contribute to improved HIV treatment outcomes. However to our knowledge, the role of methadone dosing on adherence to antiretroviral therapy (ART) has not been investigated. We sought to examine the relationship between methadone dose and ART adherence among a cohort of persons who use illicit drugs.
Methods: We used data from the ACCESS study, an ongoing prospective cohort of HIV-positive persons who use illicit drugs, which we confidentially linked to comprehensive HIV treatment data. Using generalized estimating equations (GEE) we evaluated the longitudinal relationship between methadone dose (≥ 100 vs < 100 mg/day) and the likelihood of ≥ 95% adherence to ART among ART-exposed participants during periods of engagement in MMT.
Results: Between December 2005 and May 2013, we recruited 297 individuals on MMT who were followed for a median of 42.1 months. In adjusted GEE analyses, MMT dose ≥ 100 mg/day was independently associated with optimal adherence to ART (adjusted odds ratio [AOR] = 1.38; 95% confidence interval [CI]: 1.08 - 1.77, p = 0.010). In a sub-analysis, we observed a dose-response relationship between increasing MMT dose and ART adherence (AOR = 1.06 per 20 mg/day increase, 95% CI: 1.00 - 1.12, p = 0.041).
Conclusions: Our results demonstrate a dose-response relationship between increasing MMT dose and improved adherence to ART. These findings underscore the need to optimize methadone access and dosing practices for illicit opioid use in an effort to enhance ART adherence and improve HIV outcomes.

WEPED852

Using ART experienced patients to tackle the challenges of attrition from ART in the resource constrained setting. A before-after retrospective cohort study in 10 randomly selected health facilities in Ethiopia

A. Teklu[1], K.D. Yirdaw[2]
[1]MERQ Consultancy PLC, Addis Ababa, Ethiopia, [2]ICAP, Addis Ababa, Ethiopia
Presenting author email: ateklu72@gmail.com

Background: Retention has been declining among patients on ART in Ethiopia in the last 5 years from 82% to 70%. Use of ART experienced and trained PLHIV to prepare and re-engage patients is recommended, and many countries including Ethiopia have started the program, but its effectiveness has not been adequately assessed. In this study, we evaluated the effectiveness of use of ART experienced patients in preventing attrition and re-engaging those who are lost to follow up.
Methods: A retrospective cohort study with random selection of 10 facilities as clusters was done to compare key outcome measures before and after the initiation of the adherence supporters program. Survival analysis was used to examine time to 1st lost, and time to restart after being lost to follow-up.
Results: 18,835 records were originally available out of which records with missing values were excluded (4.36%) leaving 17,897 records for analysis. Observation period ranged from 1 day to 6.1 years (median follow up time was 1.25 years). The incidence of first instance of lost to follow-up was 22.2 per 100 person-years (21.7-22.7). The risk of being lost to follow up was high after initiation of the program (HR -1.22, log rank p-value: 0.000), this may be explained partly by the fact that all patients who are lost to follow up are identified immediately by the adherence supporters. The incidence of restarting after being lost to follow up was 23 per 100 PY (95% CI 22.2-24.1 per 100 PY). The chance of restarting after being lost to follow-up was four times higher during the period adherence supporters were present (log rank p-value: 0.0000). Patients who stayed longer in care before being lost to follow-up were more likely to restart treatment than those who were lost sooner after ART initiation (5.66 times higher chance of restarting comparing time at first lost at 12 months to at < 3 months, log rank p-value: 0.0000). Time to restarting treatment was also shorter (median 37 vs 115 days).
Conclusions: Adherence supporters were effective in improving re-engagement after pateints were lost to follow up, but preventing lost follow-up remains a challenge.

WEPED853

Short-term comprehensive case management support can contribute to long-term ARV adherence for complex clients

J. Pringle, M. Compton, T. Shannon
Vancouver Coastal Health, Vancouver, Canada
Presenting author email: miranda.compton@vch.ac

Background: In Vancouver, BC, a multi-disciplinary clinical Case Management (CM) team was implemented as a key component of a region-wide Treatment as Prevention (TasP) initiative. The CM team consists of Nurses, Social Workers, Outreach Workers, Peers, and Housing Workers, and engages in outreach-based support to assist individuals who face multiple barriers to antiretroviral (ARV) adherence. The CM team works with clients to develop and execute a care plan to strengthen connections to primary care, mental health and addiction services, stabilized income and housing, and psycho-social supports. Discharged clients are either transitioned to less intensive programs, or assessed as capable of meeting healthcare needs independently.
Methods: Between November 2010 and September 2014, 481 clients were discharged from the clinical case management team. A chart audit was conducted of a random sample of 135 clients who had been discharged for a period of >6 months. Plasma Viral Load (pVL) data was examined to determine whether discharged clients had successfully achieved viral suppression (pVL≤200), suggesting improved ARV adherence.
Results: Clients within the sample ranged in age from 24-65 years, with a median age of 46. The median period of time the clients were supported by the CM team was 193 days. At intake, 67% (n=90) of clients were linked to a primary care provider and at discharge, 99% (n=133) of the clients were linked. At intake 39% (n=53) of the clients had pVL ≤200, and at discharge 67% (n=91) of clients had pVL ≤200. In the sample of clients at least 6 months post-discharge, 80% (n=108) of clients had a pVL ≤200 at most recent measure.
Conclusions: Results suggest that providing complex clients with comprehensive community-based outreach support that addresses housing, income and psycho-social supports, along with strengthening engagement with primary care, is an effective intervention toward achieving long-term health stabilization. In the months following discharge the clients continued to show an improved trajectory, as the number of clients with suppressed viral load continued to increase. An assessment of on-going needs of clients who did not achieve suppressed pVL post discharge is needed to develop interventions to meet the needs of this group.

WEPED854

The value of strategies to address attrition from care within an HIV treatment program in East Africa

J. Kessler[1], L. Li[1], G. Bakoyannis[2], K. Nucifora[1], C. Yiannoutsos[2], S. Braithwaite[1]
[1]NYU School of Medicine, Population Health, New York, United States, [2]Indiana University School of Public Health, Indiannapolis, United States
Presenting author email: jason.kessler@nyumc.org

Background: Attrition from HIV care and treatment threatens gains achieved as a result of the scale-up of antiretroviral therapy (ART) across Africa. Attrition rates vary substantially between settings. Since many patients who are lost are, in fact, dead, retention programs may be an inefficient use of scarce resources. We sought to establish the rate of attrition within a HIV treatment program in East Africa and to ascertain the value and cost-effectiveness of the implementation of a retention program within it.
Methods: We used a micro-simulation HIV model in order to account for attrition dynamics. Attrition event rates from an East African treatment program (Academic Model for Prevention and Treatment of HIV [AMPATH]) were assessed and utilized. We analyzed the health impact and value of enhancing retention in care directed activities within this setting. We compared this to simulation derived estimates of expansion of ART services to all patients in care with a CD4 count ≤500 cells/mm^3 as a measure of the potential health benefits forgone (e.g., opportunity cost) that could be gained by applying resources to other resource-constrained decisions. The analysis was considered from a payer perspective using a lifetime horizon.
Results: The impact of retention focused interventions is seen in the table. An outreach program that seeks re-link those patients who do not return for routine follow up care is associated with an incremental cost effectiveness ratio (ICER) of $1800/QALY. A strategy consisting of a retention and adherence program in addition to an outreach effort is associated with an ICER of $7800/QALY. In comparison expanding ART access to all HIV + persons with a CD4 ≤ 500 cells/mm^3 yields an ICER of $900. The value of retention programs was strongly influenced by costs of second-line ART and cost of the interventions.

	Life Years	QALYs	Cost	ICER
No intervention	19.1	10.6	$10,420	---
ART <=500 cells	19.8	11.0	$10,780	$900
Outreach	20.8	11.3	$11,710	$1,800
Reduce attrition + Outreach	26.6	13.5	$33,130	$7,800

[Impact of retention focused interventions]

Conclusions: In a setting where HIV infected persons present to care with advanced disease retention programs may have a greater health benefit than expanding treatment access, though this may not provide these health gains in a more cost - efficient manner. Further research is needed to assess the factors associated with retention focused strategies that can maximize population health.

WEPED855

Access to stable housing and adherence support services improve antiretroviral adherence among HIV and hepatitis C co-infected individuals in British Columbia

C. Puskas[1,2], K. Salters[2], S. Parashar[2], A. Cescon[2,3], Z. Cui[2], J. Zhu[2], A. Kaida[1], C. Miller[1], R. Hogg[1,2]
[1]Simon Fraser University, Faculty of Health Sciences, Burnaby, Canada, [2]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada, [3]Northern Ontario School of Medicine, Sudbury, Canada
Presenting author email: cathyp@sfu.ca

Background: Hepatitis C virus (HCV) is both a risk factor for and common comorbidity associated with HIV. Individuals with HIV/HCV co-infection face serious health challenges including risk of end-stage liver disease. The purpose of this study was to compare socio-demographic and clinical characteristics between HIV/HCV co-infected and HIV mono-infected individuals and to determine covariates of optimal ART adherence among co-infected individuals enrolled in a large cohort of HIV-positive individuals in British Columbia, Canada.
Methods: The study utilizes survey data from the Longitudinal Investigations into Supportive and Ancillary Health Services (LISA) study collected between 2007 and 2010 across British Columbia. This cross-sectional data is linked with longitudinal clinical data through the provincial Drug Treatment Plan (DTP). HCV co-infection status was obtained through self-report. Optimal ART adherence was defined as ≥95% based on pharmacy refill compliance. Multivariable logistic regression models compared optimal adherence between HIV/HCV co-infected and HIV mono-infected individuals, as well as independent covariates of optimal ART adherence among co-infected individuals.
Results: Of 912 included participants (28.2% women), 536 (58.8%) were HIV/HCV co-infected. In adjusted multivariable analysis, co-infected individuals were significantly more likely to have a history of IDU (adjusted odds ratio [AOR]: 20.8; 95% confidence interval [CI]: 11.2 to 38.5) and incarceration (AOR: 2.52; 95% CI: 1.41 to 4.51), and less likely to be optimally adherent (AOR: 0.53; 95% CI: 0.28 to 0.99). Optimal adherence among HIV/HCV co-infected participants was associated with stable housing (AOR: 1.86; 95% CI: 1.14 to 3.05) and accessing an adherence support program (AOR: 4.76; 95% CI: 2.62 to 8.57).
Conclusions: HIV/HCV co-infected individuals exhibit significantly lower ART adherence than HIV mono-infected individuals, however, stable housing and adherence support services were associated with improved adherence within this demographic. The findings highlight the importance of integrating adherence support and social services, such as housing outreach, with ART treatment programs for HIV/HCV co-infected individuals.

Socio-economic challenges in implementing treatment as prevention strategies

WEPED856

Socio-economic and clinical factors associated with late initiation of antiretroviral therapy: preliminary results from the ENGAGE cohort study

S. Kesselring[1], S. Parashar[1], A. Kaida[2], Z. Cui[1], N. Oliveira[1], G. Colley[1], C. Osborne[1], H. Samji[1], M. Kestler[3], R. Baltzer-Turje[4], L. McCandless[2], D. Nash[5], D. Moore[1], R. Hogg[1]
[1]BC Centre for Excellence in HIV/AIDS, Epidemiology and Population Health, Vancouver, Canada, [2]Simon Fraser University, Burnaby, Canada, [3]Oak Tree Clinic, Vancouver, Canada, [4]Dr. Peter AIDS Foundation, Vancouver, Canada, [5]Hunter College, New York City, United States
Presenting author email: skesselring@cfenet.ubc.ca

Background: The purpose of ENGAGE is to identify socio-economic factors associated with late initiation of antiretroviral therapy (ART) among people living with HIV in the province of British Columbia (BC), Canada. Results will inform practices to improve linkage to care in a province where ART is provided free of charge.
Methods: People living with HIV and newly initiating ART (within the previous 6 months) were enrolled in ENGAGE, a prospective cohort study nested within the provincial Drug Treatment Program (DTP). Participants complete a 1-hour structured survey collecting demographics, ART attitudes and adherence behaviours, and use of healthcare and support services. CD4 cell count and plasma viral load were obtained via linkage to the DTP. The primary outcome, 'late initiation of ART', was defined as CD4 cell count < 500 cells/μL at time of initiation. Bivariate analyses (Wilcoxon rank-sum and Fisher's exact test) were used to test the association between late initiation and socio-economic characteristics.
Results: Since December, 2013, 55 participants were enrolled in ENGAGE, representing 14% of the 380 eligible individuals. Enrollees were 15% female, median age of 40 years [IQR: 29-45], 27% reported Aboriginal ancestry, and had a median annual personal income of 13,332 CAD [IQR: 7,800-27,600]. In addition, 24% reported ever being incarcerated and 25% a history of injection drug use. The median CD4 cell count at time of ART initiation was 500 cells/μL [IQR: 310-640]. Overall, 55% of our participants were late ART initiators. In contrast, for all eligible individuals the median CD4 cell count at initiation was 410 cells/μL [IQR: 225-595], median age 40 [IQR: 31-50] and 16% were female.
Higher personal income was the only variable found to be negatively associated with late initiation (Odds ratio [OR] = 0.62, 95% Confidence Interval [CI] 0.40-0.98) per thousand-dollar increase). Female gender was marginally associated with late initiation (0R: 7.30, 95% CI 0.83-62.50) with a greater proportion of women (88%) initiating late than men (49%).
Conclusions: In this analysis, over half of the individuals initiated ART late, with disparities observed by income level. Continued efforts are needed to engage individuals in care earlier in order to fully benefit from high-quality HIV care.

WEPED857

Stigma fears undermine the scale up of HIV care and prevention in North West Province, South Africa

S. Treves-Kagan[1], W. Steward[1], L. Ntswane[2], R. Haller[1], J. Gilvydis[3], H. Gulati[3], S. Barnhart[3], S.A. Lippman[1]
[1]University of California, Center for AIDS Prevention Studies, San Francisco, United States, [2]University of Washington, International Training and Education Center for Health (ITECH) - South Africa, Pretoria, South Africa, [3]University of Washington, International Training and Education Center for Health (ITECH), Department of Global Health, Seattle, United States
Presenting author email: sarah.treves-kagan@ucsf.edu

Background: Stigma is a known barrier to HIV testing and care. Because widespread availability of antiretroviral therapy reduces mortality, some scholars have posited that HIV-related stigma could also be reduced. This view, however, focuses on overt acts of discrimination (enacted stigma). Individual beliefs about the existence of prejudice (felt stigma) may continue to drive behavior. As part of a "situational analysis" to inform a combination HIV prevention program in high prevalence communities, we examined the impact of stigma on the uptake of services.
Methods: We conducted semi-structured interviews and focus groups with 677 individuals in four low-resource subdistrict districts in North West Province, South Africa, between April 2012 and September 2013. We subsequently coded all fieldwork notes; we also conducted a more in-depth transcription and coding of 31 recorded interviews. Using a grounded theory approach, we developed codes based on themes that emerged in the data. Stigma-related codes were subsequently categorized according to manifestation (enacted stigma, felt stigma). We then examined how people sought to manage stigma and the impact it had on accessing care.
Results: Findings suggested that stigma remains a barrier to care. Although participants reported less hostility toward people living with HIV, they also felt that HIV remains highly as-

sociated with promiscuity and infidelity. Participants described community members taking steps to avoid being identified as infected, including avoiding healthcare facilities entirely, using traditional healers, or paying for private doctors. Such behaviors led to delays in testing and accessing care, and problems adhering to medications, especially for men and youth who worried that there was no other health condition that could plausibly account for their utilization of medical services.

Conclusions: Despite significantly increased availability of treatment and care, stigma continues to pose a formidable barrier. Providing access to ART alone will not end HIV-related stigma. Individuals are hesitant to seek care and support as long as they fear that doing so will lead to unintended disclosure and prejudice and discrimination. It is critical to combat this trend by increasing cultural acceptance of being seropositive, integrating HIV care into general primary care and normalizing men and youths' utilization of health care.

WEPED858

Sociodemographic barriers affecting adherence to HAART among elderly patients at a tertiary care centre in India

A. Basavaraj[1], D. Kadam[1], H. Dalal[1], A. Chandanwale[1], A. Gupta[2], A. Belluca[2], N. Gupte[3], V. Mave[3], R. Suman[1], R. Bollinger[2]
[1]B.J Medical College and Sassoon Hospital Pune, Medicine, Pune, India, [2]John Hopkins University, Medicine, Baltimore, United States, [3]BJMC CTU, Medicine, Pune, India
Presenting author email: anita.basavaraj@rediffmail.com

Background: Adherence to ART in geriatrics is affected by factors which are novel to this age group. The lost to follow up rates are very high. The impact of co-existing morbidities, the effect of toxic drugs on failing organ systems and dependency of this population to obtain medicines makes the management of HIV in this group complex. This study was done to estimate the sociodemographic barriers to HIV care among elderly patients (>55 years) at a Tertiary care centre in Pune, India.
Methods: Elderly patients (>55 years) on regular ART for more than a year (N-100) were selected from those attending OPD at BJMC, Pune. A 28 question questionnaire was administered and ART records were analysed subsequently conclusions were drawn.
Results: Study questionnaire was divided into two parts: A self assessment of drug adherence and common perceived barriers to adherence. Patients were divided into strictly adherent (<2 doses missed a month), adherent (<2 missed days) and poorly adherent (>2 missed days). Of all participants,58 patients were on non-ART medications due to associated comorbid conditions with 25 patients currently on AKT for pulmonary or extra pulmonary TB.
Barriers to adherence were assessed under the headings of perception of HIV disease and treatment, self efficacy of treatment and follow up, adverse effects and social barriers to treatment adherence.
Among the poorly adherent group, major barriers recognized were confusion due to multiple drugs (91.67%), associated co-morbidities(83.3%),inability to manage self medication (75%), dependence on caretaker for follow up(91.67%), presence of ADR's to ART drugs (100%) and widowhood (100%).
Factors associated with good adherence were adequate information about drugs (87.88%), positive perception of disease outcomes(83.33%), less fear of ADRs (81.6%) and lesser travel time to obtain medication (88.9%).
Conclusions: Lost to follow up rates among geriatric HIV patients are high. Certain factors which resulted in poor adherence among patients were lack of adequate adherence counselling, requirement of multiple drugs, presence of comorbid conditions, fear of adverse effects and lack of social support structure, especially in case of widows. Modification of these factors could lead to improved adherence to ART in this population.

Implementation of PMTCT Option B+ in various contexts

WEPED859

Six- and 12-month loss to follow-up among early implementation of Option B+: a systematic review

A.S. Rustagi[1], C. Henley[2], B. Wagenaar[2,3], J. Pfeiffer[1], K. Sherr[1,2]
[1]University of Washington, Department of Global Health, Seattle, United States, [2]Health Alliance International, Seattle, United States, [3]University of Washington, Department of Epidemiology, Seattle, United States
Presenting author email: catieh13@uw.edu

Background: Universal, lifelong provision of antiretroviral therapy (ART) for pregnant or breastfeeding HIV-positive women (Option B+) was adopted by the World Health Organization in 2013. Since then, 16 of the 22 Global Plan priority countries have endorsed Option B+ and moved towards implementation. However, uptake, retention, and clinical outcomes under Options B+ are not yet well understood. Women who feel healthy at the time of ART initiation may be more likely to be lost to follow-up (LTFU) than symptomatic women. We sought to review published literature reporting LTFU among pregnant or breastfeeding women at 6 and 12 months after initiating Option B+.
Methods: We searched Pubmed, African Index Medicus, and relevant citations using the terms "Option B+" and "universal antiretroviral therapy for HIV-infected pregnant and breastfeeding women." Studies reporting loss to follow-up among women at 6 and/or 12 months after initiation of Option B+ were included. Heterogeneity in data sources, methods of ascertaining loss to follow-up, and follow-up time precluded statistical pooling of results.
Results: Of 99 citations that met our search terms, 9 were eligible for study inclusion. Upon further review, one study was later excluded as inclusion was conditional on study retention through the breastfeeding period. Of the 8 studies included, 7 reported LTFU under Option B+. LTFU at 6 months ranged from 8-22%. LTFU at 12 months ranged from 6-23%.

Author, Year, Country	Setting	Study Population	Study Period	Study Design	Data source	n	6 mo LTFU	12 mo LTFU	Other
CDC, 2013, Malawi	all public clinics in Malawi	All women initiating OB+ in third quarter 2011 (1st quarter of implementation)	July 2011 - Sept 2012	Retrospective cohort	Registries	2,949	-	23%	-
Kieffer, 2014, Uganda	EGPAF-supported health facilities	Women accessing OB+ services	March 2013 - March 2014	Retrospective cohort	Aggregated service delivery data	9,805	12%	-	-
Kieffer, 2014, DRC and Cameroon	EGPAF-supported health facilities	Women accessing OB+ services	2013 - March 2014	Retrospective cohort	Aggregated service delivery data	1,314 (DRC); 6,657 (Cameroon)	22% (DRC)	-	89% at 90 days (Cameroon)
Kieffer, 2014, Malawi	EGPAF-supported health facilities	Women accessing OB+ services	August 2011 - March 2014	Retrospective cohort	Aggregated service delivery data	5,837	-	-	71% at 24 mo
Koole, 2014, Malawi	All public ART clinics within one district (Karonga)	All ART patients; sub-group included all women initiating OB+	2005 - 2012	Retrospective cohort	Clinic registries	586	15% (12-18%)	-	-
Price, 2014, Malawi	Karonga district	All recently postpartum women residing in DSS survey area	July 2011 - January 2013	Retrospective cohort	Interview & clinic record review	395	-	-	19% LTFU at interview
Tenthani, 2014, Malawi	all public clinics in Malawi	Women initiating OB+	October 2011 - March 2012	Retrospective cohort	MoH routine data	21,939	17.1%	-	-
Tweya, 2014, Malawi	Largest ANC clinic in Lilongwe, Malawi	Women initiating OB+; those LTFU were interviewed to ascertain the cause	2011 - 2013	Prospective cohort	Clinic registries	2,353	-	-	20% missed 1 clinic visit by >3 weeks
van Lettow, 2014, Malawi	All PMTCT/ART facilities in 6 districts	Women initiating OB+	Feb - June 2013	Cross-sectional	Aggregated clinic registry & health facility survey data	141 health facilities	Range 8-21%	Range 6-23%	-

[WEPED859 Table 1. 6- and 12-month Option B+ LTFU Rates]

Conclusions: Preliminary experiences delivering Option B+ indicate that loss to follow-up can be substantial, though some facilities are able to achieve high retention rates. Future research to define the characteristics of these high performing health facilities could be applied to maximize retention of women initiating Option B+. Gaining a better understanding of why some women remain in treatment while others are lost to follow-up will also be important to identify women who might benefit the most from efforts to reduce LTFU.

WEPED860

Option B+ in Mozambique: challenges to retention in care

J. Pfeiffer[1], M. Napua[2], R. Chapman[3], C. Henley[1], R. Hoek[4]
[1]University of Washington, Global Health, Seattle, United States, [2]Beira Operations Research Center, Ministry of Health, Beira, Mozambique, Mozambique, [3]University of Washington, Anthropology, Seattle, United States, [4]Health Alliance International, CIOB, Beira, Mozambique
Presenting author email: catieh13@uw.edu

Background: The objective of this implementation science intervention study was to develop and test a pilot intervention in six large public clinics in central Mozambique to improve implementation of new 2013 WHO "Option B+" guidelines that seek to start antiretroviral treatment (ART) among pregnant women at time of diagnosis. The "B+" approach was initiated by the Ministry of Health in selected sites in July 2013. Data from the 6 sites in this study indicate substantial loss-to-follow-up (LTFU) in the first 3 months after ART initiation. Major streamlining of links among ANC, PMTCT, and ART services is required. Results from the formative research from this study are described here. The intervention is currently being implemented in the six sites using a stepped wedge design.
Methods: The study includes a formative research, intervention design, and implementation phase. This formative research was initiated in early 2013 completed in early 2014 in each of the six study clinics and consisted of:
1) patient flow mapping,
2) collection of health systems data from ANC registries, pharmacy registries, and ART clinic databases, and staffing levels, patient waiting times, and patient flow data, and
3) patient and health worker individual interviews and focus groups.
Results: Performance at the six sites ranged from 1% to 79% of newly diagnosed HIV-positive women starting ART within 14 days of diagnosis. Only about 50% (ranging from 27% to 70% at the six sites) managed to return for their first scheduled 30-day medication refill visit. There was little training, minimal workflow modification, and few new job aids to orient health facilities to the B+ roll-out. These data revealed major systemic bottlenecks that contributed to poor adherence and retention in the first month after ART initiation. Long wait times, short consultations, and poor counseling were identified as barriers.
Conclusions: Formative research findings indicate that improved retention requires:
1) workflow modification to redefine nurse tasks, shift tasks to community health workers, and enhance patient tracking; and
2) an adherence and retention package to systematize active patient follow-up, ensure home visits by community health workers, employ text messaging, and intensify counseling by health staff.

WEPED861

Patient preferences for antiretroviral treatment during pregnancy under Option B+ in Zambezia, Mozambique

S. Brusamento[1], A. Palma[2], F. Tsiouris[3], L. Ahoua[1], M. Rabkin[3], M.E. Kruk[2]
[1]ICAP at Columbia University, Maputo, Mozambique, [2]Columbia University, Mailman School of Public Health, NY, United States, [3]ICAP at Columbia University, NY, United States
Presenting author email: serenabrusamento@columbia.org.mz

Background: Option B+, lifelong antiretroviral therapy (ART) for all HIV-infected pregnant women (PW), was implemented in Mozambique in 2013, to accelerate reductions of HIV vertical transmission. However, loss to follow up of PW enrolled in Option B+ is a challenge, and the optimal approach for B+ implementation is unknown.
We conducted a survey to identify factors associated with disclosure and reluctance to start ART on the day of HIV diagnosis.
Methods: We interviewed a random sample of HIV-infected women enrolled in HIV care in Mozambique's Zambezia Province about demographics, HIV knowledge, stigma, and preferences for HIV care. We assessed factors associated with disclosure of HIV status and preferences for timing of ART initiation. Results were compared using chi-square and t-tests, and regression analysis was used to assess factors associated with preference for timing of ART initiation.
Results: 1,020 women participated in the survey; mean age was 25.3y; 48.9% were pregnant and 85.7% were on ART. Over 80% reported that they had disclosed their HIV status to their partner or family member. Women who disclosed were more frequent non-PW vs. PW (91.1% vs. 73.9%, p< 0.001), literate (71.9% vs. 59.7%, p< 0.001) and older (mean: 25.5y vs. 24.6y, p< 0.05). In addition, the partners to whom participants had disclosed their HIV status were more frequently HIV infected (30.9% vs. 6.5%, p< 0.001). 74.5% of participants would prefer to initiate ART on the day of diagnosis vs. waiting until the next visit. PW were more likely to prefer starting immediately (78.3% vs. 70.7%). Endorsing stigma was associated with unwillingness to start immediately (OR 3.04, 95%CI 1.05-8.78).

Characteristics	Initiate ART at day of diagnosis (n=743)	Wait until next visit (n=255)	p-value
Age, mean (SD)	25.4 (5.5)	25.2 (5.3)	0.679
Currently married or living with partner n(%)	564 (75.9)	173 (67.8)	0.011
Has at least 1 child infected with HIV n(%)	74 (10.9)	32 (14.8)	**0.040**
Educational attainment n(%) No education	83 (11.2)	37 (14.5)	0.263
Any primary	336 (45.2)	118 (46.3)	
Any secondary	324 (43.6)	100 (39.2)	
On ART now n(%)	657 (88.7)	200 (78.4)	**0.000**
Pregnant (n=493) n(%)	386 (78.3)	107 (21.7)	**0.006**
Non-Pregnant (n=505) n(%)	357 (70.7)	148 (29.3)	

[Preferences for timing of ART initiation]

Conclusions: Although PW were more likely than non-PW to accept immediate ART initiation, 22% preferred to delay the start of ART, which may be a risk factor for both vertical transmission and loss to follow-up. Given the urgency of ART initiation to prevent HIV transmission to the baby, and concerns that deferring ART may decrease retention in B+ programs, understanding women's preferences and barriers to swift ART initiation may enhance the effectiveness of B+ programs in achieving the goal of eliminating pediatric HIV.

WEPED862

HIV-free survival at six weeks in a cohort of children born to HIV-positive mothers enrolled in Option B+ in Kigali: the Kabeho study

G.F. Ndayisaba[1], E.A. Bobrow[2], P. Mugwaneza[3], D. Ndatimana[1], M. Gill[2], H.J. Hoffman[4], C. Baribwira[5], L. Adair[6], L. Guay[2], A. Asiimwe[7]
[1]EGPAF, Kigali, Rwanda, [2]EGPAF, Washington DC, United States, [3]Rwanda Biomedical Centre, Kigali, Rwanda, [4]George Washington University Milken Institute School of Public Health, Washington DC, United States, [5]University of Maryland, School of Medicine, Kigali, Rwanda, [6]University of North Carolina, Chapel Hill, United States, [7]Rwanda University Teaching Hospitals, Kigali, Rwanda
Presenting author email: ndayisaba@gmail.com

Background: In April 2012, Rwanda began implementing a policy to initiate all HIV-positive pregnant women on lifelong antiretroviral treatment ('Option B+'). In April 2013, the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) and Rwanda's Ministry of Health began the Kigali Antiretroviral and Breastfeeding Assessment for the Elimination of HIV (Kabeho) Study. The study aims to assess HIV-free survival from birth to 24 months weeks of age among HIV-exposed children with mothers enrolled in Option B+.
Methods: HIV-positive women were enrolled from their third trimester of pregnancy until two weeks postpartum at 14 Kigali health facilities that serve ≥ 50 HIV-positive pregnant women/year. At enrollment, HIV and ART history, medical care, and laboratory information were collected. Delivery information and birth outcomes were recorded from maternity units as soon as possible after delivery. At 6 weeks of age, PCR for HIV diagnosis was done by the National Reference Laboratory using Roche COBAS Ampliprep/TaqMan HIV-1 qualitative test. Positive results were confirmed on second specimen.
Results: Of the 608 infants born in the cohort, 9 (1.4 %) were still births, 10 (1.6 %) spontaneous preterm deliveries and 7 (1.2 %) infants had birth defects. Of the 572 infants with known birth weight, 33 (5.8 %) had birth weight below 2,500 grams. By six weeks of age, 11 (1.8 %) additional infant deaths occurred and 7 (1.2%) of them died within the first 24 hours of life. Of the 588 children alive at six weeks, 2 (0.3%) were confirmed to be HIV-positive. The overall HIV-free survival at 6 weeks was estimated at 96.8% (95% CI: 95%-98%).
Conclusions: Provision of ART to all Kabeho Study women resulted in low mother-to-child HIV transmission (0.3%) before six weeks of age, and mortality in this HIV-exposed cohort is much lower than the 2.7% neonatal mortality rate in the 2010 Rwanda Demographic and Health Survey (DHS).

WEPED863

Optimizing health information systems for Option B+ in Swaziland

A.B. Gachuhi[1], N. Dlamini[2], D. Mudoni[2], S. Mthethwa[3], V. Okello[4], A. Zerbe[1], H. Nuwagaba-Biribonwoha[2], R. Sahabo[2], E.J. Abrams[1]
[1]ICAP at Columbia University, Research Department, New York, United States, [2]ICAP at Columbia University, Research Department, Mbabane, Swaziland, [3]Ministry of Health, Kingdom of Swaziland, SNAP, Mbabane, Swaziland, [4]Ministry of Health, Kingdom of Swaziland, Mbabane, Swaziland
Presenting author email: ab3857@columbia.edu

Background: The Option B+ approach for prevention of mother-to-child transmission (PMTCT) of HIV presents opportunities for streamlined treatment and retention for mothers and their infants. However, paper-based health information systems (HIS) are often redundant and poorly integrated across maternal-infant care. We examined documentation protocols and their implementation in the context of PMTCT.
Methods: '*Situkulwane Lesiphephile—Safe Generations*' is an implementation science research study evaluating Option B+ outcomes in the Kingdom of Swaziland using routinely collected patient-level data. Facility and healthcare worker assessments were conducted at 10 PMTCT clinics to identify and describe PMTCT service documentation under Option B+. Documentation source was tabulated against visit type, maternal and infant health indicators, and maternal and infant unique identifiers to evaluate: a) proportion of repeated data collected across documentation source, b) the burden of documentation at each visit type, and c) the presence or absence of maternal-infant linking through unique identifiers.
Results: Swaziland PMTCT HIS includes 12 documentation sources for maternal data and 4 sources for infant data. Multiple paper-based documentation sources are completed for each PMTCT visit (min 10, max 15). Many indicators are duplicated across these sources. For example, health workers must document maternal HIV status on eight separate forms for each PMTCT visit. Maternal HIV status is the only key variable routinely recorded on infant documentation sources; maternal health and treatment status are not found on any infant record (Table 1). Unique identifiers are not used to link maternal-infant pairs on any documentation source (Table 1).

Documentation Source	Maternal Documentation Sources					Infant Documentation Sources		
Key Information (Unique Identifiers, Health Indicators)	ANC Register	ANC Patient Card	HIV Chronic Care File (CCF)	HIV Patient Card	PNC Register	Child Welfare Patient (CWF) Card	DBS Log Book	Child Welfare (CWF) Register
Maternal ANC Unique Identifying Number	x	x			x			
Maternal HIV Care Unique Identifying Number			x	x				
Infant Unique Identifying Number	N/A	N/A				x	x	x
Maternal Outcome (Dead, Transfer, LTF)			x					
Infant Outcome (Dead, Transfer, LTF)								x
Maternal HIV Status	x	x	x	x	x	x	x	x
Maternal ART Status	x	x	x	x				
Infant HIV Status	N/A	N/A					x	x

[Key Information on Maternal & Infant Documentation]

Healthcare workers report an increased burden of documentation with integration of ART into ANC services and fail to routinely document all information on all forms at each visit. For example, no CD4+ count and no birth date were recorded for 17% and 16% of women, respectively, across all documentation sources.
Conclusions: The multitude and replication of maternal and infant documentation required for a single PMTCT visit burdens healthcare workers and increases risk for inconsistent, erroneous, and incomplete data. New approaches to Option B+ documentation, including introduction of electronic medical records, are urgently needed to facilitate and accurately record maternal-child health service delivery and PMTCT outcomes.

WEPED864

Acceptability of community-based mentor mothers among HIV-positive pregnant women and partners in the context of Option B plus in Kenya

I. Wanga[1], L. Abuogi[2,3], E. Akama[3], E.A. Bukusi[1,3], A. Helova[4], P. Musoke[4], W. Nalwa[5], T. Odeny[1], J.M. Turan[4], M. Onono[1]
[1]KEMRI/RCTP, Center for Microbiology Research, Kisumu, Kenya, [2]University of Colorado, Denver, Pediatrics, Denver, United States, [3]KEMRI/RCTP, Family AIDS Care and Education Services (FACES), Kisumu, Kenya, [4]University of Alabama, Birmingham, United States, [5]Ministry of Health, Migori, Kenya

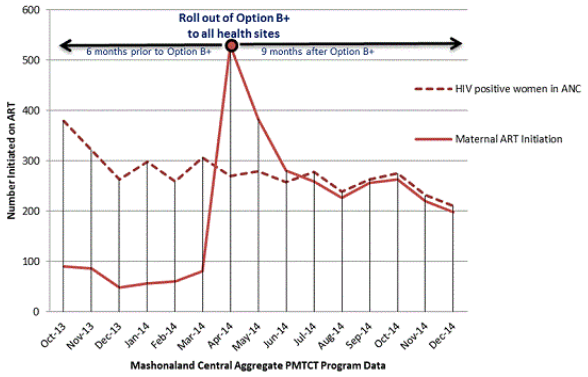
Background: Universal, lifelong ART for HIV-infected pregnant and breastfeeding women (Option B+) holds promise for improving maternal and child health but key challenges remain in achieving long-term ART adherence and retention in HIV care. Mentor mothers (HIV-infected women who have been through PMTCT and who are tasked with providing peer education and psychosocial support) have been shown to increase uptake of services, but have generally been facility-based in Kenya. In order to optimize adherence and retention in the context of Option B+, we explored the acceptability of community mentor mothers (cMMs).
Methods: A total of forty gender-matched in-depth interviews were conducted separately with HIV-positive pregnant/postpartum women and their male partners at four health facilities in Western Kenya between September-November 2014. Transcripts were transcribed verbatim, translated and then coded using Dedoose software based on the literature, themes from the interview guides and the transcripts. Excerpts from broad codes were then fine-coded using an inductive approach.
Results: Major themes in the data indicated an overall acceptability of cMMs, ideal characteristics of a cMM and potential risks. The cMMs were thought to be beneficial for stigma reduction, as well as improving women's clinic attendance and medication adherence. Participants' ideal characteristics of a cMM included age over 30 years and they preferred someone they could see as both a confidant and a role model. The cMM should preferably wear unmarked clothing that would not identify her as an HIV-related worker. There were, however, mixed responses as to whether the cMM should work in the same community where she lives, with some respondents raising concerns about inadvertent disclosure. Risks of the cMM approach included potential breaches of confidentiality and inadvertent disclosure of HIV status.
Conclusions: The cMM approach was perceived as a potentially beneficial and acceptable strategy for supporting adherence and retention of pregnant and postpartum women on ART for life. However the design for cMM interventions should minimize risks of unwanted disclosure and stigma.

WEPED865

Impact of Option B+ on maternal ART initiation rates in Mashonaland Central, Zimbabwe

G. Mujaranji[1], K. Webb[1], V. Chitiyo[1], T. Sengai[1], D. Patel[1], C. Tshuma[2], B. Engelsmann[1]
[1]Organisation for Public Health Interventions and Development (OPHID) Trust, Harare, Zimbabwe, [2]Ministry of Health and Child Care, Mashonaland Central Province, Bindura, Zimbabwe
Presenting author email: gmujaranji@ophid.co.zw

Background: Zimbabwe's PMTCT Program began its transition to Option B+ ('test and treat for life') strategy in September 2013. With an HIV prevalence of 15.9% among women in antenatal care (ANC), Option B+ presents an opportunity to improve maternal and child health through improved access to ART, reduced transmission to uninfected male partners and provide protection against vertical HIV transmission in future pregnancies in Zimbabwe. Our objective was to document changes in ART initiation rates among HIV positive women in ANC following transition to Option B+ in Mashonaland Central Province.
Methods: In April 2014, Option B+ was rolled out simultaneously to all 135 health sites in Mashonaland Central Province, serving a population of 273,372 women of childbearing age. Routinely collected data from the national PMTCT program on maternal ART initiation rates was analyzed descriptively 6 months prior and 9 months after roll out of Option B+ (Oct 2013-Dec 2014). Chi-square test was used to calculate statistical significance.
Results: The simultaneous, rapid roll out of Option B+ to all sites in Mashonaland Central resulted in significant, 457% increase in the number of HIV positive pregnant women initiated on ART in ANC $\chi^2(1, N = 5300) = 2373.43$, $p<0.0001$, from 6 months prior to 6 months after implementation of B+. In the last quarter of 2014 (Sept-Dec), among 982 women identified in ANC as HIV positive, 95.5% (n= 938) were initiated on ART (95% CI: 94.0% to 96.7%).
Conclusions: Implementation of Option B+ resulted in dramatic and significant increases in the number of HIV positive pregnant women initiated on ART in Mashonaland Central Province. Introduction of Option B+ saw an initial surge in maternal ART initiation rates as HIV positive women in care but not on ART were initiated under revised guidelines. Following this 'ART catch-up' phase, initiation rates stabilized proportionate to number of HIV positive women identified in ANC. With high ART coverage, there is need to enhance retention and adherence of mothers across the PMTCT cascade, including improved uptake of early infant diagnosis among HIV-exposed infants and timely ART initiation among infected children.



[Figure 1. Number of HIV positive women and infants initiated on ART (Oct 2013 - Dec 2014), Mashonaland Central]

WEPED866

Immediate initiation of antiretroviral therapy in PMTCT programmes is not associated with non-adherence during pregnancy: a cohort study

N. Langwenya[1], T. Phillips[1], A. Zerbe[2], G. Petro[3], L.-G. Bekker[4], J. Mcintyre[5], E.J. Abrams[2], L.B. Myer[1], Maternal & Child Health Antiretroviral Therapy (MCHART) Study
[1]University of Cape Town, Division of Epidemiology & Biostatistics, School of Public Health & Family Medicine, Cape Town, South Africa, [2]ICAP at Columbia University, Mailman School of Public Health, New York, United States, [3]University of Cape Town, Department of Obstetrics & Gynaecology, Cape Town, South Africa, [4]University of Cape Town, Desmond Tutu HIV Centre, Cape Town, South Africa, [5]Anova Health Institute, Johannesburg, South Africa
Presenting author email: landon.myer@uct.ac.za

Background: Under "Option B+" many prevention of mother-to-child HIV transmission programmes in Africa initiate pregnant women on lifelong antiretroviral therapy (ART) at their first antenatal clinic (ANC) visit. However concerns have been raised regarding patient readiness before ART initiation and whether immediate ART initiation in pregnancy may contribute to increased non-adherence.
Methods: As part of a larger study of ART use in pregnancy, we enrolled into a prospective cohort consecutive ART-eligible pregnant women making their first ANC visit at a primary care facility in Cape Town, South Africa, between April 2013 and June 2014. Before July 2013, eligibility was based on CD4 cell count ≤350 cells/μl ("Option A"), usually with a 1-2 week delay from the first ANC visit to ART initiation; thereafter all women were eligible regardless of CD4 cell count ("Option B+") and typically started ART on the same day as first ANC visit. All women received standardized counselling before starting a fixed-dose regimen. Study interviews were conducted separately from the ART service through one week postpartum and included self-reported adherence based on 30-day recall.
Results: In 618 consecutive ART-eligible women (median age, 28 years; median gestation, 21 weeks; 54% newly diagnosed with HIV), more than two-thirds of women (71%) started ART immediately; this proportion was higher under "Option B+" versus "Option A" (p< 0.001). 15% percent of women reported at least one missed ART dose. Missed doses were reported more frequently among younger women (p=0.022) and women diagnosed with HIV before the current pregnancy (p=0.015). In women initiating ART immediately, 15.2% reported a missed dose during pregnancy, compared to 14.7% of women who did not start ART at the first ANC visit (risk ratio, 1.01; 95% CI:0.88-1.15; p=0.883). This finding did not vary after adjustment for demographic and clinical measures, and was consistent when restricted to women with CD4 cell counts ≤350 cells/μl.
Conclusions: These results suggest that same-day ART initiation in pregnant women is not associated with reported missed ART doses during the antenatal period. While these results are reassuring for ART programmes implementing "Option B+", further research is required to examine adherence in care over time, particularly postpartum.

WEPED867

Viral load outcomes after ART initiation among women in a PMTCT B+ programme in Zimbabwe

H. Bygrave[1], S. Simons[2], C. Metcalf[1], T. Bonyo[2], G. Chenjirai[2], T. Roberts[3]
[1]Medecins Sans Frontieres, Southern Africa Medical Unit, Cape Town, South Africa, [2]Medecins Sans Frontieres, Harare, Zimbabwe, [3]Medecins Sans Frontieres Access Campaign, Geneva, Switzerland
Presenting author email: helen.bygrave@joburg.msf.org

Background: The WHO 2013 guidelines recommend that all HIV-infected pregnant and breastfeeding women take ART to prevent mother-to-child transmission (PMTCT). A high viral load (VL) >1000 copies/ml during pregnancy or breast-feeding is associated with higher rates of MTCT. Although antenatal attendance is high in Zimbabwe, women frequently present late in pregnancy. In Zimbabwe, routine VL testing was implemented in MSF-supported HIV programmes in 2012, with patients tested at three and twelve months post initiation, then annually. Those with a VL >1,000 copies/ml are given enhanced adherence counselling and retested after three months.
Methods: Laboratory records of VL among women aged 15 to 45 years, having routine VL testing were analysed to assess the virological response to ART. The analysis was stratified according to whether the women were pregnant (n=201), breastfeeding (n=359), or neither pregnant nor breastfeeding (n=1,064), at the time of ART initiation.
Results: Three months after starting ART, viral suppression to <1,000 copies/ml was 85.7% overall, 88.1% among women who started ART during pregnancy, 87.7% among women who started ART during breastfeeding, and 84.6% among women not in the PMTCT programme. Twelve months after starting ART, viral suppression to <1,000 copies/ml was 86.5% overall, 91.7% among women who started ART during pregnancy, 86.5% among women who started ART during breastfeeding, and 85.9% among women not in the PMTCT programme. At 3 months, the relative risk of having a VL>1,000 copies/ml among women in the PMTCT programme, compared to women not in the PMTCT programme, was 0.77 (95% CI: 0.60 - 0.99; p=0.041).
Conclusions: Although rates of virological suppression were high among all women in the cohort, a substantial number of pregnant and breastfeeding women failed to suppress their VL within 3 months of starting ART, putting their infants at ongoing risk of mother-to-child HIV transmission often at a time coinciding with the time of delivery. Guidance is urgently needed on the optimal timing and frequency of VL testing among women in PMTCT programmes, and whether ongoing prophylaxis among infants of women with a high VL is required.

WEPED868

Utility of individual tracking tool in monitoring and evaluation of prevention of mother to child transmission of HIV, Maharashtra, India

A.S. Hegde[1], P.A. Babu[2], S. Khaparde[1], N. Seguy[3], T. Mulik[4]
[1]National AIDS Control Organisation, Basic Services, New Delhi, India, [2]WHO, Case Tracking and Reporting, New Delhi, India, [3]WHO, HIV, New Delhi, India, [4]NACO, HIV, New Delhi, India
Presenting author email: drashahegde@gmail.com

Background: Maharashtra State launched the Life long ART for PMTCT in the month of February 2014. Maharashtra State AIDS Control Society designed a strong individual tracking tool and deployed it for tracking HIV positive pregnant women to monitor the retention along the PPTCT services cascade. The tracking tool also provides information for decision making at various levels in the program.
Methods: The Excel based tracking tool is initiated by 578 Integrated Counselling and Testing Center (ICTC) Counsellor and shared with 70 ART centers. The compiled excel sheet is monitored at regular intervals by district and state level authorities. Between April to September 2014, total of 1,118 HIV infected pregnant women were registered in the tool. The secondary data from the tracking tool in this period has been analyzed in this descriptive study.
Results:

- Of the total 1,118 HIV positive pregnant women, 760 (68%) were newly detected and 358 (32%) had already been detected before their current pregnancy. 646 (85%) of the newly detected cases were in WHO Clinical stage I at the time of registration. 669 (60%) of HIV infected pregnant women were less than 25 years of age and 464 (41%) were primi gravida.

Out of the total, 1095 (98%) were registered at ART center, and 1007 (91%) were initiated on lifelong ART. For 844 women the average time between HIV detection at ICTC and registration at ART Centre was 12 days, 664 women underwent CD4 testing on the same day and 712 women were initiated on lifelong ART the very next day. The baseline median CD4 count (at the time of ANC registration) was 415 (n=1019).
7% underwent MTP, 45% delivered live babies, 2% were still birth and abortions and 46% were yet to deliver.
Conclusions: This tool was critical in preventing lost to follow up of pregnant women until delivery. The finding suggests that tracking tool is an effective tool for assessing the retention in care of HIV positive pregnant women and for identifying programmatic bottlenecks. There is a need to focus on earlier identification of HIV positive women during pregnancy and decreasing the time between detection and ART registration.

WEPED869

Health facility challenges to the provision of Option B+ in Kenya

A. Helova[1], E. Akama[2], E. Bukusi[2], P. Musoke[1], W. Nalwa[2], T. Odeny[2], M. Onono[2], J.M. Turan[1], I. Wanga[2], L. Abuogi[3]
[1]University of Alabama at Birmingham, Health Care Organization and Policy, Birmingham, United States, [2]Kenya Medical Research Institute, Center of Microbiology Research, Nairobi, Kenya, [3]University of Colorado Denver, Department of Pediatrics, Aurora, United States
Presenting author email: lisa.abuogi@childrenscolorado.org

Background: Current World Health Organization guidance recommends lifelong antiretroviral therapy (ART) for all pregnant and breastfeeding women (Option B+) in settings with generalized HIV epidemics. We explored provider perspectives on potential barriers and facilitators in the provision of Option B+ in Kenya.
Methods: We conducted four focus groups with 30health care providers between September and November 2014 to explore challenges that health facilities are facing in implementation of Option B+, which has recently been rolled out in western Kenya. Transcripts were coded using the Dedoose software; based on the literature, topics from interview guides, and emerging themes from transcripts. Excerpts from broad codes were then fine-coded using an inductive approach.
Results: Major themes that emerged included a preference for Option B+ over prophylactic regimens, with the major advantage cited being elimination of CD4 count testing as requirement for treatment initiation. Shortage of drugs and staff, and the practice of same-day initiation into treatment were challenges raised. Providers expressed concern that pregnant women have little time to accept and disclose their HIV status when they are immediately initiated on treatment; which could potentially lead to stigma, conflict, or violence in the home. An additional challenge noted was the possibility of women disengaging from care if their child tests HIV-negative at 18 months and they no longer feel the need to adhere to treatment to protect their child. Suggested facilitators for long-term retention and adherence included strategies for individual clients (continuous adherence counseling, tracing of clients who are lost-to-follow-up, and text messages), couple/group strategies (couple testing, assisted disclosure, treatment buddies, and support groups), community strategies (reducing stigma, community mentor mothers), and changes in service provision (integration of ART with other services and longer clinic hours of operation).
Conclusions: This study highlights important challenges at the health facility level related to Option B+ roll-out in western Kenya. Adaptation of identified facilitators may increase linkage, retention and adherence to life-long treatment for pregnant women in Kenya, contribute towards elimination of mother-to-child HIV transmission, and improve maternal and child outcomes.

Interventions to improve retention in the PMTCT cascade, including early infant diagnosis

WEPED870

Using text messaging to maximize adherence and retention for women and infants in the context of Option B+ in Kenya

P. Musoke[1], I. Wanga[2], J. Turan[1], M. Onono[2], W. Nalwa[3], A. Helova[1], E. Bukusi[2], E. Akama[2], L. Abuogi[2,4], T. Odeny[2]
[1]University of Alabama at Birmingham, Department of Health Care Organization and Policy, Birmingham, United States, [2]Kenya Medical Research Institute, Research Care and Training Program, Centre for Microbiology Research, Kisumu, Kenya, [3]Ministry of Health, Kisumu, Kenya, [4]University of Colorado Denver, Department of Pediatrics, Denver, United States
Presenting author email: lisa.abuogi@childrenscolorado.org

Background: Key challenges in the provision of lifelong antiretroviral therapy (ART) to pregnant and breastfeeding women (Option B+) include achieving long-term ART adherence and retention in care. Evidence suggests these challenges may be addressed using mobile text messaging. However, the efficacy and acceptability of this intervention in context of Option B+ has yet to be ascertained. We evaluated the acceptability of mobile text messaging as a means of supporting women's long-term ART adherence and retention in care as Option B+ is being rolled out in Kenya.
Methods: Forty in-depth interviews with 20 HIV-positive pregnant/postpartum women and 20 male partners, as wells as 4 focus groups with 30 health workers, were conducted during the period September-November 2014 in rural Nyanza, Kenya. Transcripts were coded using the Dedoose software program based on the literature, topics from the interview guides, and emerging themes from the transcripts. Excerpts from broad codes were then fine-coded using a grounded approach.
Results: Themes that emerged in the data included overall acceptability, preferred content of messages, message sharing and potential risks of receiving HIV-related text messages. The overall acceptability of a patient-tailored mobile text messaging intervention was evident among most participants. They anticipated that the messages would provide useful and educational information, and proposed the content of messages include specific reminders for clinic visits and infant immunizations. In addition, participants recommended that messages encourage HIV testing for infants and HIV-negative partners, as well as promote "positive living" with HIV. Because mobile phone sharing was common, participants reported potential risks of inadvertent disclosure of HIV status. All participants emphasized the need to keep messages confidential. They suggested that disclosure between couples be required if partners received messages. To further reduce risk of involuntary disclosure, many participants preferred text messages be kept generic and omit any specific mention of HIV.
Conclusions: Overall, mobile text-messaging was viewed as an acceptable intervention for promotion of long-term ART adherence and retention in HIV care among pregnant women. The findings are being used to refine a text messaging intervention for pregnant/postpartum women and male partners at sites rolling out Option B+ in Kenya.

WEPED871

Exploring the delays in turnaround time for HIV early infant diagnosis in selected health facilities in Zimbabwe

R. Musarandega[1], B. Mutede[1], A. Muchedzi[1], T. Moga[1], C. Muchuchuti[1], A. Chadambuka[1], T. Ncomanzi[1], T. Nyamundaya[1], K. Maeka[2]
[1]Elizabeth Glaser Pediatric AIDS Foundation, Technical Department, Harare, Zimbabwe, [2]National Microbiology Reference Laboratory, Ministry of Health and Child Care, Harare, Zimbabwe
Presenting author email: rmusarandega@pedaids.org

Background: Early infant diagnosis (EID) is critical to the health and survival of HIV-exposed infants. The Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) has been supporting a courier to transport EID specimens and results between central collection points and processing laboratories since 2011.Until 2013, Zimbabwe had one EID laboratory, the National Microbiology Reference Laboratory (NMRL), to process specimens from around 1,440 sites. In 2014, EID testing was decentralized to two more regional laboratories in Mutare and Bulawayo cities, with EGPAF and other partners' support. EGPAF conducted an assessment of turnaround time (TAT) and causes of delay in the EID program.
Methods: A cross-sectional descriptive study was conducted in 23 health facilities, randomly selected from 7 provinces including 9 peripheral and 14 courier collection sites. EID TAT data was collected for 1,557 EID dried blood spot (DBS) samples collected between June and November 2014. Qualitative data were collected through key informant interviews with EID service providing health care workers. The TAT was time from date of specimen collection to date of delivering results to a client. Data were analyzed using Epi-Info. The study was approved by the Medical Research Council of Zimbabwe.
Results: Approximately 40% (627/1,557) of specimens assessed had complete TAT data. Overall national level TAT was 10.1 weeks against a 4 weeks standard. Specimens processed at the NMRL had the highest median TAT (13.5 weeks) compared to regional laboratories (TAT = 4.9 weeks and 4.4weeks, respectively). The longest delay in TAT was in the laboratories; the NMRL (original EID lab) contributing the most to this delay with 7.4 weeks internal TAT. Urban healthcare facilities had higher TAT (11.1 weeks) compared to rural healthcare facilities (8weeks) p=0.02. Clinics had higher TAT (11.7 weeks) compared to hospitals (7 weeks), p=0.000. Hospitals have more referral clients who take longer to collect results.

EID Process	Median TAT in weeks	Lower and Upper Quartiles	EID Process	Median TAT in weeks	Lower and Upper Quartiles	EID Process	Median TAT in weeks	Lower and Upper Quartiles
Crude Overall TAT (n=627)	10.1	(5.1; 13.9)	**EID process stage (National)**			**Type of Facility (p<0.001)**		
EID TAT by processing laboratory			Collecting site to courier pick-up	0.86	(0.0; 1.37)	Hospital	7.0	(4.0; 12.8)
National Medical Reference Laboratory (n=338)	13.5	(11.7; 16.7)	Courier pick-up to receipt at lab	1.28	(0.8; 2.2)	Clinic	11.7	(6.3; 15.0)
Mutare Provincial Hospital Laboratory (n=280)	4.9	(4.0; 7.4)	Lab receipt to lab testing	6.1	(1.9; 7.1)			
Mpilo Provincial Hospital Laboratory (n=9)	4.4	(4.0; 5.0)	Testing to dispatch from lab	0.4	(0.1; 0.7)			
Rural/Urban Setting (p=0.02)			Dispatch from lab to courier delivery point	1.4	(0.3; 6.4)			
Urban	11.1	(4.9; 14.8)	From Courier delivery point to collecting site	0.14	(0.1; 26.6)			
Rural	8.2	(5.2; 12.9)	Receipt at site to client given	2.0	(0.8; 4.2)			

[Table 1: Overall EID TAT by Processing Lab, EID process]

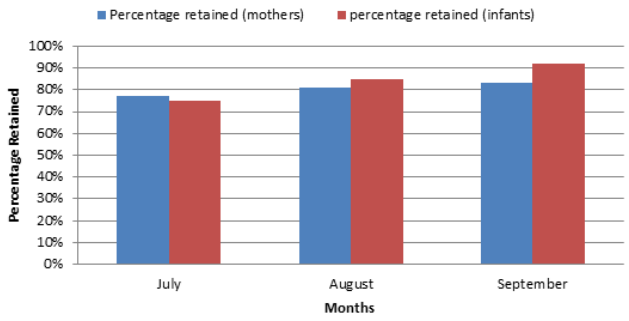
Conclusions: Overall TAT in the national EID program remains far too long. The courier system and decentralization of EID have reduced TAT in the provinces served by regional labs. EGPAF is in process of working with MOHCC to further decentralize EID process and have more sites referring specimens to the regional laboratories.

WEPED872

Improving retention of young children and women on Option B+/ART at six months in Zimbabwe: a quality improvement approach

B. Mutede, R. Musarandega, E. Tumbare, J. Muponda, E. Chinaka, P. Mthombeni, E. Jange, A. Mahomva
Elizabeth Glaser Pediatric AIDS Foundation, Technical Department, Harare, Zimbabwe
Presenting author email: bmutede@pedaids.org

Background: Retention of women and children on ART has long been a challenge in Zimbabwe, and yet is necessary for the success of Option B+. Quality improvement (QI) methods can optimize retention in HIV care and treatment. In 2014, EGPAF supported QI to optimize HIV care and treatment to obtain at least 90% client retention on ART at 6 months.
Methods: Thirty seven PMTCT District Focal Persons (DFP), a government cadre of health workers who oversee PMTCT functions, were trained and supported to coach 125 EGPAF-supported, facility-based QI teams across 62 districts. Between April and December 2014, 85 facility teams developed and implemented QI projects to improve retention of women on ART 6 months after ART initiation in ANC and 55 teams had projects to improve 6 month retention of children initiated on ART before 2 years of age. Each team was received monthly coaching from the DFP. Interventions based on use of appointment diaries and use of peers or community based health workers to track clients who missed reviews were used in >90% of sites. Facility retention data were abstracted monthly and transmitted by DFPs to EGPAF for use in QI support through peer learning sessions for coaches and facility managers. Monthly cross-sectional analysis of women and child cohorts initiated on ART 6 months prior to each reviewing month were used to track retention.
Results: A review of progress after 3 months of implementation indicated that in QI sites, the proportion of women retained on ART 6 months post ART initiation in pregnancy increased from 77% to 81.6% and that of children retained on ART 6 months post initiation increased from 76.6% to 92% over 3 months. The proportion of sites whose retention rates were above 90% for women increased from 46% before QI to 66% and retention of children had surpassed the 90% target midway through QI projects.



[Figure 1. Retention of women initiated on ART during pregnancy and infants initiated before two years of age after six months of treatment]

Conclusions: It is possible to optimize retention on ART under Option B+ through QI methods based on techniques to better track clients at sites and follow up with community health cadres. We recommend extension of these efforts beyond six months as cohorts mature.

WEPED873

Factors associated with HIV-related stigma in three African countries (Project ACCLAIM)

G. Woelk[1], M.P. Kieffer[2], D. Mpofu[3], N. Herrera[4], D. Walker[5], H. Hoffman[4], The ACCLAIM Study Group
[1]Elizabeth Glaser Pediatric AIDS Foundation, Research Department, Washington, United States, [2]Elizabeth Glaser Pediatric AIDS Foundation, Program Innovation and Policy, Lilongwe, Malawi, [3]Elizabeth Glaser Pediatric AIDS Foundation, Program Innovation and Policy, Mbabane, Swaziland, [4]George Washington University, Epidemiology and Biostatistics, Washington, United States, [5]United States Agency for International Development, Bureau for Global Health, Office of HIV/AIDS, Washington, United States
Presenting author email: gwoelk@pedaids.org

Background: In 2013, the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) undertook a baseline knowledge, attitudes and beliefs (KAPB) household survey as part of a three-arm, community-based randomized trial to improve the uptake and retention of women in MCH and PMTCT services in Swaziland, Uganda and Zimbabwe. EGPAF also assessed social and behavioral factors including HIV-related stigma using eight selected validated stigma scales for community and individual attitude measures. In this analysis, we present factors associated with stigma in the three countries.
Methods: We surveyed randomly selected households using a structured questionnaire with data entered into a database on laptops. One adult (male or female) per household was randomly selected from eligible (18-60 years) adults. We analyzed demographic, socioeconomic and HIV testing factors in relation to the mean values of the stigma scales using generalized estimating equations with a binomial distribution, a logit link function and the compound symmetry correlation structure. We used principal component analysis to identify the most discriminating stigma measures. Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated along with p-values.
Results: Over 3,000 respondents were surveyed; 1099 in Swaziland, 1140 in Uganda, 1079 in Zimbabwe. Of the eight stigma measures, two were the most discriminating: "HIV/AIDS is the result of sinning", and "It would be foolish to marry someone who is living with HIV or AIDS". After adjustment for the covariates of age, gender, marital status, education, occupation and HIV testing, "country" was found to be significantly associated ($p< 0.001$) with agreement with the statement "HIV/AIDS is the result of sinning", with ORs of 12.4 (95% CIs: 9.3, 16.6), for Uganda, and 0.52 (95% CIs: 0.39, 0.68) for Swaziland relative to Zimbabwe. Women were less likely than men to have stigmatizing attitudes (OR: 0.79, $p< 0.02$), as were those tested for HIV (OR: 0.69, $p< 0.001$). Higher levels of education, (ORs: primary, 0.66, $p< 0.003$, secondary, 0.34, $p< 0.001$, tertiary, 0.22, $p< 0.001$) were associated with less stigma, while formal employment with more stigma (OR: 1.64, p< 009).
Conclusions: High levels of HIV stigma persist in the community. Evidence-informed approaches to prevent and mitigate stigma are needed.

WEPED874

Optimizing Zimbabwe's National PMTCT Program: cost-effectiveness of a planned village health worker (VHW)-based intervention to improve mother-infant linkage to postnatal care

K. Webb[1], R. Maclean[2], B. Engelsmann[1], K.A. Freedberg[2], A. Mushavi[3], E. Hyle[2], A. Ciaranello[2]
[1]Organisation for Public Health Interventions and Development (OPHID) Trust, Harare, Zimbabwe, [2]Medical Practice Evaluation Center, Massachusetts General Hospital, Harvard Medical School, Boston, United States, [3]Ministry of Health and Child Care, National PMTCT Program, Harare, Zimbabwe
Presenting author email: karen.myllynen.webb@gmail.com

Background: Low retention of mother-infant pairs in postnatal care (PNC) reduces the effectiveness of PMTCT programs offering Option B+ (lifelong ART). We projected the clinical and economic impact of a planned village health worker (VHW)-based intervention to re-engage mother-infant pairs who fail to link to PNC after delivery in Zimbabwe.
Methods: Using the Cost-effectiveness of Preventing AIDS Complications (CEPAC) model, we simulated a cohort of Zimbabwean women identified as HIV-infected and treated with ART during antenatal care and their infants (mean maternal age: 24 years, CD4: 451/μL, breastfeeding duration: 18 months). We compared three strategies: no PMTCT program (comparator), current national program, and current program plus a VHW-based intervention to identify and re-engage in care mother-infant pairs who fail to link to PNC by 6 weeks postpartum. Based on program and published data, we modelled successful 6-week PNC linkage (current: 43%; current+VHW: 71.5%: 50% of traced defaulters linked); VHW program costs were US$35/mother-infant pair traced. Model outcomes included MTCT risk, maternal and pediatric life expectancy (LE), and lifetime healthcare costs (2013 US$). We calculated incremental cost-effectiveness ratios (ICERs) in US$/life-year saved (US$/LYS) from discounted maternal+pediatric LE and costs, defining "very cost-effective" as ICER < US$950/LYS (Zimbabwe 2013 *per-capita* GDP). Sensitivity analyses varied intervention effectiveness, intervention costs, and loss to follow-up after initial linkage to PNC (late-LTFU).

Results: Compared to no PMTCT (not shown), the current national program was projected to reduce MTCT from 26.0% to 8.8%, increase pediatric LE from 48.70 to 57.37 years, and be cost-saving. The VHW program further reduced projected MTCT risk to 7.2% and increased maternal and pediatric LE (by 0.8 and 1.9 years). The VHW program increased total projected lifetime costs - including healthcare and ART costs - by $510/mother-infant pair, but was very cost-effective (ICER US$350/LYS vs. current program). It remained very cost-effective through wide variations in cost and effectiveness. With high late-LTFU, many clinical benefits were lost.

	Model input parameters			Model results								
				Pediatric			Maternal			Combined (maternal + pediatric)[b]		
	Linkage to PNC at 6 weeks (%)	VHW program effectiveness (%)[a]	VHW cost per mother-infant pair traced (USD)	MTCT risk (18m, %)	Lifetime cost/person (USD)	LE (years)	ANC+VHW cost/person (USD)	Lifetime cost/person (USD)	LE (years)	Lifetime costs/ pair (USD)	LE (years)	ICER ($/LYS)
I. Base-case analyses												
Current program	43	0	0	7.2	1,010	57.37	280	4,070	15.38	3,630	35.06	Comparator
VHW intervention	72	50	35	7.2	890	58.14	300	4,870	17.24	4,140	36.54	350
II. Selected sensitivity analyses: VHW program effectiveness, VHW program costs, and late LTFU[c]												
Lower efficacy: 20% RTC	54	20	35	8.2	960	57.68	300	4,390	16.12	3,850	35.65	370
Higher cost: $100/ mother-infant pair traced	72	50	100	7.2	890	58.14	340	4,870	17.24	4,180	36.54	370
Increased late-LTFU (10%/year)[d]	72	50	35	7.2	550	57.72	300	2,790	12.75	2,770	33.87	280

Abbreviations: PNC: postnatal care; RTC: return to care; LTFU: lost to follow-up; VHW: village health worker program; MTCT: mother-to-child HIV transmission; m: months; USD: United States dollars; LE: life expectancy; ANC: antenatal care; ICER: incremental cost-effectiveness ratio; LYS: life-year saved; Late-LTFU: late loss to follow-up after initial linkage to PNC at 6 weeks (late-LTFU is modeled at 2.5% per year in all other scenarios).
a. VHW program effectiveness: proportion of mother-infant pairs not linking to PNC at 6 weeks who are re-engaged in care.
b. Combined outcomes shown are discounted at 3%/year. For space considerations, separate discounted results for mothers and infants are not shown; these sum to the total discounted costs and total discounted LE shown in the table.
c. Sensitivity analyses (Section II): ICERs shown compare the VHW program in each scenario to the base-case current PMTCT program.: Varying rates of late-LTFU leads to changes in projected results for both the current program and the VHW program, so results cannot be directly compared to the "current program" results in Section I.
d. Excludes postnatal transmission impact of LTFU during breastfeeding among women who initially link to PNC.

[Table. Results of model-based analysis: impact of planned VHW intervention in Zimbabwe]

Conclusions: VHW-based interventions to improve linkage to PNC will provide good value for investment in Zimbabwe. Long-term retention of mother-infant pairs in care is critical to realize these benefits and optimize outcomes of Option B+ implementation in Zimbabwe.

WEPED875

ANC-PMTCT integration at primary healthcare centers improves exposed infant service quality in a high-burden Nigerian State

E. Okpokoro[1], H. Swomen[2], F. Yunusa[2], N. Sam-Agudu[3,4,5], H. Isah[2], P. Dakum[2,5]
[1]Institute of Human Virology, Research Department, Abuja, Nigeria, [2]Institute of Human Virology, Community Medicine, Abuja, Nigeria, [3]Institute of Human Virology, Clinical, Abuja, Nigeria, [4]University of Maryland School of Medicine, Department of Pediatrics, Baltimore, United States, [5]Institute of Human Virology, University of Maryland School of Medicine, Baltimore, United States
Presenting author email: homsuk.swomen@gmail.com

Background: Nigeria accounts for 30% of the global PMTCT coverage gap. Causes include poor access to PMTCT services among Nigerians living in rural areas, largely served by Primary Healthcare Centers (PHCs). The Institute of Human Virology-Nigeria's (IHVN's) ACTION in Community (AIC) project integrates PMTCT services with antenatal care (ANC) at rural PHCs to meet the national target of 80% PMTCT coverage by 2015. This study was conducted to identify key services/processes provided to PHCs that improved Early Infant Diagnosis (EID) and appropriate Nevirapine (NVP) administration.
Methods: In 2011, we selected high-ANC flow PHCs not providing PMTCT in Benue State, North-Central Nigeria. Of 37 states, Benue had the highest antenatal HIV prevalence (12.9%). After assessments, we initiated PMTCT services with: healthcare worker training, provision of ART, linkage to Mentor Mothers and other key services/processes shown in Table 1. With PHCs as the unit of analysis, we determined proportion of PHCs performing each key service/process. Using Fisher's exact test, we performed univariate analysis to assess the association between these proportions and timely EID (by 2 months of age) and infant NVP (within 72 hours) through to 6 weeks, at the PHCs.
Results: Between 2011 and 2013, 59 PHCs were identified and activated to provide PMTCT services. Overall, 76.3% (45/59) of PHCs administered NVP within 72 hours till 6 weeks and 76% (45/59) performed EID between 6 weeks and 2 months. Almost all (58/59, 98.3%) of PHCs provided same-day HIV test results, though this was not significantly associated with PHCs performing timely EID or adequate NVP administration. Client linkage with Mentor Mothers and ART, however, were significant associations (Table 1): PHCs linked with Mentor Mothers were twice as likely to administer infant NVP (95CI 1.15-3.56; p < 0.01) and perform EID at 6 weeks (95CI 1.28-4.59; p < 0.01) compared to PHCs without.

		NVP at 72hours till 6weeks		EID at 6weeks	
Key services/processes provided at PHCs	Proportion of 59 PHCs with services N (%)	Risk ratio (95%CI)	P-value	Risk ratio (95%CI)	P-value
HIV test result received same day	58 (98.3)	-	0.24	-	0.24
Male Partner testing offered	56 (94.9)	2.35 (0.47-11.7	0.14	2.35 (0.47-11.7)	0.14
PMTCT client seen by trained Health care worker	50 (84.8)	2.52 (0.99-6.39)	<0.01	1.44 0.79--2.63)	0.19
Baseline CD4 test documented	41 (69.5)	1.36 (0.92-2.01)	0.07*	1.53 (0.99-2.36)	0.01*
Offered HAART	45 (76.3)	6.68 (1.85-24.1)	<0.01	3.18 (1.39-7.34)	<0.01
Adherence assessed	43 (72.9)	2.97 (1.43-6.18)	<0.01*	2.97 (1.43-6.18)	<0.01
Adverse events assessed	39 (66.1)	2.05(1.25-3.36)	<0.01	2.37 (1.37-4.07)	<0.01
Linked to Mentor Mother	43 (72.9)	2.01 (1.15-3.56)	<0.01*	2.42 (1.28-4.59)	<0.01
Breastfeeding counseling	50 (84.8)	1.44 (0.79-2.62)	0.19	2.52 (0.99-6.40)	<0.01
Family planning services	46 (77.9)	1.84 (1.01-3.35)	<0.01*	1.31 (0.83-2.06)	0.27
Infant Immunizations available	49 (83.1)	1.33 (0.78-2.24)	0.23	1.11 (0.72-1.71)	0.69

*Chi square analysis

[Impact of PMTCT Integration on Infant Care_Table]

Conclusions: AIC has enabled/upgraded rural PHCs to provide PMTCT services and increase coverage in high-burden state. Management of PMTCT clients by trained health care workers, ART provision and Mentor Mother support are key services/processes relevant to improving HIV-exposed infant care. These services should be in the minimum basic package for PMTCT activation at PHCs.

WEPED876

Telephonic defaulter tracing by mentor mothers for EMTCT

M.A. Simba[1], N. Sijenyi Fulton[2], W. Nango[2], E. Okonji[3], E. Scheepers[4], A. Schley[5]
[1]mothers2mothers, Programmes and Technical Support, Nairobi, Kenya, [2]mothers2mothers, Nairobi, Kenya, [3]mothers2mothers, Cape Town, South Africa, [4]mothers2mothers, Research and Strategic Information, Cape Town, South Africa, [5]mothers2mothers, Training and Education, Cape Town, South Africa
Presenting author email: anne.schley@m2m.org

Background: PMTCT retention is a national program priority in Kenya, with documentation of 66% of HIV-exposed infants lost to follow-up by 18 months of age. In 2012, the Kenyan Ministry of Health launched the strategic framework for the elimination of mother-to-child transmission of HIV (eMTCT) and keeping mothers alive, which identified five strategic directions including improving access and demand for PMTCT through meaningful involvement of HIV-positive mothers. To operationalize the role of HIV-positive women, the national guidelines for the Kenya Mentor Mother Program (KMMP) were simultaneously launched. The KMMP trains and employs Mentor Mothers (MMs) to provide peer education and psychosocial support to PMTCT clients to promote retention in care and improve client outcomes.
Methods: mothers2mothers (m2m) implements the KMMP at 30 high volume facilities in Kenya. At each facility, MMs record client information in longitudinal registers, which are updated each time a client returns to the health facility. HIV-negative pregnant women are followed-up to ensure that they return to the facility for HIV testing in the third trimester, and HIV-positive PMTCT clients are followed throughout pregnancy and up to 18-months post-partum to track and retain clients in PMTCT care. MMs record clients' details at first contact and obtain consent for telephonic follow-up in the event of missed priority appointments. Upon a missed priority appointment, MMs initiate client follow-up immediately either through SMS or a phone call, encouraging the client to return to care. In this paper, we reviewed data collected from January to December 2014 at the 30 m2m-supported KMMP facilities.
Results: The results indicate that 7,801 priority PMTCT appointments were missed during the observation period. MMs successfully reached defaulted clients 5,772 times either through a SMS or a phone call during the same period, and 4,792 (61%) of missed appointments were resolved. An average of 93% of m2m's post-natal clients had completed a 6-week EID test, compared to the national average of 45%.
Conclusions: Site level documentation and telephonic defaulter tracing by MMs is an effective and efficient method to promote retention of PMTCT clients, and should be scaled up as part the country's national KMMP effort to improve client outcomes.

WEPED877

HIV early infant diagnosis (HEID): using IQSMS tool to track HIV-positive infants; an experience from Tanga region, Tanzania

S. Jongo[1], T.S. Tulli[1], G. Binde[1], A. Madhehebi[1], D.M. Kioko[2], A. Mourad[2]
[1]Futures Group International, Dar es Salaam, Tanzania, United Republic of, [2]Catholic Relief Services, Dar es Salaam, Tanzania, United Republic of
Presenting author email: sjongo@futuresgroup.com

Background: HIV testing of exposed infants is the entry point to rapid HIV treatment, continuous follow up and monitoring from an early age. Innovative methods to track exposed infants in communities and facilities are important for successful treatment programs. To support national efforts of improving early identification and treatment of all HIV exposed infants, the Local Partners Excel in Comprehensive HIV and AIDS Service Delivery (LEAD) project, funded by the Centre for Disease Control under PEPFAR used International Quality Short Messages (IQSMs) to identify infants who were not tested at first clinic visit and six weeks after cessation of breastfeeding in 293 facilities in Tanga region for them to be tested.
Methods: The IQSMS server receives preformatted SMS monthly reports from health care providers through their mobile phones. IQSMS software is equipped with a feature used for reporting stock of HIV test kits, numbers of exposed infants, and whether they have been tested. The monthly reports submitted to the server are analysed and lists of infants who have not been tested are sent to the respective facilities whereby multidisciplinary teams, including home based care providers trace the untested infants using the infant's mother/guardian home address, mobile phones or treatment supporters contacts retrieved from the facility register.
Results: Between October 2013 and September 2014, there were 1757 registered exposed infants from 293 facilities located in remote areas with limited resources in Tanga region. A total of 1749 (99.5%) were traced and tested for HIV within 12 months of their birth using DNA-PCR, of these 50 (2.9%) were diagnosed HIV positive. Of the identified positive 39(78%) initiated treatment, 6 were reported dead and 5 were lost to follow up.
Conclusions: IQSMS tool assists program implementation in areas where challenges are inevitable. The use of IQSMS to trace exposed infants has reduced infant lost to follow up rates and can be used in different areas for program monitoring.
Recommendations: IQSMS can be adapted by countries with limited resources. It is a fast, reliable and sustainable innovation critical to ensuring that children start treatment on time thus decreasing morbidity and mortality.

WEPED878

A highly successful massive early infant HIV testing campaign in rural Mozambique

L. Cumba[1], E. Mahagaja[1], A. Júnior[1], P. Jaime[1], H. Caliche[1], D. Maitor[1], C. Cugara[1], M.P. Bravo[2], C.W. Wester[3,4], D.B. Filimão[1], A. Green[3]
[1]Mozambican Ministry of Health, Zambézia Province Department of Health, Quelimane, Mozambique, [2]Friends in Global Health, Maputo/Quelimane, Mozambique LLC, Maputo, Mozambique, [3]Vanderbilt Institute for Global Health (VIGH), Nashville, United States, [4]Vanderbilt University School of Medicine, Department of Medicine, Division of Infectious Diseases, Nashville, United States
Presenting author email: william.wester@vanderbilt.edu

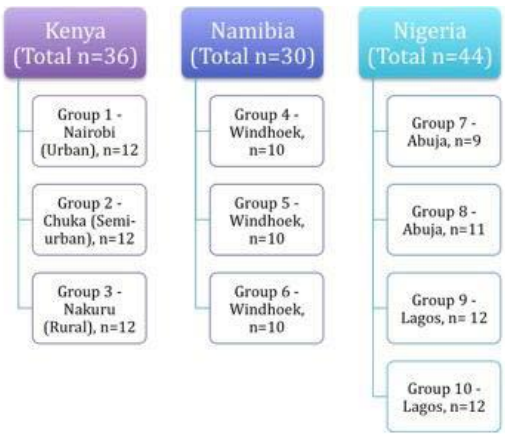
Background: Zambézia (Z), Mozambique's 2nd most populous and principally rural province, is characterized by high HIV prevalence (12.6%), poverty, and suboptimal health service access and utilization. Significant antiretroviral therapy (ART) scale-up efforts are ongoing as part of the national "*acceleration plan*", but as of the end of 2013, only 37% of eligible children nationally had been initiated on ART. Zambézia is among the poorest performing provinces with only 5,455 (20%) of the desired 27,032 currently receiving ART. We herein report outcomes from a recently implemented provincial Directorates of Health (DPS-Z) "*massive testing*" campaign focused on identifying and testing infants without known HIV status in all 22 districts of the province.
Methods: The massive testing campaign took place between May 1st - November 30st, 2014, and it included:
i) **training** of health care personnel at each health facility;
ii) **supply-chain support**, increasing distribution of HIV rapid tests and provider-initiated HIV testing and counseling (PICT) registers;
iii) **expanded service provision**, offering PICT to "at-risk" children in all service entry points with all infants testing positive immediately referred to the requisite exposed child services and ART clinics; and
iv) **weekly monitoring of pediatric indicators.** Data presented include 5-month outcomes, July - November 2014.
Results: 177 (74.7%) of Zambézia's 237 health facilities provide early infant diagnosis (EID) via HIV DNA PCR testing. Between July-November 2014, 78,760 infants greater than 2 months of age underwent HIV rapid testing with 2,549 (3.2%) testing positive. In addition, 6,221 exposed infants underwent EID with 836 (13.4%) testing positive. The majority (87.2%) of testing took place in pediatric triage clinic (53.4%) and healthy child clinic (33.8%) settings. Compared to the same period last year when massive testing campaign were not ongoing, we noted marked increases in proportion of children being linked to care (85.3%) as well as proportion of infected children (87.9%) being initiated on ART.
Conclusions: The DPS-Z-led massive pediatric testing campaign was highly successful as evidenced by increases in identified and ART-initiated children. Consistent (weekly) monitoring as well as supply-chain (reagents, ARV medications, etc.) and individual health facility-level support were integral to the success of this important initiative.

WEPED879

Women's voices: perceptions, values and preferences of women living with HIV regarding early infant diagnosis

T.N. Otieno, S. Brion, F. Anam
International Community of Women Living with HIV, Nairobi, Kenya

Background: World Health Organization (WHO) is updating guidelines that currently recommend that all infants with known or possible HIV exposure undergo virological testing at 4-6 weeks old. Infants with an initial positive diagnosis should begin anti-retroviral therapy (ART) as soon as possible. Although the testing rate of infants exposed to HIV in the first two months of life has increased since these guidelines' implementation, many still lack access to early infant diagnosis (EID), essential to timely ART initiation. WHO commissioned ICW and GNP+ to conduct a qualitative study to understand the perspectives of mothers living with HIV regarding the causes of loss-to-follow-up in terms of EID and treatment.
Methods: During June and July of 2014, a judgment sample of women living with HIV who gave birth in the past three years (n=110), recruited by national networks of women living with HIV, participated in ten focus group discussions (FGD) held in Kenya, Namibia, and Nigeria, using the same FGD questionnaire. Standard qualitative thematic analysis was applied to the FGD transcripts.



[Figure 1. FGD Demographics]

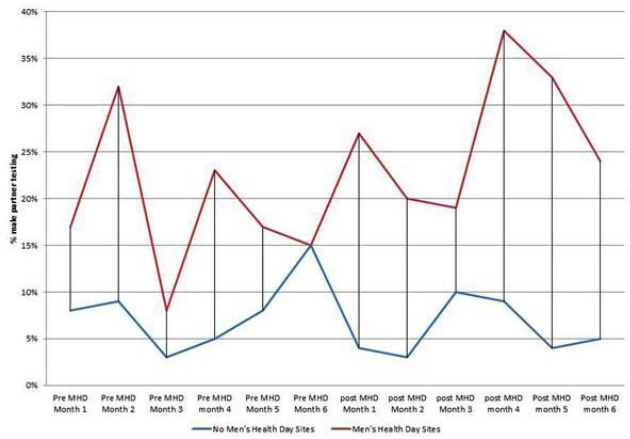
Results: FGD participants shared the following:
1. Many pregnant women are not informed about EID nor asked to give consent before their babies are tested;
2. Participants support testing within 4-6 weeks of age, but had mixed feelings about testing at birth;
3. Barriers contributing to loss-to-follow-up on infant diagnosis include lack of understanding about EID, clinic distances, and fear;
4. Participants feared that integration of EID and immunisation programs may cause inadvertent disclosure of their and the child's status;
5. Infant testing uptake depends on the quality and availability of education, peer counselling, and home/community-based testing; and
6. Participants appreciate that immediately offering ART to infants can increase child survival, but raised concerns about the side effects, toxicity, drug resistance, and running out of treatment options at young age.
Conclusions: To ensure survival of infants exposed to HIV, prevention of vertical transmission programmes must provide essential information about EID to women and support them to take necessary action for themselves and their children. Providing rapid turnaround testing at point-of-care for infants is preferred. However, barriers to current EID methods must also be addressed.

WEPED880

Engaging men for eMTCT through men's health days: experiences from Mutare District, Manicaland Province, Zimbabwe

T. Mukotekwa[1], T. Maphosa[2], C. Crand[1], S. Nezandoyi[2], P. Matyanga[1], V. Chitiyo[1], K. Webb[1]
[1]Organisation for Public Health Interventions and Development, Programs, Harare, Zimbabwe, [2]Ministry of Health and Child Care, AIDS and TB Unit, Harare, Zimbabwe
Presenting author email: tmukotekwa@ophid.co.zw

Background: The Prevention of mother to child transmission of HIV (PMTCT) program in Zimbabwe advocates for male partner HIV testing together with women attending antenatal care (ANC). Male partner testing rates (17%) remain below national target of 20%.The "Men's Health Days" initiative is a strategy to mobilise male partner involvement in PMTCT programs and increase uptake of HIV testing and counselling (HTC) among men. Our objective was to assess male partner testing at health sites in Mutare district following implementation of "Men's Health Days".
Methods: Mutare district was purposively selected due to male partner testing rates consistently below 15%. Men's Health Days (MHDs) intervention was developed collaboratively with Ministry of Health and community stakeholders to increasing rates of HTC among male partners of women in ANC. Held at health sites, the days were divided into three sessions:
1) community dialogue led by midwives to discuss pregnancy, child birth and the role of men;
2) Men's health needs;
3) Provision of free HIV counselling and testing, doctor's consultations and planning for men and health in the community.
Results: In October 2013, MHDs reached 1,539 men at 8 clinics over 10 days. A total of 402 men received HTC over 10 days approximated the number of male partners accessing HTC services district-wide the previous quarter (n= 311) Confidential post-test counselling by clinic nurses ensured those testing positive were linked to care. Dialogues provided an opportunity to educate and correct myths and misconceptions among men about contraception, pregnancy, child birth in the context of HIV. Men recommended more community-led family-based health interventions. Clinics where MHDs were conducted experienced a commendable increase in the proportion of male partner testing after the intervention compared to control sites that recorded a decline, relative change of 37% and -26%, respectively.



[Proportions of male partner HIV testing in ANC]

Conclusions: High attendance at Men's Health Days demonstrates potential of community-led efforts to increase male engagement in PMTCT. Clinic-based Men's Health Days are an effective strategy for reaching men for HIV prevention, treatment and care services. Future research should explore long-term impact on service utilisation and health outcomes among women, men and infants in communities where Men's Health Days are held.

Strategies to improve outcomes in HIV-infected children

WEPED881

Perspectives and experiences regarding disclosure of HIV status to perinatally infected children in Lima, Peru

A. Baker[1], L. Kolevic[2], A. Bayer[1,3], L. Najarro[3], J. Deville[1], R. Viani[4]
[1]University of California, Los Angeles, Los Angeles, United States, [2]Instituto Nacional de Salud del Niño, Lima, Peru, [3]Universidad Peruana Cayetano Heredia, Lima, Peru, [4]University of California, San Diego, La Jolla, United States
Presenting author email: anbaker@mednet.ucla.edu

Background: Despite global recommendations for disclosure of a child's HIV status, fewer than half of HIV-infected children at the National Institute of Child Health (INSN) in Lima, Peru have had their HIV status disclosed. Disclosure is necessary in order to improve the child's disease management, psychosocial support, medication adherence, HIV knowledge, and prevention of secondary transmission. How and when the disclosure process should take place in Peru has not been studied.
Methods: We conducted a qualitative study at INSN to explore the perceptions and experiences of healthcare workers (HCWs), disclosed and non-disclosed perinatally HIV-infected children, and their caregivers, regarding knowledge of their illness, disclosure of the child's HIV status, and appropriate approaches for HIV disclosure. Disclosed and non-disclosed HIV-infected children aged 7-17 years old (n=14) were interviewed separately from their caregivers (n=14). All HCWs of INSN's pediatric HIV clinic (n=6) were also interviewed. Transcribed interviews were analyzed using grounded theory to identify themes and relationships between themes. Coding was done using Dedoose software (Los Angeles, CA). Data were synthesized by theme and themes were analyzed within and across participant sub-groups.
Results: Disclosed children, all of whom were 12 or older, feared that others would learn of their HIV status and that they would be rejected from family, friends and future sexual partners. Children also wanted to be told their diagnosis earlier. Non-disclosed children expressed frustration taking daily medications and frequent doctor's visits. Regarding non-disclosed children, caregivers and HCWs reported greater difficulty with medication adherence. Caregivers and HCWs also discussed their motivations to disclose HIV status to the child, including desire to educate the child before their sexual debut, improve medication adherence, and tell the child the truth, especially before discovery of their status through some other means. Caregivers and HCWs expressed need for more training with the HIV disclosure process.
Conclusions: Among those caring for non-disclosed children, there was perceived difficulty with antiretroviral adherence, and fear of potential secondary transmission. Disclosed children require ongoing education and support. Culturally appropriate guidelines and training for HCWs and caregivers are needed to support disclosure of a child's HIV status as a process starting at an appropriate age.

WEPED882

Where are the children? Results from a successful pediatric intensified case finding initiative in a Kenya HIV program

M. Kitheka[1], J. Sunguti[2], S. Mutwiwa[1], M. Mudany[1], S. Bii[3], I. Malonza[1]
[1]Jhpiego Kenya, Nairobi, Kenya, [2]ICAP Kenya, Embu, Kenya, [3]USAID Kenya, Nairobi, Kenya
Presenting author email: moses.kitheka@jhpiego.org

Background: The estimated Pediatric HIV prevalence in Kenya is 0.9% with approximately 101,000 children living with HIV. There has been marked delay in Pediatric Antiretroviral Therapy (ART) initiation, with majority of the children remaining undiagnosed, started late on ART, with many succumbing to death early. The MOH has intensified efforts to identify all HIV infected children and enrol them on ART in order to eliminate Pediatric HIV deaths.
Methods: APHIA plus KAMILI project supports HIV care services in 136 health facilities in eastern and central Kenya. The project started a Pediatric intensified case finding initiative to identify, diagnose and treat all eligible children. This exercise started in June 2014 through to September 2014. All program officers were sensitized on the initiative and given a weekly tracking log for all eligible Pediatric clients. This included systematic chart review of files, flagging of any eligible children in MCH clinic, Early Infant Diagnosis website, and the HIV clinic. All the patient files were also standardized according to existing Standard operation procedures to ensure all required services. Aggregated data analysis was done using routine MOH reporting tools.
Results: As at December 2014, there are 3064 Pediatric current on ART. There was a 58% increase in the new paediatric ART clients from an average of 111 new clients per quarter in 2013 to 175 clients per quarter in 2014. In April-June 2014, 120 (52 male, 68 female) new clients were started on ART, a 35% increase from 89 (40 male; 49 female) paediatrics in Jan-Mar 2014. In July-Sep 2014, the total new children enrolled on ART increased by 140% from 120 to 287 clients (134 male, 153 female). In Oct- Dec 2014 after the intensified activity ended, 193 (104 male, 89 female) children were started on ART, a 33% decline from the previous quarter.

Conclusions: Through intensified case finding it is possible to find additional eligible children and initiative them on ART. These efforts need to be sustained to reach every eligible child for ART and support in identifying all "missed opportunities" for Pediatric ART.

WEPED883

ART and pre-ART treatment outcome among adolescents in Zimbabwe, results from a routine program

K. Kranzer[1], F. Vogt[2], M. Nyathi[3], M. Dixon[3], H. Gunguwo[3], W. Ndebele[3], R. Ferrand[1,4]
[1]London School of Hygiene and Tropical Medicine, London, United Kingdom, [2]Medicins Sans Frontieres, Operation Centre Barcelona, Harare, Zimbabwe, [3]Mpilo ART Clinic, Bulawayo, Zimbabwe, [4]Biomedical Research and Training Institute, Harare, Zimbabwe
Presenting author email: rashida.ferrand@lshtm.ac.uk

Background: Adolescents have emerged as a priority group for HIV prevention and care services especially in sub-Saharan Africa. However, antiretroviral treatment (ART) outcomes for this age group are rarely reported and data on pre-ART outcomes are completely lacking.
Methods: All HIV-infected adolescents (aged 10-19 at time of presentation) presenting at a public sector hospital clinic in Bulawayo, Zimbabwe between February 2004 and November 2011 were included in the analysis. HIV care at the hospital was provided by the public sector in partnership with Medecins Sans Frontieres (MSF) and other organisations. Survival analyses were performed to calculate crude mortality, loss to follow-up and ART initiation rates. Proportions in care, dead and lost to follow-up stratified on ART or pre-ART were calculated for different time points.
Results: A total of 2255 HIV-infected adolescents presented to the HIV service. The median age was 13.2 (IQR 11.4; 15.3) and 1189 (53%) were girls. The median follow-up time was 1.57 years (IQR 0.62; 3.17). A baseline CD4 count was available for 49% (N=1098): median CD4 count was 220 (IQR 95-390). The crude ART initiation rate was 219/100PY (95%CI 209-230) with a median time to ART initiation of 21 days (IQR 9; 61). Crude mortality and loss to follow-up rates were 4.4 (95%CI 3.9-5.1) and 7.8 (95%CI 7.0-8.7) respectively. Proportions alive, lost to follow-up and dead at 4, 12 and 24 months are presented in table 1.

Outcome	N (%) 0-4 months	N (%) 0-12 months	N (%) 0-24 months
Alive, in care, on ART	1498 (66.4%)	1568 (69.5%)	1535 (68.1%)
Death, on ART	46 (2.0%)	88 (3.9%)	116 (5.1%)
Transfer, on ART	13 (0.6%)	37 (1.6%)	68 (3.0%)
Loss to follow-up, on ART	44 (2.0%)	84 (3.7%)	136 (6.0%)
Alive, in care, not on ART	510 (22.6%)	313 (13.9%)	212 (9.4%)
Death, not on ART	27 (1.2%)	32 (1.4%)	38 (0.7%)
Transfer, not on ART	8 (0.4%)	10 (0.4%)	15 (0.7%)
Loss to follow-up, not on ART	109 (4.8%)	123 (5.5%)	135 (6.0%)

[Table 1: Outcomes stratified by treatment]

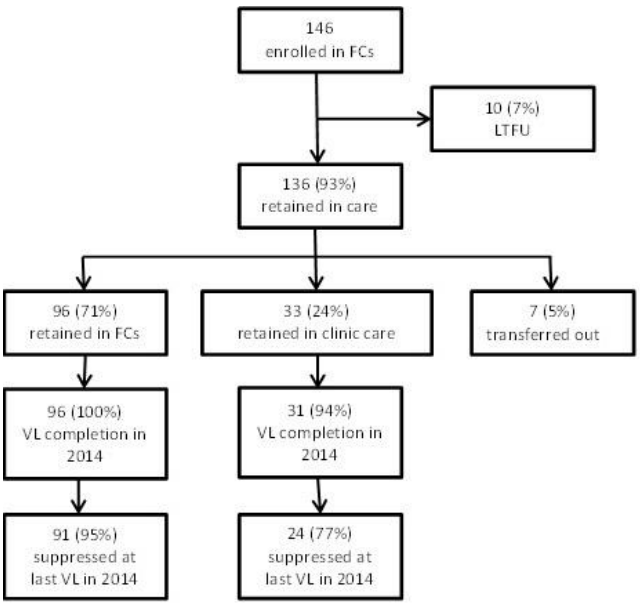
Conclusions: Overall this program showed minimal delay in treatment initiation and the overall ART treatment initiation rate was high. However a considerable proportion of all loss to follow-up (50%) happened in the pre-ART period.

WEPED884

Promoting paediatric antiretroviral treatment (ART) adherence and retention: outcomes of children receiving ART in family ART adherence clubs in Khayelithsha, South Africa

L. Wilkinson[1], R. Henwood[1], G. Patten[1], C. Kilani[1], N. Dumile[1], F. Gwashu[1], N. Mantangana[1], L. Twentiey[2], A. Shroufi[1]
[1]Medecins Sans Frontieres, Cape Town, South Africa, [2]Western Cape Provincial Department of Health, Cape Town, South Africa
Presenting author email: msfocb-capetown-deputymed@brussels.msf.org

Background: Community models of care supporting long term retention are relevant not only for adult ART populations but also for children. Family ART adherence clubs (FCs) adjusted Médecins Sans Frontières' adherence club model for family units. Fifteen children stable on ART and their caregivers (whether on ART or not) meet at the clinic every 2 months, receive support and ART supply in their club. Child disclosure forms a key part of group discussions. Children have their viral load (VL) taken twice a year with a follow-up clinical consultation.
When a child has a raised VL, requires clinical follow-up, or neither child nor caregiver attends their scheduled club visit, they return to mainstream care, including enhanced adherence support.
Methods: Patients enrolled in FCs from March 2011-September 2013 were included. Study endpoint was 30 November 2014. Patient baseline characteristics; longitudinal VL data, retention in care outcomes and child disclosure status were collected from clinic records. Patients with no recorded clinic or FC visit for three months were counted as lost to follow-up (LTFU).
Results: 146 children and 71 caregivers on ART enrolled. 45% (65) of children were female and median age was 9.1 years (IQR 6.8-11.3). Median time on ART prior to FC enrolment was 5.3 years (IQR 3.6-6.4) and in FCs was 2.7 years (IQR 1.7-3.5). Retention and virologic outcomes are reflected in diagram.



[Retention outcomes of children in family clubs]

Of those children retained in clinic care, 15 (45%) exited the FC due to a high VL while the remaining 17 (55%) were suppressed and exited due to missing their scheduled club visit or for other clinical reasons. Median time in a FC until exit was 1.9 years (IQR 1.3-3.3).
Of those children retained in FC care, 16 (100%) 7-10 years achieved partial disclosure and 57 (79%) older than 10 years achieved full disclosure.
Conclusions: FCs ensure quick access to ART for children and their caregivers stable on ART, supporting high rates of paediatric retention and adherence. FCs allow for family-centered HIV care with less interruption of daily family activities; promotion of school attendance; and an optimal setting for empowering caregivers to manage child disclosure.

Building country ownership in HIV care and prevention

WEPED885

A comparison of the institutionalization of ART programs in four categories of health facilities in Uganda

H. Zakumumpa[1], O. Galarraga[2], S.C. Bennett[3], F. Ssengooba[1]
[1]Makerere University, School of Public Health, Kampala, Uganda, [2]Brown University, School of Public Health, Providence, United States, [3]Johns Hopkins University, School of Public Health, Baltimore, United States
Presenting author email: zakumumpa@yahoo.com

Background: In 2004, Uganda commissioned a national antiretroviral therapy (ART) scale-up program with external donor support. There has been limited post-implementation research evaluating program sustainability since the trial roll-out phase. Without donor support, the sustainment of interventions is most likely to occur when they become an integral part of an organization. We sought to measure the extent of institutionalization of ART programs in health facilities in Uganda and compare institutionalization scores by health facility type.
Methods: Level of Institutionalization (LoIn) scales developed by Goodman, et al(1993) were used to measure the extent of institutionalization of ART programs at 195 health facilities in 42 districts of Uganda which received donor support between 2004 and 2009 to initiate ART services. Health facilities were categorized as Public, Private for Profit (PFP), Private Not for Profit (PNFP) and HIV Research Clinics. The 45-item questionnaire measured institutionalization based on four 'sub- systems' theorized to make up an organization (Production, Maintenance, Supportive, Managerial) assessed against two levels of institutionalization; routines (lower) and niche saturation (higher). Data were collected between December 2013 and April 2014. Descriptive statistics were generated and used to describe organizational characteristics and calculate and then rank health facilities into quartiles based on their mean institutionalization scores.

Results: The overall mean institutionalization score for participating health facilities was 3.5 (Range, 1-4) and the mean score for niche saturation, the highest level of institutionalization, was 3.2 (Range,1-4). Of the four systems, the production sub system, concerned with ART product delivery activities, scored the highest mean component score. The Managerial sub system ,concerned with coordinating the operations of other sub-systems, had the lowest mean component score. PFP health facilities had the lowest mean institutionalization score. PNFP health facilities had a higher overall mean institutionalization score than Public facilities. There was a statistical significance in the correlation between institutionalization scores and health facility type (pvalues< 0.05).
Conclusions: Programs aimed at enhancing the institutionalization of ART interventions in PFPs are recommended. ART program evaluation and supervision need strengthening across health facilities. Mainstreaming best practices from health facilities with the highest institutionalization scores could enhance sustainability of ART programs in Uganda and other resource-limited settings.

Changes in policy and practice

WEPED886

Putting into perspective how criminalization of certain practices is impeding evidence-based policy formulation in Malawi

K. Phiri[1], E. Njiwa[2], A. Makawa[3]
[1]Liberty Consulting, Zomba, Malawi, [2]University of Malawi, Chancellor College, Zomba, Malawi, [3]Baylor College of Medicine, Lilongwe, Malawi
Presenting author email: kenphiri@yahoo.co.uk

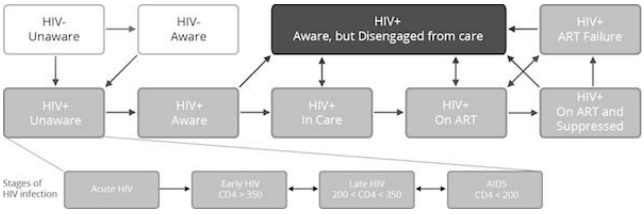
Background: Policies based on local research evidence are critical in the management of HIV and AIDS. However, continued criminalization of certain practices discourages researchers from conducting research in populations which undertake those practices, thereby impeding evidence-based policy formulation. Approximately 50% of all health research in Malawi is conducted through the Malawi College of Medicine and its various affiliates. We investigated the amount of HIV/AIDS related-research in gays, lesbians and commercial sex workers that has been conducted through the Malawi College of Medicine and its affiliates from 2012 - 2014. Malawi, one of the countries hardest hit by AIDS, still criminalizes same-sex partnerships and commercial sex work.
Methods: We used key words HIV, AIDS, ART, CD4, HTC, VCT, VMMC and their definitions, sex, partners and condoms to search the research study database for the College of Medicine Research and Ethics Committee (COMREC) for HIV/AIDS-related studies submitted for ethics approval from 2012 - 2014. We then cross-referenced the results with key words gay, men having sex with men, MSMs, homosexuals, lesbians, women having sex with women, commercial sex workers, CSWs, street girls, call girls and prostitutes. We also manually read through all the titles of submitted studies. Where clarification was required, study investigators were contacted.
Results: In 2012 COMREC reviewed 158 studies, of which 36 were HIV/AIDS-related with 1 (2.8%) focusing on gays. The same study focused on lesbians and commercial sex workers. In 2013 COMREC reviewed 169 studies, of which 32 were HIV/AIDS-related, with no study (0%) focusing on gays, no study (0%) focusing on lesbians and 1 (3.1%) commercial sex workers. In 2014, COMREC reviewed 159 studies, of which 20 were HIV/AIDS-related, with 1 study (5.0%) focusing on gays, no study (0%) focusing on lesbians and no study (0%) focusing on commercial sex workers.
Conclusions: Far too inadequate research to guide evidence-based policy formulation for management of HIV/AIDS in gays, lesbians and sex workers is being conducted in Malawi. Health workers may therefore be using arbitrarily policies to manage HIV/AIDS in these populations.

WEPED887

Economic and epidemiological impact of early antiretroviral therapy (ART) initiation in India depends on the HIV continuum of care

M.V. Maddali[1], D. Dowdy[2], A. Gupta[1,2], M. Shah[1]
[1]Johns Hopkins University, School of Medicine, Baltimore, United States, [2]Johns Hopkins University, Bloomberg School of Public Health, Baltimore, United States
Presenting author email: manoj.maddali@jhmi.edu

Background: Recent WHO guidance advocates early ART initiation at higher CD4 counts to improve survival among people living with HIV and reduce HIV transmission. Models suggest early ART initiation in India is cost-effective, but have not considered that suboptimal engagement in care may limit potential benefits.
Methods: Our dynamic compartmental model of the Indian HIV epidemic replicates transmission, disease progression, and health system engagement among Indian adults (15-64 years), stratified by sex, HIV risk-profile, and serostatus. Primary outcomes were prevalence, incident cases, AIDS-related deaths, quality-adjusted-life-years (QALYs), and costs over a 20-year time-horizon, assessing how the impact of early ART initiation was modified by the HIV continuum of care (i.e. screening, linkage, retention in care, ART usage).
Results: Assuming optimal levels of engagement in HIV care after diagnosis, we project 882,000 new HIV infections and 532,000 AIDS-related deaths in India over twenty years with current practice (ART delayed until CD4 ≤350 cells/mm^3). In this idealized care continuum, earlier ART initiation could avert 306,000 new infections (36% reduction) and 79,000 AIDS-related deaths (15% reduction), at a cost-effectiveness of $504/QALY-gained. However, when incorporating realistic gaps in care (i.e. incomplete linkage and long-term retention), projections of 20-year outcomes (ART initiation at CD4 ≤350) rose to 1,277,000 new HIV infections and 999,000 AIDS-related deaths. In this more realistic setting, early ART initiation remained highly cost-effective ($568/QALY-gained) but averted only 234,000 new infections (18% reduction) and 94,000 AIDS-related deaths (9% reduction). Implementing early ART initiation with expanded screening for high-risk groups (i.e. test and treat strategies) offered only modest benefits at current rates of care-retention (283,000 new infections averted; 22% reduction). Alternatively, a 50% reduction in the rate of disengagement from care more than doubled the impact of early ART initiation, averting 445,000 new HIV infections (35% reduction) and 331,000 AIDS-related deaths (33% reduction).
Conclusions: Early ART initiation in India is highly cost-effective, but has modest absolute benefits in reducing new HIV infections and averting AIDS mortality if current rates of retention persist. Sustained economic investments and improved strategies to strengthen the HIV continuum of care are required to realize the full potential of early ART initiation.



[Model schematic our dynamic compartmental model]

Care Continuum	ART Initiation	New HIV infections	AIDS-related deaths
Idealistic	Delayed ART initiation	882,000 (Reference)	532,000 (Reference)
Idealistic	Early ART initiation	576,000 (36% reduction)	453,000 (15% reduction)
Realistic	Delayed ART initiation	1,277,000 (Reference)	999,000 (Reference)
Realistic	Early ART initiation	1,043,000 (18% reduction)	905,000 (9% reduction)
Realistic	Early ART initiation and annual targeted screening	994,000 (22% reduction)	870,000 (13% reduction)
Realistic	Early ART initiation and 50% reduction in rate of disengagement in care	832,000 (35% reduction)	668,000 (33% reduction)

[Early ART initiation impact over 20 years]

WEPED888

What does a national response to closing the gap in pediatric and adolescent HIV treatment cost? Zambian costing model for universal pediatric treatment

E. McCarthy[1], G. Munthali[2], M. Lu[3], S. Diamond[4], P. Haimbe[5], P. Navario[6], N. Shaffer[7], E. Ghanotakis[8], A. Mwango[2]
[1]Clinton Health Access Initiative, Applied Analytics Team, Lusaka, Zambia, [2]Ministry of Health, Lusaka, Zambia, [3]Clinton Health Access Initiative, Kampala, Uganda, [4]Clinton Health Access Initiative, Washington, DC, United States, [5]Clinton Health Access Initiative, Lusaka, Zambia, [6]New York University, Global Institute of Public Health, New York, United States, [7]World Health Organization, HIV/AIDS, Geneva, Switzerland, [8]Elizabeth Glaser Pediatric AIDS Foundation, Washington, DC, United States
Presenting author email: emccarthy@clintonhealthaccess.org

Background: Zambia has set aggressive targets for its HIV treatment program. The recently adopted national guidelines call for access to treatment for all 149,000 HIV-positive children < 15 years and renewed focus on the 38,500 HIV-positive adolescents. These groups have lagged behind adults in treatment coverage. Zambia's government needed to understand the cost of pediatric and adolescent treatment scale-up under these new guidelines for informed budgeting, forecasting and implementation decisions.
Methods: We conducted a macro-level cost analysis from the government perspective with a 5-year time horizon (2014-2018) including the following variable costs: antiretroviral drugs, cotrimoxazole, CD4 tests, viral load tests, and health worker salaries. Fixed and programmatic costs were excluded. Using Avenir Health's AIDS Impact Model, we estimated patient volumes and age. We collected cost estimates from the Ministry of Health. Five scale-up scenarios

- varying treatment eligibility guidelines, pace of scale-up and drug regimen choices - were analyzed and compared in an Excel-based mathematical model.

Results: Under World Health Organization (WHO) HIV treatment guidelines, average cost per patient year is estimated at US$453 for children and US$249 for adolescents. If scale-up were to follow the aggressive rate needed to reach universal access (defined as 95% coverage) by 2015 and close the gap between coverage of adults and children, total program costs for pediatrics are estimated at US$48.8 million in 2014 and then on average US$60 million per year through 2018. Adolescent total program cost is estimated at $US5.8 million in 2014, growing steadily until US$9.9 million in 2018. The Zambian national guidelines have a higher estimated cost than WHO pediatric guidelines due to Zambia's decision to include all children < 15 rather than all < 5 years, and drug regimen recommendations.

Conclusions: In Zambia, a modeling exercise provided policy-makers and planners with the evidence on costs to develop a budgetary roadmap that will allow them to expand HIV treatment to children and adolescents, enabling treatment levels to soon reach that of adults and advance to full coverage. The model and process can be applied in new contexts where governments need to make informed policy and implementation decisions to efficiently scale-up HIV treatment.

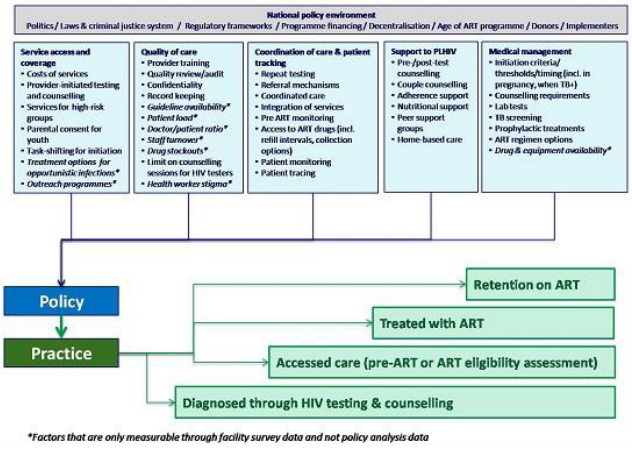
WEPED889

From policy to practice? A comparison of national HIV policy implementation in six sub-Saharan African countries with generalised HIV epidemics

A. Wringe[1], K. Church[1], K. Machiyama[1], X. Gómez-Olivé[2], E. Geubbels[3], A. Dasgupta[1], M. Njage[4], B. Zaba[1], D. Michael[5], E. Mpandaguta[6], F. Kiweewa[7], A. Nyaguara[8], T. Lutalo[9], J. Todd[1]
[1]London School of Hygiene and Tropical Medicine, Population Studies, London, United Kingdom, [2]MRC/Wits Rural Public Health and Health Transitions Research Unit, Johannesburg, South Africa, [3]Ifakara Health Institute, Ifakara, Tanzania, United Republic of, [4]Consultant, Nairobi, Kenya, [5]National Institute of Medical Research, Mwanza, Tanzania, United Republic of, [6]Manicaland HIV/STD Prevention Project, Harare, Zimbabwe, [7]Makerere University School of Public Health, Kampala, Uganda, [8]Kenya Medical Research Institute, Kisumu, Kenya, [9]Rakai Health Sciences Program, Kampala, Uganda
Presenting author email: alison.wringe@lshtm.ac.uk

Background: Understanding contradictions between HIV policies and their implementation is essential for improving the effectiveness of national HIV programmes. As part of a study to investigate HIV mortality in African health and demographic surveillance sites (HDSS) in six countries, we compared national policies on HIV testing, HIV care and treatment, and retention in care with survey data from health facilities serving the HDSS populations in order to assess policy implementation.

Methods: A policy extraction tool was developed to review and compare 120 national HIV policy documents published in Kenya, Malawi, South Africa, Tanzania, Uganda, and Zimbabwe between 2003 and 2013, covering delivery of testing, prevention of mother-to-child transmission, and HIV care and treatment services. 139 purposively-sampled health facilities in nine HDSS sites in the same countries were surveyed between October 2013 and May 2014 using a structured questionnaire covering the same services. A conceptual framework (figure 1) and related indicator tool were developed to identify and compare HIV policies and programme implementation by factors that influence HIV-related adult mortality across the HIV care continuum including
i) service access;
ii) quality of care;
iii) service coordination and patient tracking;
iv) patient support and v) medical management.



[Fig1:Conceptual framework of policy implementation]

Results: Provision of HIV testing services closely followed national policy in all sites, with the exception of provider-initiated testing and counselling which was explicit policy in all countries, but not systematically implemented in all the facilities surveyed. Malawi emerged as having the closest relation between its progressive HIV care and treatment policies, designed to maximise the numbers of infected persons accessing antiretroviral therapy, and their implementation. In contrast, Zimbabwe's relatively detailed policies in relation to HIV testing and access to care and treatment did not translate into service provision across most of the facilities surveyed. There was wide variation between countries' policies to encourage retention in care and treatment programmes, and also in relation to their implementation among the facilities surveyed in each country.

Conclusions: Wide variation was observed in the degree of implementation of HIV policies influencing service access and retention across the diagnosis-to-treatment cascade in the six countries which may contribute to HIV mortality differences between sites.

WEPED890

Evaluating pricing policies of pharmaceutical companies as a rationale for introducing measures related to removal of intellectual property barriers to scale up access to HIV treatment

S. Golovin[1], T. Khan[2]
[1]International Treatment Preparedness Coalition in Eastern Europe and Central Asia, St. Petersburg, Russian Federation, [2]International Treatment Preparedness Coalition in Eastern Europe and Central Asia, Kiyv, Ukraine
Presenting author email: sergey.golovin@itpcru.org

Background: Currently, Russia is facing a growing HIV epidemic. The number of people receiving treatment is over 160,000, but the number of people in need is nearly twice as many. The monitoring of the government procurement of antiretrovirals shows that for many drugs prices have remained high over a 3-year period.
Experience shows that some countries have successfully used regulatory tools related to intellectual property (TRIPS flexibilities) to reduce prices for antiretrovirals. In 2014, ITPCru analyzed the pricing trends to see whether they can be used as a rationale for introducing such measures.

Methods: To evaluate the pricing trends for antiretrovirals, 5051 tenders were analyzed in 2012-2014. The key research parameter was minimal price. To evaluate the generic drug landscape, the official drug register was used; as search entries, international non-proprietary names were used. Two groups of drugs were selected based on the criteria of the presence/absence of generic versions. The choice of drugs is based on an already available analysis of the most popular drugs used in Russia. The patent landscape and the regulatory instruments available for use in Russia were analyzed using semi-structured interviews and literature review.

Results: We found that in the group of drugs with generics, the price decrease varied from 113% (abacavir, number of generics - 2) to 1946% for lamivudine (number of generics drugs - 6), whereas in the group of patented drugs without generic versions the price decrease varied between 1% (raltegravir, atazanavir and lopinavir/ritonavir) and 9% (darunavir). The interviews and literature review have shown that there is a range of tools related to IP available under the current regulatory framework to force companies to reduce prices, including compulsory licenses and patent opposition.

Conclusions: The study has confirmed that in the absence of generic versions, brand companies do not change their pricing policies voluntarily; in contrast, competition drives the prices down by a great margin. Based on the result of the drug procurement monitoring, interviews with experts and literature review, it is proposed to introduce measures related to removing IP barriers which can be used according to the current laws, such as compulsory licensing and patent opposition.

WEPED891

How to translate high level political targets into programmatic planning for key populations at country level?

B. Mathers[1], A. Verster[2], M. Rodolph[3], K. Sabin[4], J.M. Garcia Calleja[3]
[1]UNSW, Sydney, Australia, [2]WHO, HIV Dept, Geneva, Switzerland, [3]WHO, Geneva, Switzerland, [4]UNAIDS, Geneva, Switzerland
Presenting author email: versteran@who.int

Background: Globally, 40% to 50% of all new HIV infections among adults are estimated to occur among key populations (KP) and their immediate partners. KP are defined as men who have sex with men, people who inject drugs, people in prisons and other closed settings, sex workers and transgender people. WHO recommends an evidence-based package of interventions for the prevention, diagnosis, treatment and care of HIV among KP. Coverage rates for these interventions among KP are currently only reported by about 50% of countries and many are well below the UNAIDS targets of '90 -90- 90' by 2020 needed to counter the AIDS epidemic.

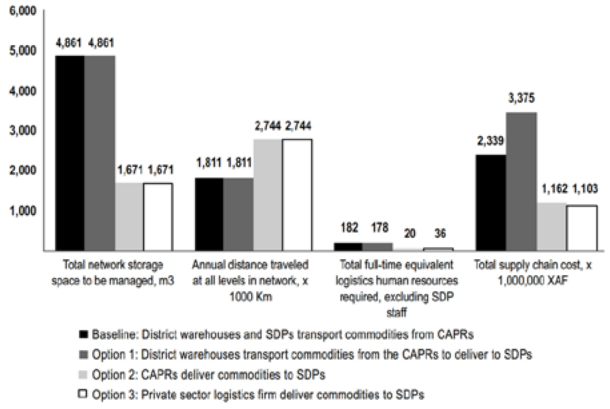
Methods: A technical tool was developed to set targets and measure the availability, coverage, and quality for the recommended interventions. It also includes indicators for assessing the key factors related to the enabling environment and examining the outcome and impact of efforts to address HIV among KP. This tool was developed by reviewing relevant existing guidance and in consultation with relevant stakeholders (UN partner agencies, academia, community representatives, programme managers, donors and implementers) to reach consensus on the proposed framework, indicators and indicative targets. The framework of this tool is based on the 2009 technical tool to set targets for PWID that was revised in 2012.
Results: By proposing indicative targets and a set of practical indicators with guidance on data collection and interpretation, this tool sets out to support national programmes and donor agencies to programme and monitor national HIV responses for KP.
Conclusions: It is widely acknowledged that an effective AIDS response needs to effectively include and address key populations. This tool provides countries with guidance to set ambitious, yet achievable, targets for each intervention of the essential package for KP and measure progress as countries work towards achieving the UNAIDS '90-90-90' targets.

WEPED892

Addressing the unmet need for ART among HIV+ women and newborns in Cameroon through strengthening the supply chain of PMTCT commodities

E. Nfor[1], K. Kakanda[2], G. Buki[3], A. Kane[4], J. Dongang[4]
[1]Management Sciences for Health, Center for Pharmaceutical Management/SIAPS, Gainesville, United States, [2]MSH, CPM/SIAPS, Arlington, United States, [3]Management Sciences for Health, CPM/SIAPS, Kigali, Rwanda, [4]MSH, CPM/SIAPS, Yaounde, Cameroon
Presenting author email: enfor@msh.org

Background: The Government of Cameroon and its partners have made major investments in the last decade in prevention, treatment, and care of HIV-infected patients. However, unmet need for antiretroviral therapy (ART) among HIV-positive pregnant women remains high at 66%. Critical to satisfying this need is ensuring adequate availability of prevention of mother-to-child transmission (PMTCT) commodities for rollout of new Option B+ guidelines.
The Cameroon supply system consists of a cost recovery system for essential medicines and other health commodities and a free-of-charge system for priority commodities including those for PMTCT and ART. This study examines options for improving the supply and availability of these commodities.
Methods: Supply chain (SC) operational data was collected in July 2014 from central (CENAME) and 4 regional warehouses (CAPRs); 10 district stores; and 30 service delivery points (SDPs), including ART and PMTCT sites. The study also included seven central private-sector logistics firms. In addition, SC cost data was obtained from CENAME and CAPRs financial statements audited in 2013. Data collected served for analysis of three options to improve effectiveness of delivering PMTCT commodities, based on the four variables detailed in Figure 1.
Results: Asset utilization within the cost recovery system ranged between 73% and 89% while inventory turnover was at 1.5. Therefore, a reliable supply of medicines to SDPs is ensured. However, for PMTCT and ART commodities, distribution to the SDPs was unreliable (in 2013, 40% of prescriptions remained unfilled). Meanwhile, results of the options analysis indicated that the model of CAPRs delivering PMTCT commodities to SDPs was the most desirable. Although the distance traveled was higher, the need for network storage space was minimal. Moreover, its total cost and human resource requirements were more favorable.



[Figure 1: PMTCT and ART supply options analysis]

Conclusions: As a result of disseminating the findings, the Ministry of Health adopted Option 2. PMTCT free-of-charge commodities are also amenable to being managed within the existing effective cost recovery system.

Capacity building initiatives

WEPED893

A novel instrument to assess capacity to consent for healthcare among individuals with problematic substance use and who are homeless or unstably housed

D. Taylor[1], A. Ho[2], L.C. Mâsse[2], N. Van Borek[3], N. Li[4], M. Patterson[4], G. Ogilvie[2], J. Buxton[2]
[1]BC Centre for Disease Control, Clinical Prevention Services, Vancouver, Canada, [2]University of British Columbia, Vancouver, Canada, [3]McMaster University, Hamilton, Canada, [4]Simon Fraser University, Burnaby, Canada
Presenting author email: darlene.taylor@bccdc.ca

Background: Individuals who misuse substances and who are homeless or unstably housed (IMSH) are at higher risk of acquiring HIV, sexually transmitted infections and blood-borne infections. They also have greater medical needs than the general population; however, providing healthcare with informed consent is challenging as many IMSH have impaired cognition due to substance use. A Capacity Assessment Instrument for People who misuse Substances (CAIPS) has been developed to assist clinicians in deciding if their clients lack capacity to consent to healthcare (CTC-HC).
Methods: Eleven items were identified by examining existing capacity assessment instruments and by interviewing nurses who deliver services to IMSH. A panel of experts assessed the items for construct and content validity and the items were revised as needed. A validation study was conducted with veteran outreach nurses by comparing the CAIPS instrument to two gold standards:
1) a clinical assessment by a psychiatrist and
2) assessment with the MacArthur Assessment Tool for Treatment (MacCAT-T).
Reliability was examined by calculating a Chronbach's alpha. A confirmatory factor analysis was conducted to determine dimensionality. Sensitivity and specificity were determined using the composite CAIPS score compared to each gold standard.
Results: The final CAIPS instrument consists of items that address understanding, voluntariness, orientation, ability to communicate, sustained attention, distorted reality, appreciation, reasoning, expression of choice, decision making demands, and physical indication of substance use. A total of 302 individuals (182 [60.3%] male; 124 [41.1%] Caucasian) participated in the validation phase. The CAIPS instrument demonstrated good internal reliability (Cronbach's alpha: 0.861 - 0.893) and inter-observer reliability (weighted kappa statistic of 0.657). The factor analysis confirmed the unidimensionality assumption. Sensitivity was 0.75 - .81 and a specificity was 0.63 - 0.51.
Conclusions: The CAIPS instrument is a reliable tool with moderate validity and is the first validated capacity assessment instrument available to assess CTC-HC among IMSH. It is hoped that this new instrument will enable nurses to make informed decisions surrounding the capacity of their clients and, in turn, will result in increased health equity for IMSH. Future research is required to validate the instrument with other healthcare professionals such as physicians and paramedics.

WEPED894

HIV and STI prevalence among men who have sex with men in 3 major cities in Uganda

N. Ritah
Nakimbugwe Foundation for HIV/AIDS, Research Department, Kampala, Uganda
Presenting author email: nabbosaritah8@gmail.com

Background: Although there is increasing evidence of the risks associated with HIV acquisition and transmission among MSM in Uganda, practically nothing is known about other sexually transmitted infections (STIs) in this population.
Methods: A total of 712 MSM were recruited between August and September, 2010 through respondent-driven sampling (RDS) from Kampala (43.3%), Masaka (29.5%) and Mbarara (27.2%).
In addition to information elicited about reported STI and risk behaviors, screening for Syphilis (S), Chlamydia trachomatis (CT), Gonorrhaea (GN) and Hepatitis B (HBV) were also conducted.
Results: Most of the MSM were aged 18-25years and a large proportion (>60%) reported having multiple male and female partners with whom they often had unprotected sex. Whilst 31% reported STIs in the past 12 months, only 26 (3.7%) reported STI symptoms at the time of the survey. Weighted prevalence of STIs ranged from 0.5-1.9% for syphilis, 4.2-8.9% for gonorrhea, 0-34.5% for Chlamydia and 21.4-21.9% for hepatitis B. Population based estimates of HIV was highest in Masaka (34.9%) followed by Kampala (15.2%) and Mbarara (11.3%). Overall, prevalence of STIs was low in Masaka and Mbarara.
However, in Kampala, prevalence of Chlamydia was highest among MSM who had casual sex partners [AOR=2.6 (1.2-5.5)] and among those who self-identified as homosexual [AOR=2.8 (1.3-6.0)]. Similarly, hepatitis B infection was more likely among the more educated [AOR=1.7 (1.01-2.7)] and MSM who had sex with men exclusively compared with those who had with both men and women [AOR=2.0 (1.2-3.3)].This study afforded many MSM first time opportunities of being tested and treated for STIs.

Conclusions: There is a large unmet need for MSM in Uganda. This calls for an urgent need for targeted screening and vaccination to prevent the untoward squealed of STIs among MSM in Uganda.

WEPED895

Fleet management system: a useful tool in improving efficiency and effectiveness in PMTCT and pediatric ART service support in Elizabeth Glaser Pediatric AIDS Foundation Zimbabwe programs

J. Shonhe[1], A. Magoronga[2], T. Ndoro[2], L. Katirayi[3]
[1]Elizabeth Glaser Pediatric AIDS Foundation, Procurement and Logistics, Chitungwiza, Zimbabwe, [2]Elizabeth Glaser Pediatric AIDS Foundation, Operations, Harare, Zimbabwe, [3]Elizabeth Glaser Pediatric AIDS Foundation, Vancouver, Canada
Presenting author email: lkatirayi@pedaids.org

Background: In an effort to strengthen support to the national PMTCT and pediatric ART program, the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) acquired 40 vehicles between 2011 and 2013 to enhance PMTCT and pediatric treatment service delivery. Thirty-seven vehicles were deployed to support all 62 districts throughout the country. Given the size and spread of the area covered, effective fleet management was a challenge. There was no independent way of verifying the trips made against the approved travel plans. Irresponsible driving, speeding, and general abuse of the vehicles was occurred. One major accident was reported and maintenance and service costs increased up to September 2013. Monitoring the position and use of the vehicles during site support trips with absolute accuracy from the EGPAF office in Harare became necessary.
Methods: Between September 2013 and April 2014, EGPAF installed a fleet management system with telematics, GPS tracking, and anti-theft mechanisms. The system allowed for real time tracking of vehicles, and it generated reports or alerts on reckless driving. All field vehicles were geo-fenced within their respective districts to control and monitor the trips made against approved plans. Manual vehicle logbooks were compared by the Logistics Team with an online logbook generated by the system in order to check if the program vehicles were utilised as planned and approved.
Results: Several benefits accrued as a direct result of the system. All vehicles were monitored at all times. In six months, maintenance costs were reduced by 12% for all vehicles. During the same period, fuel efficiency increased by 33% and no accidents were recorded after system installation. Speeding alerts decreased from 51 during the October 2013 (first month of system installation) to only one during the month of April 2014.
Manual logbook recordings compared exactly with the online logbook system of approved monthly travel plans. In summary, the system sustained the vehicles in a roadworthy and usable state up to the end of the program.
Conclusions: The installation of the fleet management system strengthened efficient use of program vehicles, ensuring that donor resources achieved the maximum benefit in country program implementation.

WEPED896

Lesotho's HIV clinical mentorship program from 2005-2015: a health systems strengthening approach

D. Thomas[1], E. Mandara[2], P. Ramphalla[3], A. Masheane-Moseneke[4]
[1]Canadian Association of Hepatology Nurses, Vancouver, Canada, [2]Clinton Health Access Initiative, Dar es Salaam, Tanzania, United Republic of, [3]PEPFAR, Centre for Disease Control, Maseru, Lesotho, [4]Government of Lesotho, Disease Control, Maseru, Lesotho
Presenting author email: denise.thomas@fnha.ca

Background: Clinical mentoring is a critical component of the Government of Lesotho's comprehensive approach to scale-up of HIV prevention, treatment and care. It is the link between the gap from pre service training and clinical practice, allowing health care workers to practice new skills and develop confidence in their own clinical abilities with the support of an experienced clinician.
Methods: A retrospective review of a national HIV Clinical Mentorship Program, designed based on 6-week implementation experience in 2005; five (5) expatriate clinical mentors from Namibia, Canada, and USA. Standard reporting tools allow each mentor to tailor on-site training and skills transfer, local mentor evaluation of their ability to impart new guidelines, referrals and linkages along the cascade of HIV prevent and care. Using monitoring and evaluation provides impact evidence to inform program planning and response-guided mentoring. The quality improvement model incorporates plan-do-study-act cycles (PDSA), this approach is where clinicians pilot a change for improvement on a small scale, observe the results, and adjust or expand it based upon results.
The methodology focuses on simple, low-cost solutions that can be implemented with limited resources to address implementation barriers.
Results: Promising practices at the individual, health systems and patient level resulted in improvements including:
1. Partnerships established with local health care providers to collectively address health system challenges;
2. Transition from an out sourced program to a national driven and owned program; and
3. Monitoring and evaluation tools contingent on mentor self reporting and health care provider responses.

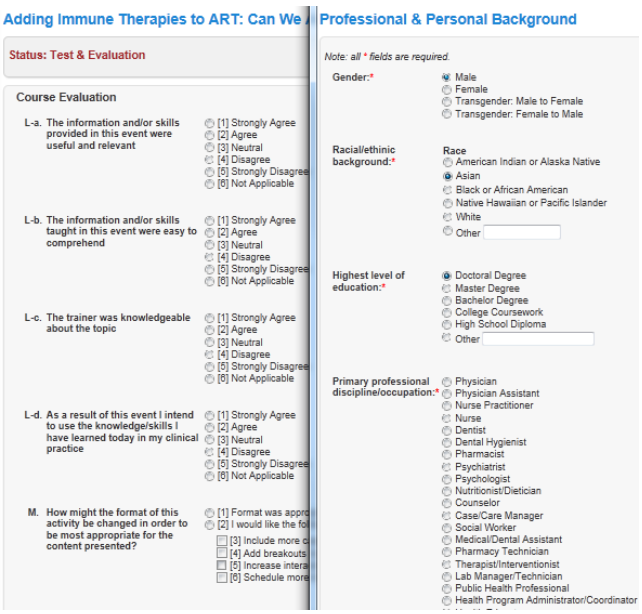
Conclusions: Results from Lesotho's HIV clinical mentorship program and interest from other countries suggest that individual, health systems, patient level and quality improvement with the model for improvement are interventions that increased quality of care in Lesotho. Using these methods, Lesotho's HIV clinical mentors increase change at twice the rate of expatriate mentors and increases local country ownership. 10-years of country program implementation experience suggests HIV clinical mentorship is an essential in-service program that contributes to strengthened health system linkages and individual health care providers' confidence to scale up new guidelines and is a high impact approach to high quality health care provider support.

WEPED897

An assessment of New York State (NYS) Department of Health HIV-HCV-STD clinical education initiative (CEI) online training program by healthcare providers

D. Wang, A. Luque
University of Rochester Medical Center, Rochester, United States
Presenting author email: dongwen_wang@urmc.rochester.edu

Background: Since 2009, the NYS HIV-HCV-STD CEI online training program has developed 238 multimedia learning modules, 97 online CME/CNE courses, 12 interactive case simulation tools, and various other resources. These resources are delivered to tens of thousands clinicians through web, mobile apps, email newsletters, and online social networks. CEI website has recorded 142,261 user sessions and 724,995 pageviews from 170+ countries, ranked by Google as a top site for HIV-HCV-STD clinical education. Here we report an assessment of CEI online training program, focusing on clinicians' evaluation of resources, their self-reported knowledge increase, intention to use knowledge, and analyses of clinicians' professional/personal background.
Methods: We selected all 12 online courses from CEI's new student portal, with an online questionnaire for evaluation.



[Data collection from the new CEI Student Portal]

Measurements of resource evaluation and utilization included usefulness/relevance, easy comprehension, trainers' knowledge, appropriate format, knowledge increase, intention to use knowledge, and intention to change practice. We analyzed clinicians' demographics, education level, profession, years in practice, employment settings, patient caseload, and services provided as the co-variants.
Results: From October to December 2014, we recorded 335 completions of CEI online courses. The clinicians' evaluations were positive (useful/relevant, 88.66%; easy comprehension, 87.76%; knowledgeable trainer, 91.04%; appropriate format, 84.18%). In terms of impact, 83.58% indicated plan to use the knowledge learned, 46.27% indicated >=1 level knowledge increase, and 44.19% providing direct patient services indicated intention to make changes in practice.

Measures	# of Positive Responses	Percentage	# of Neutral and Negative Responses	Percentage	Total # of Responses
useful and relevant	297	88.66%	38	11.34%	335
easy to comprehend	294	87.76%	41	12.24%	335
knowledgeable trainer	305	91.04%	30	8.96%	335
intend to use knowledge	280	83.58%	55	16.42%	335
format appropriate	282	84.18%	53	15.82%	335
increasing knowledge	155	46.27%	180	53.73%	335
will change practice	76	22.69%	259	77.31%	335
will change practice (excluding those don't provide direct patient services)	76	44.19%	96	55.81%	172

[Clinicians' Evaluation of Online Resources]

Co-variant analyses showed:
1) clinicians from rural areas, with a small caseload (<=10 patients/month), and not yet providing direct patient services (but planning to) had the most positive evaluations;
2) the individual courses taken, clinicians providing particular types of services, and years of practice had mixed responses, and;
3) clinicians' demographics, education levels, professions, and employment settings made no differences.

Conclusions: Initial assessment has shown that the CEI online courses are very positively evaluated by its clinician audience. While certain responses may depend on individual courses and particular clinical services, clinicians from rural areas, with a small caseload, and new to the field of HIV-HCV-STD care are likely to have across-the-board benefits to participate in the CEI online training program to incorporate the learned into clinical practice.

WEPED898

Strategic approach to establishing an international pharmacology specialty laboratory in a resource-limited setting

T.G. Monera[1], D. Duri[2], T. Mudzviti[1], F. Makita[1], T. Mtisi[3], C. Maponga[1], G. Morse[4], UZ-IPSL Development Team
[1]University of Zimbabwe College of Health Sciences, School of Pharmacy, Harare, Zimbabwe, [2]University of Zimbabwe College of Health Sciences, Medical Microbiology, Harare, Zimbabwe, [3]Ministry of Health and Child Care, Harare, Zimbabwe, [4]SUNY Buffalo, Buffalo, United States
Presenting author email: moneratg@yahoo.co.uk

Background: There has been a growing number of clinical studies involving drug interventions conducted in Zimbabwe. Unfortunately, laboratory facilities with expertise in the assay of drugs in biological samples (often the primary outcome) is limited. Specimen have had to be shipped abroad for analysis. A collaboration between the Schools of Pharmacy at the University of Zimbabwe and the State University of New York at Buffalo, sought to address this gap by establishing a Pharmacology Specialty Laboratory in Zimbabwe. This paper describes the progress, challenges and strategies.
Methods: The laboratory was established with the assistance of the Aids Clinical Trials Group. An award was made in 2011 for its establishment as a developmental Pharmacology Specialty Laboratory The process involved five major steps; namely acquisition of start-up equipment, human resources training, development of quality management systems, HPLC method transfer and validation, laboratory licensure, certification and accreditation.
Results: Two HPLC machines were donated through the University at Buffalo. Eight scientists and technicians have been trained in laboratory operations, quality management systems and HPLC techniques. Standard operating procedures have been developed and staff trained. HPLC method transfer and partial validation have been done for plasma nevirapine and efavirenz Initial laboratory space at the University was inadequate. Some target drugs required more sensitive assays. Strategic partnerships with the national drug regulatory authority and a private biomedical institute, enabled location of bigger laboratory space and access to LC/MS/MS for development tenofovir and atazanavir hair assays. The prevailing socioeconomic situation has limited available technical support and supplies. Reliance on regional vendors has further constrained the limited developmental laboratory funding. Close liaison with an established regional International Pharmacology Specialty Laboratory and the Aids Clinical Trials Group Clinical Pharmacology Quality Assurance program has been helpful in locating cost-effective vendors and achieving the goals. Finalization of ISO15189:2003 accreditation and CPQA Certification requirements is currently underway.
Conclusions: Significant progress has been realized in the establishment of an International Pharmacology Specialty Laboratory in Zimbabwe. Strategic partnerships have been beneficial in addressing the challenges faced.

WEPED899

Building capacity for implementation and sustainability of harm reduction training to prevent HIV transmission in Tijuana, Mexico

E. Patiño[1,2,3], M.L. Rolón[1,2], J. Arredondo[1], T. Rocha[1], H.O. Olivarría Horcasitas[4], M.G. Rangel Gómez[5], S.A. Strathdee[1], L. Beletsky[1,6]
[1]University of California San Diego, Division of Global Public Health, La Jolla, United States, [2]Universidad Xochicalco, Escuela de Medicina, Tijuana, Mexico, [3]Dirección Municipal de Salud, Tijuana, Mexico, [4]Instituto de Capacitación y Adiestramiento Profesional, Tijuana, Mexico, [5]Secretaría de Salud, Tijuana, Mexico, [6]Northeastern University, School of Law & Bouvé College of Health Sciences, Boston, United States
Presenting author email: efrainpatinom@hotmail.com

Background: Policing practices (e.g., syringe confiscation) are pervasive HIV risk factors among people who inject drugs (PWID) in the Mexico-US border region and other settings. We sought to develop creative, cost-effective training tools to educate police officers about occupational and public health elements of HIV prevention in Mexico and other resource-constrained settings. The development of the training also served as an experiential learning exercise for forensic science students in a college setting.
Methods: Our binational team included faculty and graduate students from US and Mexican universities, and the Department of Municipal Public Safety in Tijuana, Mexico. We developed basic educational modules that bundled harm reduction training with occupational safety for active duty police officers in Tijuana. Training focused on policing behaviors and prevention of HIV and viral hepatitis risks related to needle-stick injuries. We piloted these educational materials with forensic science students, who then created original videos to enhance harm reduction messages for the police, using smart-phones. The educational modules and smartphone videos were then piloted with police academy instructors.
Results: Over a four-month period, 30 forensic science students received the educational modules and created 3 videos:
(1) inappropriate frisking that could expose to needle-stick injuries,
(2) on-site visits to drug treatment centers in Tijuana highlighting evidence-based drug treatment, and;
(3) an in-depth interview with a rehabilitated drug user to generate awareness on the path to rehabilitation and reduce stigma.
A total of 15 police academy instructors were trained. All enthusiastically embraced the content of the training modules and provided feedback for refining materials. Approval was granted by the Tijuana Mayor and Police Academy Director to integrate the training modules and videos into regular police refresher training, offered by trained police academy instructors.
Conclusions: This multi-sectoral, binational collaboration led to low-cost approaches to develop and sustain harm reduction training for active duty police officers. These modules form the basis of a structural intervention for active duty police officers that aims to reduce the incidence of needle-stick injuries as well as policing behaviors that are well-established drivers of needle sharing among PWID.

WEPED900

Training internal medicine residents in the care and treatment of HIV-1 infected patients: a model to increase physician providers for HIV patient care

L. Saravolatz, S. Valenti, S. Szpunar, R. Hilu, L. Johnson
St John Hospital and Medical Center, Internal Medicine, Grosse Pointe Woods, United States

Background: Currently there are approximately 4500 HIV providers in the United States; 50% will retire within the next 10 years leaving a shortage of HIV trained providers. A proposed solution to this problem is to train internal medicine residents to be primary care providers in the care and treatment of HIV-1 infected patients.
Methods: All internal medicine residents at St. John Hospital and Medical Center in Detroit, Michigan, entering our residency program between July 1, 2012 and July 1, 2014, were trained over the course of their three-year residency program in many aspects of the care and treatment of HIV-infection. Training included HIV lectures, on-line training, and a clinic course with one-on-one mentoring by an Infectious Disease, HIV Specialist. Knowledge was tested before and after the training; data were analyzed using the paired t-test.
Results: Eighty internal medicine residents completed three years of HIV training (2012, 2013 entrants); 30 residents took both a pre- and post-test. Overall, the post-intervention mean score (86.95%±6.3) was significantly higher than the pre-intervention mean (51.35%±14.9), p< 0001). When assessed by program year (PG), there were significant gains in knowledge from baseline to post-intervention for all three years (PGY1: Pre 43.3%±24.2 Post: 89.7%±4.0 p=0.005; PGY2: Pre 55.4%±11.3, Post 87.9%±6.9, p< 0.0001; PGY 3: Pre 53.2%±12.4, Post 82.8%±4.7, p=0.014). S
ubjective reports for the one on one HIV-1 clinical training rated the experience as "excellent" to "very good" by 98% of the participants with 60% expressing more knowledge and confidence in the care of HIV patients than prior to the training period.
Conclusions: During this program, HIV clinical knowledge increased at each level of training. The clinical mentoring was associated with an increased comfort level in providing HIV

care. Incorporating HIV didactic and clinical rotations increased the knowledge and comfort level of internal medicine physicians in training and may provide an answer for addressing the HIV physician manpower shortage. Incorporating HIV training should be considered in the curriculum of internal medicine resident training programs.

WEPED901

m-Health: intervention to rapidly link Xpert MTB/RIF rifampicin resistant patients to treatment intitation in South Africa

L. Stewart-Isherwood[1], F. Olsen[1], P. Madumo[1], L. Scott[2], L. Berrie[1], W. Stevens[1,2]
[1]National Health Laboratory Service, National Program Unit, Johannesburg, South Africa, [2]University of the Witwatersrand, Molecular Medicine and Haematology, Johannesburg, South Africa
Presenting author email: lynsey.isherwood@nhls.ac.za

Background: GeneXpert technology has improved the rapid diagnosis of multi-drug resistant tuberculosis (MDR-TB) patients, however, the gap between diagnosis and treatment initiation and subsequently retention in care, remains large. m-Health is a promising solution to real time linkage to care and is being investigated for MDR-TB patients in South Africa through the development of a prototype MDR-TB android application (APP).
Methods: The MDR-TB treatment APP is named 'Treat TB' and has been designed for android platforms by the National Priority Program of the National Health Laboratory Service in Johannesburg, South Africa, as an extension to the existing national network of 2960 SMS bi-directional printers. The 'Treat TB' prototype has to date been implemented in one of eight trial sites in two districts of Johannesburg, using one Lenovo 3G enabled tablet placed within the clinic and two laboratory based Lenovo monitoring tablets. The following variables are being measured to determine the value of m-Health over existing laboratory paper-based clinic result reporting: time to treatment initiation, clinic workload reduction, ease of use, end-user value added satisfaction, training requirements, computer literacy and cadre of staff, impact of connectivity downtimes and patient identification mapping.
Results: The Treat TB required five months software development. Implementation training could be performed within one hour across staff cadres (one data capturer, two nurses, one social worker, two clinicians). Data capture through drop-down, selection boxes and minimum free text fields took on average 10 minutes per patient. One software upgrade has occurred requiring additional training. Sporadic and variable signal connectivity increased data capture delays and ease of use. Implementation currently is performed without real time automated communication with Gauteng Department of Health TB co-ordinators and MDR-TB patients; therefore time to treatment initiation still takes on average 12 days from diagnosis.
Conclusions: The Treat TB APP was successfully developed and shown to be easily implemented in an MDR-TB treatment initiation facility, however, requires real time automation to further reduce the turnaround time to treatment initiation. Access of this APP by all health care workers in all levels of the cascade of care may also be achieved through functionality available on personal smart phone devices.

WEPED902

Engaging aboriginal communities and organizations in research: lessons learned from stable homes, strong families

M. Amirault[1], P. Brownlee[1], J. Anaquod[2], S. Greene[3], C. Hill[4], A. Ion[3], R. Jackson[3], R. Masching[1], S. Nyman[5], P. Paul[6], S. Stonechild[7]
[1]Canadian Aboriginal AIDS Network, Dartmouth, Canada, [2]Canadian Aboriginal AIDS Network, Regina, Canada, [3]McMaster University, School of Social Work, Hamilton, Canada, [4]Canadian Aboriginal AIDS Network, Ohsweken, Canada, [5]Canadian Aboriginal AIDS Network, Victoria, Canada, [6]Canadian Aboriginal AIDS Network, Fredericton, Canada, [7]Canadian Aboriginal AIDS Network, Toronto, Canada
Presenting author email: reneem@caan.ca

Background: Conducting research with Aboriginal communities necessitates developing positive relationships within the community long before data collection begins. This process is important to maximize leadership within communities and organizations that are critical to supporting the research process. *Stable Homes, Strong Families* (SHSF) demonstrates the successes and challenges of relationship building in community-based research (CBR). SHSF is a national project that aims to develop cultural understandings of housing and home amongst Aboriginal peoples living with and affected by HIV and AIDS in order to influence housing policy and programs.
Methods: Relationships were developed between Aboriginal HIV service organizations, academic researchers and community leaders prior to grant submission. Following receipt of funding, a strategy to hire, train and support local Peer Research Associates (PRAs) to plan and lead digital storytelling (DS) workshops along with the research team was developed. Five workshops were held with 22 participants across Canada from June 2013 to November 2014.
Results: Our CBR approach highlighted a number of important lessons for working in partnership with diverse Aboriginal communities across Canada and conducting research with PRAs who also bring diverse identities and experiences. Time must be invested to develop partnerships even before the grant is finalized and submitted. PRAs should be trained and supported in all aspects of the research. Early engagement with Elders, community supports and organizations is critical to understanding the needs of participants, to creating a safe space where the research will be conducted and ensuring local Aboriginal cultural protocols are respected.
Conclusions: Community engagement and partnership development are as important as generating data and are essential to effective, community-driven knowledge translation activities. Lessons learned regarding key considerations for partnerships between Aboriginal communities and researchers will critically inform our analysis of data from the DS workshops.

WEPED903

Challenges and facility-level solutions identified by frontline healthcare workers to scale up high quality paediatric HIV treatment and care

H.S. Soeters[1], N. Sugandhi[2,3], L. Hatane[1], T. Runciman[1], D. Mark[1,4]
[1]Paediatric AIDS Treatment for Africa, Cape Town, South Africa, [2]Clinton Health Access Initiative, New York, United States, [3]Icahn School of Medicine Mount Sinai, New York, United Kingdom, [4]University of Cape Town, Department of Psychology, Cape Town, South Africa
Presenting author email: heleen@teampata.org

Background: There are an estimated 5.8 million HIV-infected children and young people in sub-Saharan Africa, yet only 24% of eligible children are receiving ART. Policy makers and programme managers require an informed understanding of service barriers and bottlenecks to providing paediatric and adolescent care at the frontline in order to translate health polices into more responsive practice.
Methods: The PATA 2014 Continental Summit was held in December 2014 to mobilize local action, share innovations and best practices, and disseminate guidance and technical updates. Thirty-seven health facilities from 18 sub-Saharan African countries, represented by 142 frontline HIV healthcare workers, five ALHIV and YPLHIV, and eight Ministry of Health representatives, participated in the summit which used expert plenaries, interactive workshops and peer-peer exchange to identify facility-level barriers, share best practices and generate concrete plans to take facility-specific action. Descriptive statistics and framework analysis were used to analyse reported barriers and planned facility interventions.
Results: The mean age of participants was 40 years, with a female majority (76%). Counsellors, community healthcare workers and social workers were most represented (28%). Collectively, health facilities cared for 53,048 children and adolescents in care (mean per facility, 487). Frontline healthcare worker and stakeholder groups reported key challenges and shared best practices along the continuum of care (Table 1).

Theme	Key challenge/s	Best practice/s
HIV case finding	Lack of entry points for testing children and adolescents	Routine HIV testing in high yield settings; Community education and demand generation
Linkage to HIV treatment and care services	Lack of child- or adolescent-friendly services; Stigma and myths	Healthcare worker training, mentorship, sensitization and job aids
Adherence and retention	Poor caregiver support	Caregiver support
Community and multisectoral engagement	Poor linkages and referrals with related health services; Staff shortages, negative attitudes and poor knowledge; Lack of child- or adolescent-friendly services	Community education and demand generation
Operational infrastructure and staffing	Staff shortages, negative attitudes and poor knowledge	Developing active linkages and referrals with related health services; Child- or adolescent-friendly services

[Table 1]

Healthcare workers designed 37 related quality improvement interventions to effect practical change at facility-level. Interventional activities and services focused on community health education and demand generation; healthcare worker training, mentorship, sensitization and job aids; and child- or adolescent friendly services. In summit evaluations, >90% of participants reported that expert input was valuable, peer-peer exchange helped in identifying bottlenecks and solutions, and intervention planning helped to clarify and define goals they could achieve over 12 months.
Conclusions: Frontline HIV healthcare workers and stakeholder groups identified major challenges in providing quality paediatric and adolescent HIV treatment and care, and developed practical solutions for implementation. Convening healthcare workers to provide capacity-building, sensitization and support can motivate and inform facility-designed interventions and services that respond to the needs of children and adolescents living with HIV.

WEPED904

Moving from theory to practice: ensuring capacity building and the application of GIPA/MIWA principles in conducting community-engaged research among women living with HIV in Canada

J. Gahagan[1], N. O'Brien[2,3], A. Carter[4,5], T. Conway[6,7], J. Thomas-Pavanel[6], S. Wertheimer[8], K. Proulx-Boucher[2], W. Tharao[9], S. Greene[10], D. Dubuc[2], S. Buhler[11], K. Beaver[6], A. Kaida[4], A. de Pokomandy[2,3], M. Loutfy[6]
[1]Dalhousie University, Health Promotion Division, Halifax, Canada, [2]McGill University Health Centre, Chronic Viral Illness Service, Montreal, Canada, [3]McGill University, Family Medicine, Montreal, Canada, [4]Simon Fraser University, Faculty of Health Sciences, Burnaby, Canada, [5]British Columbia Centre for Excellence in HIV/AIDS, Vancouver, Canada, [6]Women's College Hospital, Women's College Research Institute, Toronto, Canada, [7]International Community of Women Living with HIV, North America (ICWNA), Toronto, Canada, [8]Canada's Source for HIV and Hepatitis C Information (CATIE), Toronto, Canada, [9]Women's Health in Women's Hands CHC, Toronto, Canada, [10]McMaster University, Social Work, Hamilton, Canada, [11]Interagency Coalition on AIDS and Development, Ottawa, Canada
Presenting author email: angela_kaida@sfu.ca

Background: Although the importance of the core principles of the Greater Involvement of People Living with HIV/AIDS (GIPA) and the Meaningful Involvement of Women Living with HIV/AIDS (MIWA) are recognized in capacity building initiatives such as community-engaged, participatory research with Women Living with HIV (WLHIV), deeply rooted ethical tensions continue to stymie the realization of these principles in practice. How we address these various, intersecting ethical tensions can have significant implications for WLHIV, particularly those who are engaged in HIV research as Peer Research Associates (PRAs).
Methods: Drawing on the process of a longitudinal, community-engaged research study operating across Canada in British Columbia, Ontario, and Quebec, the Canadian HIV Women's Sexual and Reproductive Health Cohort Study (CHIWOS) examined the ethical tensions that emerge when moving the GIPA/MIWA principles from theory to practice in the Canadian context.
Results: A variety of tensions were noted in moving GIPA/MIWA from theory to practice. Among these tensions were issues of meaningful participation of WLHIV Peer Research Associates (PRAs), including appropriate compensation; role clarity, recognition, and a sense of overall well-being. Among these tensions were: needing transparency around having WLHIV working in CHIWOS while balancing the need to protect HIV-status confidentiality; facilitating maximum involvement while ensuring proper recognition and compensation under budget constraints; balancing the need to be supportive given the impact of the research on their personal lives while prioritizing professionalism; and supporting PRAs to navigate insider versus outsider roles on the research team and community they are researching.
Conclusions: The importance of recognizing these intersecting tensions is paramount to the shift from GIPA/MIWA as theoretical constructs to the practice of undertaking community-engaged research in Canada In an effort to proactively address tensions which can emerge when moving GIPA/MIWA from principle to practice, research teams must embrace open, flexible, and creative approaches. Such approaches are aimed at recognizing and engaging WLHIV within the broader funding landscape, ongoing HIV-related stigma, including issue of disclosure, and the intersecting determinants of health all of which can negatively impact on the ways in which we animate GIPA/MIWA principles. Recommendations for ways to address these tensions will be offered.

WEPED905

The district monitoring forum: a forum to support data driven decision-making to inform patient management in the South African ART programme

C. White[1], R. Pretorius[2], J. Ndirangu[1], J. Quevedo[1], Y. Pillay[2], P. Barron[2]
[1]Clinton Health Access Initiative, Pretoria, South Africa, [2]South African National Department of Health, Pretoria, South Africa
Presenting author email: cwhite@clintonhealthaccess.org

Background: The South African National Department of Health (NDoH) introduced a standardised ART monitoring system in 2011 comprised of standardised ART clinical records and a standardised in-facility monitoring tool. Whist implementation is still in progress data is now available for 1.3 million patients in the central data repository and the country has produced two annual reports presenting the programme outcomes. With an aim to strengthen the use of the system and improve data-driven decisions country-wide trainings were conducted to guide interrogation and use of the data. This research aims to share the achievements in improved reporting data use discussions; the district monitoring forum (DMF).
Methods: Twenty-eight trainings organised by the NDoH were prepared using data from each province and district where the trainings were held. Data was drilled down to the facility-level and included interpretations to demonstrate data usage and emphasise the importance of data completeness. A sample agenda was supplied to guide discussion in the DMF.
Results: Comparison of cohort data representativeness between 2012/13 and 2013/14 demonstrated an increase of data availability from 18.4% to 54.7%. Training demonstrated the use of the ART monitoring system to support in-facility patient management and also provided guidance on the generation of reports to support management. The training supplied attendees with a sample agenda to guide the establishment of forums in each district and guide strengthened data usage.
Conclusions: Training and support, as well as expanded implementation of the system from 1,296 facilities in Dec 2013 to 2,139 in October 2014, has increased data availability. Data representativeness increased by 36.3% (range 23.3% - 89.7%) in this reporting period. The DMF demonstrates the importance of data completeness and routine engagement with data to inform the management of the ART programme in the facility. It also creates an opportunity for facilities to share their best practices; to seek advice or support about how to manage a challenge they are currently experiencing; and facilitates the identification of where district level supervisory oversight visits might be required. The use of data in district-level reviews of patient enrolment, quality of care indicators, including retention informs and improves patient management.

WEPED906

The utility of HIV support groups in advancing implementation research in resource-limited settings

S. Sithole[1,2], T. Mudzviti[3], D. Chagwena[3], F. Mazambara[3], M. Zende[3], G.D. Morse[1,2], C.C. Maponga[3]
[1]NYS Center of Excellence in Bioinformatics and Life Sciences, Translational Pharmacology Research Core, Buffalo, United States, [2]University at Buffalo, School of Pharmacy and Pharmaceutical Sciences, Buffalo, United States, [3]University of Zimbabwe, School of Pharmacy, Harare, Zimbabwe
Presenting author email: samsithole@gmail.com

Background: The primary function of HIV support groups in sub-Saharan Africa was initially to promote HIV awareness and psychosocial well-being among people living with HIV, however, they have since evolved to serve as platforms upon which other sustainable initiatives may be explored. In order to address the global vision to eradicate HIV/AIDS as a public health threat by 2030, it is prudent to investigate how support groups can be integrated with academic programs that seek to conduct implementation research in this area. The purpose of this study was to describe the process of how HIV support groups can be strengthened to support implementation research in resource-limited settings.
Methods: PARI adult HIV support group is based at an opportunistic infection clinic in Zimbabwe and was established in 2006. We instituted different levels of membership including peer-to-peer counselors, trainers, project leaders and general facilitators to provide an organizational structure which can be utilized to discuss research projects, enroll participants in studies and provide feedback to members. The multidisciplinary framework of the program allows for all group meetings and clinical services to be conducted at this location. PARI support group is closely linked with two tertiary academic institutions whose graduate students and fellows are engaged in implementation research. It is sustained by HIV-positive members who meet monthly and actively participate in various psychosocial and microeconomic initiatives.
Results: To date, twenty-three international abstracts and four published articles in the area of pharmacovigillance, nutrition, adherence, microeconomics and capacity building have been generated through the PARI support group. Additionally, groundwork for implementation of the latest global HIV treatment and prevention strategies such as treatment as prevention among sero-discordant couples is underway. Lastly, benefits from the support group initiatives have also been realized, particularly in life skills training and income-generating activities. Data show that an average of US$42 was earned as extra monthly income from June 2013 to June 2014 for participating members.
Conclusions: The support group model has been successfully utilized to generate clinical and implementation data. Going forward, the introduction of HIV eradication interventions should include HIV support groups since they are capable of supporting and sustaining clinical research.

WEPED907

Description and evaluation of stage 1 of the ASHM Asia and Pacific regional leadership and mentoring program 2014

L. Crooks[1,2], N. Medland[3,4]
[1]Australasian Society for HIV Medicine, Executive, Sydney, Australia, [2]La Trobe University, Public Health and Human Biosciences, Melbourne, Australia, [3]Australasian Society for HIV Medicine, Sydney, Australia, [4]Monash University, Central Clinical School, Melbourne, Australia
Presenting author email: levinia.crooks@ashm.org.au

Background: We set out to support regional delegates to attend the AIDS 2014 Conference in Melbourne and through providing a short term period of study and participation in a leadership course, maximise the benefit of these delegates. We also sought to develop an ongoing durable network and mentoring program.

Methods: 15 local civil society groups (CSG) came together to develop the program and ASHM negotiated support from the Australian development agency. Each CSG developed a scholarship program which included the conference and leadership course. The course ran for 2 days before and after the conference. Mentoring was provided during the conference and a mentoring has continued among many groups post the conference. Skills building workshops held after the conference included: Quality, Outcomes Based Management, Mentoring as well as translational skills to assist delegates to share the experiences abstract and manuscript writing, using survey techniques and writing for the web.

Results: 10 agencies submitted 15 application of which 8 agencies ran 10 course. AusAID supported full scholarship for 277 delegates (clinicians, government, MSM, TG, SW) from regional lower and middle income countries. A small number of delegates were funded from other sources.

The 2 day Leadership course was exposed delegates to high level leader, IAS President and President elect, the Hon Michael Kirby, leaders from regional countries and experts in leadership, management. The focus was on engagement of key populations. It evaluated very highly and delegates report taking inspiration from these leaders. Delegates used the mentoring space and mentoring software and report this helped them to navigate the conference.Skills workshops were very highly evaluated delegates indicated that objectives were met and they would apply the skills learned.

Conclusions: The evaluation of part one of the program indicates that it was highly successful. It has also established greater ongoing linkages between the Australian CSGs and their regional counterparts and we will evaluate that over time. As a strategy of combining resources and value adding to a conference it was superb. It also provided delegates with sustained exposure south-south and across interest and professional groups. The IAS should support programs like this at all its meetings.

Late Breaker Posters

Track A

Monday, 20 July 2015

MOLBPE01

Low frequency HIV drug resistance in Ugandan patients failing ART with susceptible HIV Sanger genotyping

R. Gibson[1], F. Kyeyune[2,3], I. Nankya[3], S. Metha[3], J. Akao[3], E. Ndashimye[3], R.A. Salata[2], P. Mugyenyi[3], M.E. Quinones-Mateu[2,4], E. Arts[1]
[1]University of Western Ontario, Microbiology and Immunology, London, Canada, [2]Case Western Reserve University, Cleveland, United States, [3]Joint Clinical Research Centre, Kampala, Uganda, [4]University Hospitals Case Medical Center, Cleveland, United States
Presenting author email: richard.gibson@schulich.uwo.ca

Background: We recently described that despite close monitoring and adherence to treatment over 10% patients failed treatment with every year of a first line treatment regimen (Kyeyune *et al* 2013 *AIDS* 27:1899). Only 70% of HIV-infected individuals failing antiretroviral therapy in Kampala, Uganda had a drug resistant HIV-1 genotype based on Sanger sequencing. We suspect that the remaining 30% had low frequency drug resistance mutations, which may impact on treatment outcomes.
Methods: Three patient groups were selected: those that failed treatment and (1) had dominant resistance as controls (N=27), and (2) lacked dominant drug resistant (N=38), and (3) had NNRTI and FTC/3TC resistance but lacked thymidine analog mutations (TAMs) (N=50). We used two novel HIV-1 genotyping assays based on oligonucleotide ligation assay (OLA) and a deep sequencing assay (DEEPGEN™HIV) to quantify minority HIV-1 drug resistant variants.
Results: DEEPGEN™HIV and OLA both detected low-level drug resistant mutations as low as 1% in most patients where Sanger failed to detect. Low-level drug resistance mutations were detected by DEEPGEN™HIV in 53% (20/38) of patients with lacking any HIV drug resistant mutations based on standard Sanger sequencing.
Mutations associated with resistance to NRTI (e.g., M41L, D67N, M184V) and NNRTI (e.g. K103N, Y181C) were quantified, ranging from 1% to 17.6%. With treatment failures and the absence of TAMs, OLA identified low frequency TAMs in 60% (30/50) of these patients. A subset analyses using DEEPGEN™HIV confirmed the low frequency TAMs detected by OLA. For all 88 patients failing first line treatment but lacking dominant drug resistance, the treatment regimens were not changed and thus, we are currently assessing treatment outcomes following the Sanger drug resistance testing.
Conclusions: These low frequency drug resistant variants detected in antiretroviral-experienced individuals failing treatment, may have significant consequences on current or future outcomes, especially if treatment is not modified based on a susceptible HIV-1 genotype (Sanger) report. Preliminary data suggests that patients with minority drug resistance variants associated with treatment failure did not respond to the continuation of the same treatment regimen.

Tuesday, 21 July 2015

TULBPE02

Novel activators of latent HIV-1 from natural products

I. Tietjen[1,2], K. Andrae-Marobela[3], X.T. Kuang[4], B.M. Abegaz[5], D. Fedida[2], Z.L. Brumme[1,6], M.A. Brockman[1,4,6]
[1]Simon Fraser University, Faculty of Health Sciences, Burnaby, Canada, [2]University of British Columbia, Anesthesiology, Pharmacology, and Therapeutics, Vancouver, Canada, [3]University of Botswana, Department of Biological Sciences, Gabarone, Botswana, [4]Simon Fraser University, Department of Molecular Biology and Biochemisty, Burnaby, Canada, [5]African Academy of Sciences, Nairobi, Kenya, [6]University of British Columbia, British Columbia Centre for Excellence in HIV/AIDS, Vancouver, Canada
Presenting author email: itietjen@sfu.ca

Background: While "shock-and-kill" strategies have the potential to eliminate latent HIV, they have yet to succeed in clinic, in part because existing latency activators display toxicity and do not uniformly activate latent viral reservoirs. Thus, new chemical leads with reduced toxicity, improved efficacy, and/or ability to synergize with existing agents are needed. Natural products are a promising but undervalued resource for identifying new anti-latency agents that may act via distinct mechanisms.
Methods: We examined 9 extracts from plants used by traditional healers in Sub-Saharan Africa to treat HIV symptoms and 85 pure compounds obtained from the pan-African Natural Product Library (p-ANAPL), which also derive from traditional medicinal plants. Extracts and compounds were screened using the J-Lat 9.2 GFP-reporter T cell line that contains an integrated NL4.3-Δenv/Δnef proviral genome. TNFα was used as a control. Natural products that induced GFP expression in >5% cells while retaining >30% cell viability at 5 µg/mL were assessed for 50% activation and cytotoxic concentrations (EC_{50} and CC_{50}), intracellular $p24^{Gag}$ expression, and synergism with histone deacetylase inhibitors (HDACi) panobinostat and romidepsin.
Results: Medicinal plant extract "Mokungulu" at 5 µg/mL induced GFP expression in >5% cells and $p24^{Gag}$ production, but displayed ~3-fold less cytotoxicity than panobinostat or romidepsin. Pure compound "p61" at 5 µg/mL also activated GFP expression. Interestingly, both products exhibited synergy with panobinostat and romidepsin, inducing GFP expression in up to 50% of cells when combined with suboptimal doses of HDACi and up to a 38-fold increase in mean GFP intensity vs. untreated cells (*i.e.,* both similar to 50 ng/mL TNFα). We also identified 6 pure compounds that activated nearly 100% of cells but with lower intensity (i.e. 2 to 7-fold increased mean GFP intensity vs. untreated cells) with no evidence of toxicity.
Conclusions: We have identified potential new HIV latency activators of natural origin guided by indigenous medicinal knowledge. These agents display low toxicity and synergy with HDAC inhibitors currently under evaluation, indicating that they may be promising lead compounds for additional study.

TULBPE03

CD4 mimetics sensitize HIV-1-infected cells to ADCC

J. Richard[1,2], M. Veillette[1,2], N. Brassard[1], S.S. Iye[3], M. Roger[1,2], L. Martin[4], M. Pazgier[5], A. Schön[6], E. Freire[6], J.-P. Routy[7], A.B. Smith rd[3], J. Park[3], D.M. Jones[3], J.R. Courter[3], B.N. Melillo[3], D.E. Kaufmann[1,2,8], B.H. Hahn[3], S. Permarl[9], B.F. Haynes[9], N. Madani[10,11], J. Sodroski[10,11], A. Finzi[1,2,7]
[1]The CHUM Research Center, Montreal, Canada, [2]University of Montreal, Montreal, Canada, [3]University of Pennsylvania, Philadelphia, United States, [4]dCEA, iBiTecS, Service d'Ingénierie Moléculaire des Protéines, Gif sur Yvette, France, [5]University of Maryland School of Medicine, Baltimore, United States, [6]The Johns Hopkins University, Baltimore, United States, [7]McGill University, Montreal, Canada, [8]Ragon Institute of Massachusetts General Hospital, Massachusetts Institute of Technology, and Harvard, Cambridge, United States, [9]Duke Human Vaccine Institute, Duke University Medical Center, Duke, United States, [10]Dana-Farber Cancer Institute, Boston, United States, [11]Harvard School of Public Health, Boston, United States

Background: Prevention of HIV-1 transmission and progression likely requires approaches that can specifically eliminate HIV-1-infected cells. There is increasing evidence supporting a role of Antibody-Dependent Cell-Mediated Cytotoxicity (ADCC) in controlling HIV-1 transmission and disease progression. Importantly, the interaction of HIV-1 envelope (Env) glycoproteins with the CD4 receptor was recently reported to be required for efficient exposure of ADCC-mediating Env epitopes. In that context, HIV-1-infected cells presenting HIV-1 Env in the CD4-bound conformation on their surface were found to be preferentially targeted by ADCC-mediating antibodies present in sera of HIV-1-infected individuals. However, HIV-1 has evolved a sophisticated mechanism to avoid exposure of ADCC-mediating Env epitopes by downregulating CD4 and by limiting the overall amount of Env at the cell surface.
Methods: Rationally-designed CD4-mimetic compounds (CD4mc) have been shown to induce thermodynamic changes in HIV-1 Env similar to those induced by CD4 and sensitize HIV-1 particles to neutralization by otherwise non-neutralizing CD4-induced antibodies. In this study, we explored the capacity of such compounds to promote the CD4-bound conformation of Env and thereby sensitize HIV-1-infected cells to ADCC mediated by sera, cervico-vaginal lavages and breast milk from HIV-1-infected individuals, using a FACS-based ADCC assay.
Results: We observed that certain CD4mc induce the CD4-bound conformation of Env and thereby sensitize cells infected with primary HIV-1 isolates to ADCC mediated by prevalent and easy-to-elicit antibodies present in sera from early converters and chronically-infected individuals. Importantly, CD4mc also enhanced recognition and ADCC-mediated elimination of HIV-1-infected cells by antibodies present in breast milk and cervico-vaginal lavages of HIV-1-infected women. Finally, we identified one CD4mc with the capacity to sensitize endogenously-infected *ex-vivo*-amplified primary CD4 T cells to ADCC killing mediated by autologous sera and effector cells.
Conclusions: By pushing Env into the CD4-bound conformation, CD4mc might represent an alternative and/or complementary approach to currently-available drugs for preventing viral transmission and might represent a new strategy aimed at eradicating the viral reservoir.

TULBPE04

Enhancement of microbiota in healthy macaques results in robust beneficial modulation of mucosal and systemic immune function

E. Haddad[1], T. Hensley-McBain[2], R. Cubas[3], J. Gile[2], C. Miller[2], J. Estes[4], S. Langevin[5], R.K. Reeves[6], N. Klatt[2]
[1]Drexel University, Philadelphia, United States, [2]University of Washington, Department of Pharmaceutics, Seattle, United States, [3]VGTI-Florida, Port Saint Lucie, United States, [4]National Cancer Institute, AIDS and Cancer Virus Program, Fredrick, United States, [5]University of Washington, Department of Microbiology, Seattle, United States, [6]Beth Israel Deaconess Medical Center, Boston, United States
Presenting author email: klattnr@uw.edu

Background: With more than thirty million HIV-infected individuals worldwide, developing an effective vaccine to prevent new HIV infections remains a top priority in contemporary biomedical research. Given the critical role of mucosal surfaces in susceptibility of HIV infection, it is imperative that we induce effective mucosal responses.
However, current approaches to enhance mucosal immunity have not been successful in preventing HIV acquisition.
Methods: Modulating the microbiota in the GI tract is a safe and well-tolerated approach to enhance mucosal and overall health, and here we hypothesized that altering TLR signaling via microbiome enhancement may improve mucosal immunity. Thus we treated five macaques (SIV-) with the probiotic (PBio) VSL3 and sampled colon, rectum, blood and LN from prior to PBio treatment, and at days 28 and 80 post-treatment. We assessed cellular and humoral immunity and inflammation.
Results: rikingly, we found that PBio therapy resulted in significantly increased T follicular helper cells (Tfh; CD4+PD-1^{high}CXCR5^{high}, p=0.0085). In addition, immunohistochemistry confirmed that LNs had increased follicles after PBio treatment. Given the ability for Tfh to induce B cell responses, we measured surface IgA and IgG expression on B cells, and observed increased frequencies of B cells expressing IgA in the LN (p=0.0151) and colon (p=0.0072). To determine the method for increased Tfh, we measured IL-23 production by antigen presenting cells (APCs), and found significantly increased frequencies of IL-23+APCs in the colon (p=0.0173), which correlated with the frequency of LN Tfh (p=0.0358).
Conclusions: These data have potential implications for using PBio therapy to alter mucosal immunity in the context of vaccination or preventative approaches. In particular, the immunomodulatory properties of probiotic therapy in conjunction with HIV vaccination may provide an opportunity for enhanced mucosal HIV vaccine responses that could improve protection from infection by improving immune defenses at the mucosal portal of entry.

Wednesday, 22 July 2015

WELBPE06

CD4 T cell reconstitution following cART is immediate as is CD4+T cell depletion following treatment interruption: coupling the whole-body imaging of the CD4 pool and of the immune system activation

M. Di Mascio[1], S. Srinivasula[2], I. Kim[3], P. DeGrange[4], A. St. Claire[1], C. Paik[5], H.C. Lane[6]
[1]Division of Clinical Research, NIAID, NIH, Bethesda, United States, [2]Biostatistics Research Branch, Leidos Biomedical Research, Inc., FNLCR, Frederick, United States, [3]Applied/ Developmental Research Directorate, Frederick National Laboratory, Frederick, United States, [4]Integrated Research Facility, NIAID, NIH, Frederick, United States, [5]Radiopharmaceutical Laboratory, Nuclear Medicine, Radiology and Imaging Sciences, Clinical Center, NIH, Bethesda, United States, [6]Laboratory of Immunoregulation, NIAID, NIH, Bethesda, United States
Presenting author email: mdimascio@niaid.nih.gov

Background: The number of peripheral blood (PB) CD4+ T cells typically increases within weeks of initiating antiretroviral treatment (cART). Similarly, decreases are observed within the first month following interruption of cART. It remains an open question whether these immediate changes in CD4 cell counts are mainly the result of changes in trafficking between lymphoid tissues (LT) and the PB, or true reconstitution/depletion of the total body pool. In previous work we have demonstrated the feasibility of imaging the whole-body CD4-pool in vivo using a radiolabelled anti-CD4 monoclonal antibody (mAb) and single photon emission computed tomography (SPECT).
The present study was designed to examine changes in the whole-body CD4-pool and immune system activation in the setting of cART using the F(ab´)2 fragment of anti-CD4 labeled with Tc-99m (for SPECT imaging) and FDG (for PET imaging), respectively
Methods: A group of 19 SIV-infected rhesus macaques (PB CD4-counts: 28-1556 cells/μl) started cART, of which 7 were imaged longitudinally. Another group of 9 SIV-infected and treated animals (PB CD4-counts: 176-1661 cells/μl) interrupted cART, of which 1 was imaged longitudinally
Results: At month 1 post-cART initiation, CD4 counts in the PB increased an average of 38% (P< 0.01,n=19). No significant changes were noted in CD8 T cell or B cell counts. Whole-body imaging revealed a 15.1 to 19.2% (P< 0.05,n=7) increase in the splenic pool of CD4 cells despite decreased FDG-uptake (n=2). Conversely, at month 1 post-cART interruption, CD4 counts in the PB decreased an average of 34% (P< 0.05,n=9), again without significant changes observed in CD8 T cell and B cell counts. Whole-body imaging revealed a 30% decrease in the splenic pool of CD4 T cells (n=1)
Conclusions: Gains or losses in CD4 count happen rapidly in both the peripheral blood and the spleen. Lymphoid tissues experience increase/decrease up to 30% of the CD4 pool within just 4 weeks from initiation or interruption of cART, respectively. The increases are associated with a decrease in cell activation suggesting that cART has an immediate effect on CD4 T cell survival

Track B

Monday, 20 July 2015

MOLBPE07

Marked gender differences in mortality on ART in lower- and middle-income countries: a systematic review and meta-analysis

S.W. Beckham[1], C. Beyrer[2], P. Luckow[3], M. Doherty[4], E. Negussie[4], S. Baral[2]
[1]*Johns Hopkins School of Public Health, Epidemioloogy, Iringa, Tanzania, United Republic of,* [2]*Johns Hopkins School of Public Health, Epidemioloogy, Baltimore, United States,* [3]*Geisel School of Medicine at Dartmouth, Hanover, United States,* [4]*World Health Organization, HIV/AIDS, Geneva, Switzerland*
Presenting author email: sarah.beckham@jhu.edu

Background: Across all low- and middle-income countries, men and women comprise similar proportions of people living with HIV who are eligible for antiretroviral therapy (ART). However, men account only 41% of those receiving ART. There has been limited study of men's experiences and outcomes in ART programs, despite a number of studies suggesting that men have higher mortality rates than women in HIV treatment. The aim of this systematic review (SR) and meta-analysis (MA) was to assess differential mortality between men and women living with HIV and on ART in low- and middle-income countries (LMIC).
Methods: A SR and MA was conducted of published observational studies reporting mortality of adult (≥15) men and women in ART treatment programs in LMIC. PubMed, Ovid Global Health, and Embase were searched. Random effects meta-analysis was conducted overall, by geographic region, and by quartiles of time and months on ART (≤ 12, 13-33, 34-60, 61+).
Results: After duplicates were removed, 11,889 records were screened, and 6,726 full text articles were assessed for eligibility. There were 69 included studies reporting 87 hazard ratios (HR), with a total sample size of 249,027 men and 375,067 women, and total follow-up time of 2981 months. The pooled HR (pHR) was 1.37 (1.31-1.43), indicating an overall 37% increased hazard of death for men while on ART. Across Sub-Saharan Africa, the pooled HR was 1.33 (1.26-1.39), and in Asia, it was 1.58 (1.42-1.75). In subgroup analyses by quartiles of time on ART, the pHR increased significantly over time on ART: ≤ 12 months pHR=1.27 (1.18-1.36); 13-33 months pHR=1.35 (1.22-1.49); 34-60 months pHR=1.44 (1.33-1.56); and 61-144 months pHR=1.49 (1.22-1.82) (time trend p=0.055).
Conclusions: These analyses demonstrate that men living with HIV have consistently and significantly greater hazards of mortality compared to women while on ART in LMIC. This effect persisted and increased over time on treatment, suggesting that longer term retention and adherence may be key to improving men's outcomes. The clinical and prevention benefits of ART will only be realized if programs can improve male engagement, diagnosis, earlier initiation of therapy, clinical outcomes and can support better long-term retention in care and treatment adherence.

MOLBPE08

Elvitegravir (EVG) / cobicistat (COBI) / emtricitabine (FTC)/ tenofovir disoproxil fumarate (TDF) is superior to ritonavir (RTV) boosted atazanavir (ATV) plus FTC/TDF in treatment naïve women with HIV-1 infection (WAVES Study)

K. Squires[1], C. Kityo[2], S. Hodder[3], D. Hagins[4], A. Avihingsanon[5], Y. Plotnikova[6], E. Koenig[7], F. Post[8], K. White[9], S.-S. Chen[9], H. Cao[9], A. Cheng[10], J. Szwarcberg[10], WAVES Study Investigators
[1]*Thomas Jefferson University, Medicine, Philadelphia, United States,* [2]*Joint Clinical Research Centre, Kampala, Uganda,* [3]*West Virginia Clinical and Translational Science Institute, Morgantown, United States,* [4]*Chatham County Health Department, Savannah, United States,* [5]*Thai Red Cross AIDS Rsch Ctr, Bangkok, Thailand,* [6]*GUZ Irkutsk Reg.Cter Prevent, Irkutsk, Russian Federation,* [7]*Zona Universitaria/, IDEV, Santo Domingo, Dominican Republic,* [8]*Kings College London, London, United Kingdom,* [9]*Gilead Sciences, Inc., Foster City, United States,* [10]*Gilead Sciences, Foster City, United States*

Background: Women are under-represented in HIV antiretroviral therapy (ART) studies. The Women AntiretroViral Efficacy and Safety study (WAVES) is the first all-women, international, randomized, double-blind, phase 3 trial designed to evaluate the safety and efficacy of EVG/COBI/FTC/TDF versus ATV+RTV+FTC/TDF.
Methods: HIV1 infected, ART naïve women were randomized (1:1), in a double-blind, global study (North America, Europe, Africa, Asia). Entry criteria included HIV RNA>500 copies(c)/mL and estimated GFR≥ 70 mL/min. Women who become pregnant had the option to continue on study drug. The primary efficacy endpoint was the proportion of women achieving a HIV1 RNA < 50 c/mL at Week 48. Safety was assessed throughout the study.
Results: 575 women were enrolled (EVG/COBI/FTC/TDF, n=289 vs ATV+RTV+FTC/TDF, n= 286). Demographic and baseline characteristics were balanced and reflect the global nature of the study (Table 1). The median age was 35 years and 78% had asymptomatic HIV infection. EVG/COBI/FTC/TDF was statistically superior to ATV+RTV+FTC/TDF, with 87.2% and 80.8%, respectively, achieving HIV-1RNA < 50 c/mL at week 48 (adjusted difference 6.5%, 95% CI 0.4% to 12.6%). Mean increases in CD4 cell counts were similar (Table 1). No subject experienced virologic failure with resistance in the EVG/COBI/FTC/TDF arm, compared to 3 (1%) in the ATV+RTV+FTC/TDF arm (M184V/I). Both regimens were generally well tolerated, with most adverse events being mild (grade 1) in severity. Mean decreases in eGFR were small and similar at week 48 (-4.5 vs -2.3 mL/min, p=0.15) with no discontinuations due to renal adverse events (AEs) in the EVG/COBI/FTC/TDF arm. Percent changes in BMD at week 48 were similar at spine (-3·09 vs -3.26, *p*=0.69) and hip (-3.02 vs -2·55, *p*=0·37). Of the 24 pregnancies reported, 13 women elected to continue study drugs.
Conclusions: EVG/COBI/FTC/TDF was superior to ATV+RTV+FTC/TDF at 48 week, and demonstrated its safety and efficacy for the treatment HIV1 infection in women. Recruitment, enrollment and retention of women in large multinational trials is feasible.

Characteristic	EVG/COBI/FTC/TDF n=289	ATV+RTV+FTC/TDF n=286	P value
Median BL Age (years)	34	35	0.86
Race (%)			0.23
Black	49.5	46.5	-
White	44.3	41.5	-
Asian	3.1	5.9	-
Median BL CD4 (cells/µl)	344	370	0.40
Median BL HIV-1 RNA (copies/ml)	28,840	36,310	0.62
Mean change of CD4 at week 48 (cells/µl)	221	212	0.40
Week 48 HIV RNA<50 copies/ml (%)	87.2	80.8	0.034
Discontinuations (AE, n)	5	19	-
Virologic Failure (%)	9	11.9	-
Emergent Resistance (n)	0	3	-

[Table 1]

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TULBPE09

Use of oral DAA-based regimens in HIV-HCV co-infected patients in a real life setting - interim analysis from the ANRS CO13 HEPAVIH cohort

D. Salmon-Ceron[1,2], K. Lacombe[3,4], L. Esterle[5], C. Gilbert[5], L. Piroth[6], F. Bani-Sadr[7], A. Laurent[8], H. Aumaitre[9], E. Billaud[10], J. Chas[11], S. Dominguez[12], A. Gervais[13], C. Lascoux-Combe[14], P. Miaihles[15], D. Neau[16], I. Poizot-Martin[17], E. Rosenthal[18], D. Zucman[19], F. Dabis[20,21], P. Sogni[2,22], L. Wittkop[20,21], ANRS CO13 Hepavih
[1]*APHP -Hôpital Cochin, Service de Médecine Interne et Pathologie Infectieuse VIH, Paris, France,* [2]*Université Paris Descartes, Paris, France,* [3]*APHP -Hôpital Saint Antoine, Service des Maladies Infectieuses et Tropicales, Paris, France,* [4]*Université UPMC, Paris, France,* [5]*Inserm U897 - Epidémiologie-Biostatistique, ISPED, Université Bordeaux, Bordeaux, France,* [6]*CHU Dijon, Département d'Infectiologie, Dijon, France,* [7]*CHU Reims - Hôpital Robert Debré, Service de Médecine interne et de Maladies Infectieuses et Tropicales, Reims, France,* [8]*CHU Toulouse - Hôpital Purpan, Service de Médecine interne, Toulouse, France,* [9]*CH Perpignan, Service des Maladies Infectieuses et Tropicales, Perpignan, France,* [10]*CHU Nantes, Service des Maladies Infectieuses et Tropicales, Nantes, France,* [11]*APHP - Hôpital Tenon, Maladies Infectieuses et Tropicales, Paris, France,* [12]*APHP - Hôpital Henri Mondor, Immunologie clinique et maladies infectieuses, Créteil, France,* [13]*APHP-Hôpital Bichat Claude Bernard, Maladies infectieuses et tropicales Hépato-gastro-entérologie, Paris, France,* [14]*APHP - Hôpital Saint Louis, Service des Maladies Infectieuses et Tropicales, Paris, France,* [15]*CHU Lyon, Service des Maladies Infectieuses et Tropicales, Lyon, France,* [16]*CHU Bordeaux, Service des Maladies Infectieuses et Tropicales, Paris, France,* [17]*APHM-Hôpital Sainte Marguerite, 9Service d'Immuno-Hématologie Clinique, Marseille, France,* [18]*CHU Nice - Hôpital L'Archet 1, Service de Médecine interne Cancérologie, Nice, France,* [19]*Hôpital Foch, Médecine interne, Suresnes, France,* [20]*Université de Bordeaux, Inserm U897- Epidémiologie-Biostatistique, ISPED, Bordeaux, France,* [21]*CHU de Bordeaux, Bordeaux, France,* [22]*APHP - Hôpital Cochin, Département des maladies du foie - Hépatologie, Paris, France*
Presenting author email: laure.esterle@isped.u-bordeaux2.fr

Background: It is widely recommended to treat chronic hepatitis C in HIV co-infected patients, considering its worse evolution and prognosis in these patients. Several new oral direct active agent (DAA)-based regimens can be used, with often quite similar antiviral activity.
Methods: HIV-HCV co-infected patients enrolled in the ANRS CO13 HEPAVIH cohort who initiated an oral DAA-based regimen were included. We report safety, end of treatment (EOT) response and sustained virologic response (HCV-RNA < 15 UI/mL) at 12 weeks (SVR12).

Results: We included 245 patients, of those, 133 patients reached EOT (54%) and 62 patients SVR12 (25%). Median age was 53 years [IQR: 49-55], 78% were male, 98% were on antiretroviral therapy (ART), 90% had an HIV viral load < 50 copies/mL, and median CD4 was 530/mm^3 [IQR: 310-715]). Sixty-nine percent of the patients were cirrhotic, and 71% had failed to respond to previous treatment. HCV genotype (Gt) repartition was as follows: Gt1, 58%; Gt2, 4%; Gt3, 13%; Gt4, 25%.HCV-RNA was undetectable at the end of treatment (EOT) in 99% of the patients (95% confidence interval (CI): 96%-100%) and global SVR12 was 90% (CI: 80-96). Overall, EOT response was 100% in both non-cirrhotic and cirrhotic patients. Two premature stops for safety reasons were observed.EOT and SVR12 according to baseline characteristics and DAA prescribed regimen are presented in Table 1.

Table 1: Proportion of patients with EOT and SVR12 according to baseline characteristics and mostly prescribed anti-HCV treatment regimen

Cirrhotic status	Genotype	Most frequent combinations and durations	Undectable HCV viral oad at EOT (%, n/N)	SVR 12 (%, n/N)
non cirrhotics	1	SOF + DCV 12W	100% (7/7)	100% (2/2)
non cirrhotics	1	SOF + LDV 12W	100% (2/2)	-
non cirrhotics	1	SOF + DCV 24W	100% (4/4)	-
non cirrhotics	3	SOF + PR 12W	100% (2/2)	100% (1/1)
non cirrhotics	4	SOF + LDV 12W	100% (2/2)	-
	4	SOF + DCV 12W	100% (3/3)	100% (1/1)
Cirrhotics	1	SOF + DCV 24W	100% (36/36)	89% (17/19)
Cirrhotics	3	SOF + DCV 24W	100% (6/6)	100% (2/2)
Cirrhotics	4	SOF + DCV 24W	100% (8/8)	100% (3/3)

DCV: Daclatasvir; LDV: Ledipasvir; PR: Pegylated interferon-ribavirin; SOF: Sofosbuvir; W: Weeks. [Table 1]

Conclusions: In this real-life prospective french national cohort, oral-DAAs based regimens showed high efficacy and excellent tolerability in HIV-HCV co-infected patients in a large variety of clinical settings.

TULBPE10

Efficacy and safety of 12 and 8 weeks of simeprevir (SMV) plus sofosbuvir (SOF) in treatment-naïve and -experienced patients with chronic HCV genotype 1 infection without cirrhosis: OPTIMIST-1

P. Ruane[1], P. Kwo[2], N. Gitlin[3], R. Nahass[4], D. Bernstein[5], S. Rojter[6], E. Schiff[7], M. Davis[8], Z. Younes[9], R. Kalmeijer[10], M. Peeters[11], O. Lenz[11], B. Fevery[11], G. De La Rosa[12], J. Scott[13], R. Sinha[10], J. Witek[10]

[1]Ruane Medical & Liver Health Institute, Los Angeles, United States, [2]Division of Gastroenterology and Hepatology, Department of Medicine, Indiana University, Indianapolis, United States, [3]Atlanta Gastroenterology Specialists, Atlanta, United States, [4]ID Care, Hillsborough, United States, [5]Hofstra North Shore Long Island Jewish School of Medicine, Manhasset, United States, [6]National Research Institute, Los Angeles, United States, [7]University of Miami Schiff Center for Liver Disease, Miami, United States, [8]Digestive CARE-South Florida Center of Gastroenterology, West Palm Beach, United States, [9]GASTRO ONE, Germantown, United States, [10]Janssen Research and Development, LLC, Titusville, United States, [11]Janssen Infectious Diseases BVBA, Beerse, Belgium, [12]Janssen Global Services, LLC., Titusville, United States, [13]Janssen Global Services, LLC., High Wycombe, United Kingdom

Presenting author email: pjruane@ruanemedical.com

Background: In a Phase II study (COSMOS), oral, once-daily (QD) combination SMV (Hepatitis C virus [HCV] NS3/4A protease inhibitor)+SOF (HCV nucleotide-analogue NS5B polymerase inhibitor)±ribavirin for 12 or 24 weeks (wks) achieved high sustained virologic response (SVR) rates and was well tolerated in treatment-naïve and prior null responder patients (pts), including METAVIR F3-F4 pts. This Phase III, randomised, open-label study (OPTIMIST-1; NCT02114177) evaluated efficacy and safety of 8 and 12 wks of SMV+SOF, in treatment-naïve or -experienced HCV genotype (GT)1-infected pts without cirrhosis.

Methods: Randomisation (1:1; stratified by HCV GT1 subtype ±Q80K, IL28B GT, treatment history) to 12 or 8 wks of SMV 150mg QD+SOF 400mg QD. Superiority of each treatment arm vs a historical control (HC; from published data), was assessed. Primary efficacy endpoint was SVR 12 wks after end of treatment (SVR12).

Results: In total, 310 pts received treatment (male, 55%; median age, 56 years; Black/African American, 18%; IL28B CC, 27%; GT1a/1b 75/25%; treatment-naïve [n=218, 70%]; treatment-experienced [n=92, 30%]). SVR12 with 12 wks of SMV+SOF (97% [95% confidence interval (CI), 94-100%]) was superior to HC (87%). SVR12 with 8 wks of SMV+SOF (83% [95% CI, 76-89%]) did not achieve superiority vs HC (83%).

Other endpoints are summarised (Table). Adverse events (AEs) occurred in 103 (67%) and 97 (63%) pts receiving 12- or 8-wk treatment, respectively (mainly Grade 1/2 [64% and 61%]). Most frequent AEs: headache, fatigue and nausea (12-wk arm: 14%, 12% and 15%; 8-wk arm: 17%, 15% and 9%, respectively).

AEs of interest, increased bilirubin and rash, occurred in 1 (1%) and 10 (7%) pts in the 12-wk arm vs 1 (1%) and 12 (8%) pts in the 8-wk arm, respectively. No pts discontinued treatment due to an AE. Serious AEs were infrequent (12-wk arm, 1 pt [1%]; 8-wk arm, 3 pts [2%]). No deaths occurred. Pt-reported outcomes significantly improved from baseline to SVR12 in both treatment arms (Table).

Conclusions: SMV+SOF for 12 wks was superior to HC and SMV+SOF for 8 wks did not achieve superiority vs HC in treatment-naïve and -experienced HCV GT1-infected pts without cirrhosis. SMV+SOF was well tolerated.

	SMV 150mg QD+SOF 400mg QD			
	12-wk arm		8-wk arm	
SVR12[a] (n/N [%])	150/155 (97)		128/155 (83)	
Treatment-naïve	112/115 (97)		88/103 (85)	
Treatment-experienced	38/40 (95)		40/52 (77)	
HCV GT1a	112/116 (97)		92/116 (79)	
HCV GT1b	38/39 (97)		36/39 (92)	
IL28B CC	43/43 (100)		38/41 (93)	
IL28B non-CC	107/112 (96)		90/114 (79)	
On-treatment failure[b] (n/N [%])	0		0	
Viral relapse[c] (n/N [%])	4/154 (3)		27/155 (17)	
Pt-reported outcomes (Mean change from baseline [SD] in pts with/without SVR12)	SVR12	No SVR12	SVR12	No SVR12
HCV-SIQv4 OBSS[d]	-3.9 (0.96)	6.7 (7.07)	-2.9 (0.87)	3.4 (2.82)
FSS[e]	-0.5 (0.15)	1.4 (0.99)	-0.6 (0.12)	-0.0 (0.22)
CES-D[f]	-0.2 (0.73)	5.3 (5.33)	-2.5 (0.61)	4.2 (1.94)
EQ-5D VAS[g]	4.1 (1.40)	-7.0 (7.51)	6.5 (1.39)	-0.6 (2.63)

[a]HCV RNA <25 IU/mL detectable/undetectable 12 wks after end of treatment; [b]HCV RNA <25 IU/mL detectable or ≥25 IU/mL at end of treatment; [c]HCV RNA <25 IU/mL undetectable at end of treatment and ≥25 IU/mL during follow-up; [d]HCV-SIQv4 OBSS, Hepatitis C Symptom & Impact Questionnaire version 4 Overall Body System Score (range 0 [no symptoms] to 100 [maximum severity for all 29 symptoms], mean reduction of ≥5 points is clinically important); [e]FSS, Fatigue Severity Scale (range 1 [no fatigue] to 7 [severe fatigue], mean reduction of 0.6 points is clinically important); [f]CES-D, Center for Epidemiologic Studies Depression Scale (range 0 [no depressive symptoms] to 60 [severe depression on 20 symptoms], mean reduction of ≥3 points is clinically important); [g]EQ-5D VAS, EuroQol-5 Dimension questionnaire Visual Analogue Scale (range 0 [worst possible health] to 100 [perfect health], mean increase of ≥5 points is clinically important).

[Table. SVR12 (overall and sub-groups) and pt-reported outcomes]

TULBPE11

Efficacy and safety of 12 weeks of simeprevir (SMV) plus sofosbuvir (SOF) in treatment-naïve or -experienced patients with chronic HCV genotype 1 infection and cirrhosis: OPTIMIST-2

E. Lawitz[1], G. Matusow[2], E. Dejesus[3], E. Yoshida[4], F. Felizarta[5], R. Ghalib[6], E. Godofsky[7], R. Herring[8], G. Poleynard[9], A. Sheikh[10], H. Tobias[11], M. Kugelmas[12], R. Kalmeijer[13], M. Peeters[14], O. Lenz[14], B. Fevery[14], G. De La Rosa[15], J. Scott[16], R. Sinha[13], K. Boven[13], J. Witek[13]

[1]Texas Liver Institute, University of Texas Health Science Center, San Antonio, United States, [2]The Gastroenterology Group of South Jersey, Vineland, United States, [3]Orlando Immunology Center, Orlando, United States, [4]University of British Columbia, Vancouver, Canada, [5]Private practice, Bakersfield, United States, [6]Texas Clinical Research Institute, Arlington, United States, [7]University Hepatitis Center at Pointe West Infectious Diseases, Bradenton, United States, [8]Quality Medical Research, Nashville, United States, [9]Digestive Health Specialists, Winston-Salem, United States, [10]Gastrointestinal Specialists of Georgia, Marietta, United States, [11]Concorde Medical Group, New York, United States, [12]South Denver Gastroenterology, P.C., Denver, United States, [13]Janssen Research and Development, LLC., Titusville, United States, [14]Janssen Infectious Diseases BVBA, Beerse, Belgium, [15]Janssen Global Services, LLC., Titusville, United States, [16]Janssen Global Services, LLC., High Wycombe, United Kingdom

Presenting author email: kboven@its.jnj.com

Background: Hepatitis C virus (HCV)-infected patients (pts) with cirrhosis are historically a difficult-to-treat pt population. In a Phase II study (COSMOS), high sustained virologic response 12 weeks (wks) after end of treatment (EOT; SVR12) rates were achieved in METAVIR F4 treatment-naïve and prior null responder pts treated with an all oral, once-daily (QD) combination of SMV (HCV NS3/4A protease inhibitor)+SOF (HCV nucleotide-analogue NS5B polymerase inhibitor) for 12 or 24 wks, regardless of the presence or absence of ribavirin. The OPTIMIST-2 (NCT02114151) study aimed to demonstrate superiority of 12 wks of SMV+SOF, in treatment-naïve or -experienced (including interferon (IFN)-intolerant) HCV genotype (GT)1-infected pts with cirrhosis compared with a historical control (composite of the SVR12 rates of approved direct-acting antiviral/IFN+ribavirin regimens).

Methods: Treatment-naïve or -experienced pts with chronic HCV GT1 infection and documented presence of cirrhosis received SMV 150mg QD+SOF 400mg QD for 12 wks. The primary efficacy endpoint was SVR12 in the overall population. Safety and pt-reported outcomes were assessed.

Results: 103 pts received treatment (male, 81%; median age, 58 years; Black/African American, 18%; IL28B CC, 28%; GT1a/1b, 70/30%; treatment-naïve [n=50, 49%]; treatment-experienced [n=53, 52%]). SVR12 with SMV+SOF (84% [95% confidence interval: 76, 91]) met the primary endpoint of superiority to the historical control (70%). Other endpoints are summarised (Table). Adverse events (AEs) were observed in 72 (70%) pts, these were mainly Grade 1/2 (64%). Most frequent AEs: fatigue (20%), headache (20%) and nausea (11%). AEs of interest, increased bilirubin and rash, occurred in 2 (2%) and 16 (16%) pts, respectively. Three (3%) pts discontinued at least 1 drug due to an AE. Serious AEs were infrequent (5 pts [5%]). One pt died in a motor vehicle accident. Pt-reported outcomes improved from baseline to follow-up wk 12 with clinically important improvements in quality of life for pts who achieved SVR12 (Table).

Conclusions: SMV+SOF for 12 wks achieved superiority in SVR12 rates vs the historical control in treatment-naïve and -experienced HCV GT1-infected pts with cirrhosis and was generally well tolerated.

	12 wks of SMV 150mg QD+SOF 400mg QD	
SVR12[a] (n/N [%])	86/103 (84)	
Treatment-naïve	44/50 (88)	
Treatment-experienced	42/53 (79)	
HCV GT1a	60/72 (83)	
HCV GT1b	26/31 (84)	
IL28B CC	25/29 (86)	
IL28B non-CC	61/73 (84)	
On-treatment failure[b] (n/N [%])	3/103 (3)	
Viral relapse[c] (n/N [%])	13/103 (13)	
Pt-reported outcomes (Mean change from baseline [SD] in pts with/without SVR12)	SVR12 (n=79)	No SVR12 (n=13)
HCV-SIQv4 OBSS[d]	-5.9 (1.5)	-5.3 (2.9)
FSS[e]	-0.6 (0.2)	-0.7 (0.4)
CES-D[f]	-3.5 (1.1)	-3.5 (1.9)
EQ-5D VAS[g]	10.8 (2.1)	3.7 (5.1)

[a]HCV RNA <25 IU/mL detectable/undetectable 12 wks after EOT; [b]HCV RNA <25 IU/mL detectable or ≥25 IU/mL at EOT; [c]HCV RNA <25 IU/mL undetectable at EOT and ≥25 IU/mL during follow-up; [d]HCV-SIQv4 OBSS, Hepatitis C Symptom & Impact Questionnaire version 4 Overall Body System Score (range 0 [no symptoms] to 100 [maximum severity for all 29 symptoms], mean reduction of ≥5 points is clinically important); [e]FSS, Fatigue Severity Scale (range 1 [no fatigue] to 7 [severe fatigue], mean reduction of 0.6 points is clinically important); [f]CES-D, Center for Epidemiologic Studies Depression Scale (range 0 [no depressive symptoms] to 60 [severe depression on 20 symptoms], mean reduction of ≥3 points is clinically important); [g]EQ-5D VAS, EuroQol-5 Dimension questionnaire Visual Analogue Scale (range 0 [worst possible health] to 100 [perfect health], mean increase of ≥5 points is clinically important).

[Table. SVR12 (overall and sub-groups) and pt-reported outcomes]

TULBPE12

The cost-effectiveness and budgetary impact of a two-drug dolutegravir-lamivudine regimen for the treatment of HIV infection in the United States

M. Girouard[1,2], P. Sax[3], R. Parker[1,4,5], B. Taiwo[6], K. Freedberg[1,2,4], R. Gulick[7], M. Weinstein[8,9], A.D. Paltiel[10], R. Walensky[1,3,11]

[1]Massachusetts General Hospital, Medical Practice Evaluation Center, Boston, United States, [2]Massachusetts General Hospital, Division of General Internal Medicine, Boston, United States, [3]Brigham and Women's Hospital, Division of Infectious Diseases, Boston, United States, [4]Harvard University Center for AIDS Research, Boston, United States, [5]Massachusetts General Hospital, Biostatistics Center, Boston, United States, [6]Northwestern University Feinberg School of Medicine, Division of Infectious Diseases, Chicago, United States, [7]Weill Medical College of Cornell University, New York, United States, [8]Harvard T.H. Chan School of Public Health, Department of Health Policy and Management, Boston, United States, [9]Harvard T.H. Chan School of Public Health, Department of Biostatistics, Boston, United States, [10]Yale School of Public Health, New Haven, United States, [11]Massachusetts General Hospital, Division of Infectious Diseases, Boston, United States

Background: US first-line ART regimens for HIV cost $31,000-$35,000/person/year (average wholesale price). Pilot studies are evaluating two-drug therapy with dolutegravir (DTG) and lamivudine (3TC) partly to reduce this cost; the efficacy of this regimen is unknown. We examined the cost-effectiveness and budgetary impact of implementing DTG+3TC regimens in the US.

Methods: We used the CEPAC-US simulation model to project the clinical and economic outcomes of ART-naïve patients under three initial ART strategies (vs. No ART): 1) SOC: standard of care with coformulated DTG/abacavir(ABC)/3TC; 2) INDXN/MAIN: a 48-week induction regimen of DTG/ABC/3TC, followed by DTG+3TC maintenance if virologically suppressed; and 3) 2-DRUG: an initial two-drug regimen of DTG+3TC. Model inputs included: 48-week virologic suppression SOC 93%, INDXN/MAIN 93%, and 2-DRUG 88%. After 48-week virologic suppression, later virologic failure was: SOC 0.1%/month, INDXN/MAIN 0.6%/month, and 2-DRUG 0.6%/month. Patients experiencing virologic failure switched to protease-inhibitor (PI)-based second-line regimens. ART costs were calculated using Medicaid branded/generic discounts (23%/70%): DTG/ABC/3TC $24,500/year; DTG+3TC $15,200/year; and PI-based regimens $30,000/year. For the budgetary impact analysis, we assumed that only patients without a history of treatment failure would be eligible for DTG+3TC maintenance and that ~14,000 incident cases/year presented for ART initiation.

Results: SOC, INDXN/MAIN, and 2-DRUG had the same 5y-survival rates (90%); undiscounted quality-adjusted life expectancies among the strategies varied by < 0.20y. At 5y, the proportion of those remaining on first-line ART was SOC 97%, INDXN/MAIN 94%, and 2-DRUG 89%. Incremental cost-effectiveness ratios were INDXN/MAIN $22,500/QALY and SOC >$500,000/QALY; 2-DRUG was a weakly dominated strategy (Table). Cost-effectiveness results were robust to plausible variation in rates of initial suppression, late failure, and drug costs. With 50% uptake of an INDXN/MAIN strategy for eligible US HIV-infected patients, the potential 1y and 5y cost savings were $1.09B and $5.74B.

	Undiscounted Results					Discounted Results		
Strategy	**Proportion of patients alive at 5 years %**	**Proportion of patients alive at 10 years %**	**Proportion of patients on 1st-line ART at 5 years[a] %**	**Proportion of patients on 1st-line ART at 10 years[a] %**	**Quality Adjusted Life Expectancy *QALY***	**Lifetime Per-Person Cost *2014 USD***	**Quality Adjusted Life Expectancy *QALY***	**ICER[b] *$/QALY***
No ART	53	21	0	0	5.90	118,600	4.98	-
Two Drug	90	79	89	88	22.56	324,900	14.11	Weakly dominated[c]
Induction/Maintenance	90	79	94	93	22.67	325,000	14.17	22,500
Standard of Care	90	80	97	96	22.75	431,800	14.20	>500,000

ART: antiretroviral therapy; USD: US dollars; QALY: quality-adjusted life years; ICER: incremental cost-effectiveness ratio

[a]Proportion of patients on 1st-line ART is out of all patients alive and on ART.

[b]ICERs are evaluated using a willingness-to-pay threshold of 2014 $100,000.

[c]By convention, a strategy is labeled "weakly dominated" if it costs more and is less effective than some combination of other strategies.

[Base case clinical and economic model outcomes]

Conclusions: Initial HIV treatment with a 3-drug dolutegravir-based 48-week induction followed by a 2-drug dolutegravir-based maintenance regimen is very cost-effective, results in negligible differences in clinical outcomes, and would save over $5 billion in ART costs in the US over the next five years. A clinical trial proving the non-inferiority of this strategy has the potential for substantial cost savings in HIV care.

Wednesday, 22 July 2015

WELBPE13

Efficacy and safety of switching to simpler single tablet regimen of elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF) in HIV-1/hepatitis B co-infected adults in North America and Japan (NCT02071082): week 24 results

J. Gallant[1], J. Brunetta[2], G. Crofoot[3], P. Benson[4], A. Mills[5], C. Brinson[6], A. Cheng[7], W. Garner[8], M. Fordyce[9], M. Das[9], S. McCallister[9]

[1]Southwest CARE Center, Santa Fe, United States, [2]University of Toronto, Family and Community Medicine, Toronto, Canada, [3]Gordon Crofoot MD, PA., Houston, United States, [4]Be Well Medical Center, Berkley, United States, [5]Southern California Men's Medical Group, Los Angeles, United States, [6]Central Texas Clinical Research, Austin, United States, [7]Gilead Sciences, Inc., HIV Therapeutics and Development Operations, Foster City, United States, [8]Gilead Sciences, Inc., HIV Biostatistics, Foster City, United States, [9]Gilead Sciences, Inc., HIV Clinical Research, Foster City, United States

Presenting author email: jgallant@southwestcare.org

Background: A single tablet with co-formulated elvitegravir, cobicistat, emtricitabine, and tenofovir alafenamide (E/C/F/TAF) has demonstrated high efficacy and improved renal and bone safety in Phase 3 trials; TAF has excellent anti-HBV activity in a Phase 1b study. This Phase 3b open- label study is the first to evaluate the efficacy and safety of switching to single tablet E/C/F/TAF in HIV/HBV co-infected patients.

Methods: Virologically suppressed adults (HIV-1 RNA < 50c/mL ≥6 mos) with chronic HBV infection, no cirrhosis, and eGFR>50 mL/min switched to E/C/F/TAF. Week (W) 24 viral suppression rates for HIV (HIV-1 RNA < 50c/mL FDA snapshot algorithm) and HBV (HBV DNA < 29IU/mL Missing=Failure Analysis), biochemical (ALT normalization), serological (HBsAg/HBeAg loss and seroconversion), and safety endpoints are reported.
Results: Participants were older (median age 51), predominantly male (92%), 70% white, 18% black, and 10% Asian. Prior to enrollment, most [69/72 (96%)] patients were on a TDF-containing regimen and the majority were on a regimen containing ≥2 pills. At baseline, 71/72 (99%) had HIV-1 RNA < 50c/mL and 62/72 (86%) had HBV DNA < 29IU/mL. At W24, 68/72 (94%) had HIV-1 RNA < 50c/mL, 62/72 (86%) had HBV DNA < 29IU/mL, and 67/72 (93%) had normal ALT, including 5 of 10 with baseline abnormal ALT. No patients met pre-specified ALT flare criteria (confirmed serum ALT > 2 ×Day 1 value and >10 × ULN); the patient who lost HBsAg and gained HBsAb had a grade 3 ALT abnormality. One of 71 HBsAg-positive patients had HBsAg loss with seroconversion; another individual (1/30 HBeAg-positive patients) experienced HBeAg loss with seroconversion. There was no change in eGFR (-1.2, p=0.38). Renal tubular proteinuria decreased with switch to E/C/F/TAF: urine median RBP/Cr ratio decreased from 98.8µg/g to 91.0µg/g (p=.001); urine median beta-2M/Cr ratio decreased from 138.8µg/g to 92.0µg/g (p<0.001). Most AEs were mild/moderate; one patient had an AE (increased weight/appetite) leading to study discontinuation. Three treatment-emergent SAEs (acute myocardial infarction and two pneumonias) unrelated to study drug occurred.
Conclusions: Through W24, simplifying to single tablet E/C/F/TAF effectively maintained HIV and HBV virologic suppression while improving liver and renal safety endpoints. E/C/F/TAF shows promise for treating HIV/HBV co-infection.

WELBPE14

Elevated serum free light chains are a potential biomarker for malignancies in HIV-1-infected individuals

T. Belsches[1], L. Assi[2], R. Parson[3], D. Boldt-Houle[3], B. Macatangay[4], C. Rinaldo[5]
[1]University of Pittsburgh Medical Center, Internal Medicine, Pittsburgh, United States, [2]The Binding Site, Birmingham, United Kingdom, [3]The Binding Site, San Diego, United States, [4]University of Pittsburgh Medical Center, Infectious Disease, Pittsburgh, United States, [5]University of Pittsburgh Medical Center, Clinical Virology, Pittsburgh, United States
Presenting author email: belschestc@upmc.edu

Background: While HIV-positive individuals have higher levels of serum free immunoglobulin light chains (sFLC) at baseline secondary to chronic B cell hyperactivation, elevated sFLC have been shown to be a potential predictor for HIV-associated non-Hodgkin and Hodgkin lymphomas. Given that other cancers are also associated with increased inflammation and immune dysfunction, our objective was to determine if elevated sFLC are a potential biomarker for other malignancies as well.
Methods: This retrospective, case-control study compared sFLC levels at <2 years and 2 to 5 years prior to cancer diagnosis in HIV-1 seropositives from the Multicenter AIDS Cohort Study with cancer (non-Hodgkin lymphoma, Hodgkin lymphoma, Kaposi's sarcoma, and solid-organ non-AIDS-defining malignancies, n=91) to cancer-free HIV-1 seropositives (n=71) matched for age, race, HCV status, time with HIV, time taking antiretrovirals, and sample availability at equivalent time points. sFLC were measured with the Freelite® quantitative sFLC assays using stored serum samples obtained from 1986-2012.
Results: Age (41.4±2.7 vs 41.4±2.2), race (94.5±4.8% vs 97.2±3.9% Caucasian), sex (100% vs 100% male), years since HIV-1 diagnosis (7.7±1.3 vs 8.7±1.6), and years on highly active antiretroviral therapy (1.9±0.8 vs 2.4±0.9) were similar for cases and controls. Participants with cancer had a lower CD4 T cell count (median 263 range 0-1132 vs 461, 6-1460, P<0.001), whereas plasma HIV-1 RNA was not different (median 600, range 0-1,261,000 vs 0, 0-165100, P=0.24) with 21 cases and 20 controls virally suppressed. Participants with cancer had elevated K and λ levels at < 2 years (K 50.0±8.5 vs 43.3±17.8, P=0.011, λ 38.4±5.0 vs 26.3±3.7, P=0.001) and 2-5 years (K 51.1±16.7 vs 40.9±18.1, P=0.021 and λ 35.9±9.7 vs 24.4±3.4, P=0.010). When compared to their matched cancer-free controls, non-Hodgkin/Hodgkin lymphomas (n=17) had elevated K and λ levels at <2 years and 2-5 years prior to cancer diagnosis. Solid-organ non-AIDS-defining malignancies (n=32) and Kaposi's sarcoma (n=42) did not have significantly elevated sFLC.

	<2 years prior to cancer diagnosis			2-5 years prior to cancer diagnosis		
	All cancer cases (n=85)	All controls (n=67)		All cancer cases (n=90)	All controls (n=70)	
Kappa, mean±SD	50.0±39.3	43.3±72.8	P=0.011	51.1±79.8	40.9±76.2	P=0.021
Lambda, mean±SD	38.4±23.3	26.3±15.2	P=0.001	35.9±46.4	24.4±14.1	P=0.014
	NHL/HL cases (n=16)	Controls matched to NHL/HL (n=13)		NHL/HL cases (n=17)	Controls matched to NHL/HL (n=14)	
Kappa, mean±SD	71.5±56.1	38.0±27.7	P=0.047	91.3±166	33.1±124	P=0.046
Lambda, mean±SD	45.8±24.9	27.6±13.9	P=0.035	56.0±97.8	25.9±12.7	P=0.102

[Table 1. sFLC values of cases and controls]

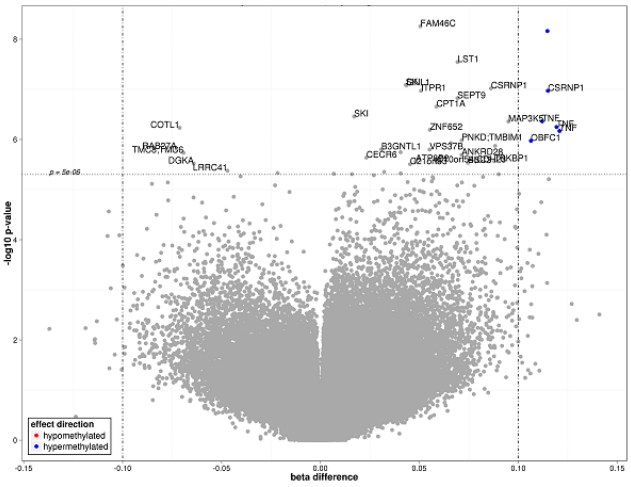
Conclusions: HIV-1-positive individuals with multiple malignancies have elevated serum free light chains as early as 2 to 5 years prior to their cancer diagnosis. sFLC should be considered as a biomarker for assessing risk for HIV-1-associated non-Hodgkin and Hodgkin lymphomas.

WELBPE15

Telomere length shortening and DNA methylation disruptions occur early following HIV seroconversion

J. Leung[1], J. Liu[1], N. Fishbane[1], S. Xu[2], R. Chen[1], J. Macisaac[3], M.-J. Milloy[4,5], E. Vucic[6], W. Lam[6], K. Hayashi[4], M. Kobor[3], J. Montaner[4,5], D. Sin[1,7], P.R. Harrigan[4], S.F.P. Man[1,7]
[1]St. Paul's Hospital, Centre for Heart Lung Innovation, Vancouver, Canada, [2]St. Paul's Hosital, Centre for Heart Lung Innovation, Vancouver, Canada, [3]University of British Columbia, Centre for Molecular Medicine and Therapeutics, Vancouver, Canada, [4]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada, [5]UBC-Division of AIDS, Department of Medicine, Vancouver, Canada, [6]BC Cancer Research Centre, Vancouver, Canada, [7]St. Paul's Hospital, Division of Respiratory Medicine, Vancouver, Canada
Presenting author email: janice.leung@hli.ubc.ca

Background: Persons living with human immunodeficiency virus (HIV) have demonstrated a higher risk of accelerated aging. Whether this occurs immediately following HIV seroconversion or throughout the chronic infection period is unknown.
To address this knowledge gap, we measured telomere length and DNA methylation changes longitudinally following documented HIV seroconversion in injection drug users within the Vancouver Injection Drug Users Study.
Methods: We measured peripheral leukocyte telomere length (LTL) and performed peripheral blood DNA methylation in 31 HIV-negative participants who subsequently contracted HIV. These were analyzed at three time points: pre-HIV (T1), early post-HIV (T2, mean 2.0 years after T1), and late post-HIV (T3, mean 2.2 years after T2). T1 and T2 samples were available for all subjects with 19 subjects also providing a T3 sample. LTL was measured using quantitative polymerase chain reaction methods. DNA methylation profiles were obtained using the Illumina Infinium 450K DNA methylation platform. CpG sites differentially methylated between T1, T2, and T3 were identified using paired limma analysis after correction for CD4 cell counts, with a Benjamini-Hochberg false discovery (FDR)-adjusted p-value <0.05 considered significant.
Results: LTL decreased significantly between T1 and T2 (mean±standard deviation 227±46 vs. 201±48 kbp/genome, paired t-test p=0.045), but there was no significant difference between T2 and T3 (201±48 vs. 186±27 kbp/genome, paired t-test p=0.244). 36 CpG sites corresponding to 33 unique genes were differentially methylated between T1 and T2, while there were no significant CpG sites distinguishing T2 from T3. Six CpG sites with both a beta methylation difference >0.1 and an FDR-adjusted p-value < 0.05 between T1 and T2 were identified; five of these corresponded to three genes (*CSRNP1*:tumor suppression, *TNF*:pro-inflammatory cytokine, and *OBFC1*:telomere protection) with the remaining CpG site corresponding to an unknown gene (Figure). The 33 genes differentially methylated between T1 and T2 were highly enriched for apoptotic pathways.



[Figure. Pre-Post HIV methylation differences, adjusting for CD4T count difference]

Conclusions: Telomere shortening and DNA methylation changes along apoptotic pathways occur early following HIV seroconversion, while no difference could be shown in these measures during the late HIV period. Hypermethylation in the *OBFC1* gene suggests that telomere protection is impaired soon after HIV seroconversion and could lead to telomere shortening.

WELBPE16

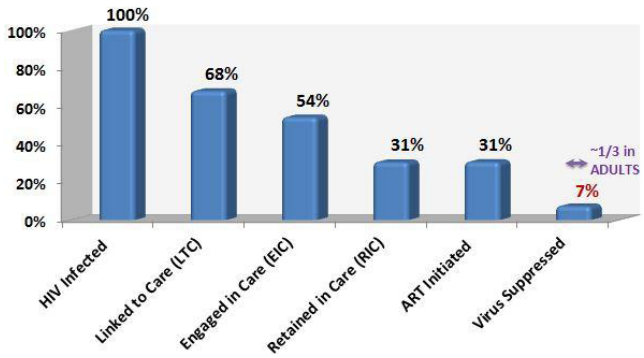
The HIV continuum of care for adolescents and young adults (12-24 years) attending 13 urban US centers of the NICHD-ATN-CDC-HRSA SMILE collaborative

B.G. Kapogiannis[1], J. Xu[2], K.H. Mayer[3,4], J. Loeb[2], L. Greenberg[2], D. Monte[2], L.J. Koenig[5], M. Banks-Shields[6], D. Fortenberry[7], and the ATN/SMILE Collaborative
[1]National Institute of Child Health and Human Development, Bethesda, United States, [2]Westat, Rockville, United States, [3]The Fenway Institute, Fenway Health, Boston, United States, [4]Beth Israel Deaconess Medical Center, Boston, United States, [5]Centers for Disease Control and Prevention, Atlanta, United States, [6]Health Resources and Services Administration, Rockville, United States, [7]Indiana University, Indianapolis, United States
Presenting author email: kapogiannisb@mail.nih.gov

Background: The HIV Continuum of Care (CoC) is a major focus of US HIV prevention and care efforts. Approximately one-quarter of all new infections occur among youth ages 13-24 years. Adolescent HIV providers and youth face enormous challenges across the HIV CoC, but few empirical youth-specific data are available.
Methods: The Strategic Multisite Initiative for the Identification, Linkage and Engagement in Care of HIV-infected youth (SMILE) collaborative between the NICHD/NIH-sponsored Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN), CDC and HRSA, forged local collaborations between health departments and ATN sites to help HIV-infected youth link to youth-friendly care, and evaluated each milestone of the HIV CoC for adolescents. Numbers of HIV-infected youth referred, linked (≤42 days after referral), engaged (≥1 additional visits within ≤16 weeks after linkage) and retained (≥1 additional visits within ≤52 weeks of engagement) in care were recorded, along with socio-demographics. Viral suppression was defined as a participant having achieved a plasma HIV viral load (VL) below the assay´s limit of detection (BLD) during the study period. VL suppression was examined by socio-demographics, risk behaviors, antiretroviral therapy (ART) and healthcare utilization, and ATN site using Cox Proportional Hazards models.
Results: 1548 HIV-infected youth ages 12-24 years were identified through SMILE between 10/2012 and 09/2014. Among 733 subjects (47.4%) with biomedical data at baseline, the mean age was 20.6±2.3 years, most were males (81%) and non-Hispanic black (72%). Seventy percent identified as either homosexual or bisexual. The median VL was 23,234 (0-10^7) copies/mL and the mean CD4 count was 463±252 cells/mL.

		Unadjusted HR (95% CI)	*p-value*	Adjusted HR (95% CI)	*p-value*
Study interval window (REF = Linked to care)	Engaged in care	2.16 (0.29 - 16.00)	0.4521	2.30 (0.31 - 17.16)	0.4175
	Retained in care	1.40 (0.19 - 10.24)	0.7406	1.53 (0.21 - 11.37)	0.6757
Log10 HIV VL at linkage (continuous)		0.75 (0.64 - 0.87)	0.0002	**0.64 (0.53 - 0.76)**	**<.0001**
Most current ART (REF = No)	Yes	2.54 (1.59 - 4.05)	<.0001	**3.10 (1.86 - 5.18)**	**<.0001**
Data sharing plan (REF = Formal data sharing)	Limited, Sharing of de-identified information monthly	3.21 (1.80 - 5.71)	<.0001	**2.33 (1.22 - 4.47)**	**0.0106**
	No formal, informal, no data sharing, and others	2.88 (1.67 - 4.99)	0.0002	**2.78 (1.51 - 5.11)**	**0.0010**
Time from HIV testing to referral (REF = >3 months)	0-7 days	1.17 (0.69 - 1.99)	0.5569	1.64 (0.93 - 2.91)	0.0883
	>7 days to 6 weeks	1.64 (1.00 - 2.69)	0.0495	**2.52 (1.50 - 4.23)**	**0.0005**
	>6 weeks to 3 months	1.49 (0.81 - 2.75)	0.1960	**2.08 (1.08 - 4.04)**	**0.0294**

[Table 1. Likelihood of Viral Suppression with Covariables]



[Figure 1. HIV continuum of care for 1,548 adolescents and young adults (12-24 yrs) attending 13 urban US centers of the NICHD-ATN-CDC-HRSA SMILE Collaborative - Oct 2012 - Sept 2014]

Conclusions: Prior studies have suggested that HIV-infected US youth are less likely to know their status than adults. The SMILE collaborative has demonstrated that youth with HIV had high levels of plasma viremia and advanced infection at diagnosis. While they linked to care at similar rates as adults, youth achieved disproportionately low rates of virologic suppression. Interventions are urgently needed to improve knowledge of undiagnosed HIV-infection, access to care, medication adherence and long-term VL outcomes in youth.

WELBPE17

Efavirenz-based therapy could simplify LPV-based therapy initiated before the age of 2 in HIV-infected children not exposed to single dose NVP to prevent mother-to-child transmission (PMTCT) in West-Africa

V. Leroy[1,2], M. Amorissani-Folquet[3], C. Yonaba[4], M. Coulibaly[5], D. Avit[6], K. Malateste[2], T. Toni[7], M. Barry[8], S. Dattez[2], M. Timité-Konan[6,9], N. Méda[5,10], P. Van de Perre[11], P. Lepage[12], R. Salamon[2], S. Blanche[13], C. Seguin-Devaux[14], for the MONOD ANRS 12206 Study Group
[1]Inserm U897, University of Bordeaux, Bordeaux, France, [2]Institute of Epidemiology and Public Health, University of Bordeaux, Bordeaux, France, [3]Service de pédiatrie, CHU de Cocody, Abidjan, Cote D'Ivoire, [4]Service de Pédiatrie, CHU Yalgado Ouédraogo, Ouagadougou, Burkina Faso, [5]Centre de Recherche International en Santé, Site ANRS, Projet MONOD ANRS 12206, Ouagadougou, Burkina Faso, [6]Programme PACCI, Site ANRS, Projet MONOD-ANRS 12206, Abidjan, Cote D'Ivoire, [7]Laboratoire du CeDReS, Abidjan, Cote D'Ivoire, [8]Laboratoire du CHU Charles de Gaulle, Ouagadougou, Burkina Faso, [9]Service de pédiatrie, CHU de Yopougon, Abidjan, Cote D'Ivoire, [10]Université de Ouagadougou, Ouagadougou, Burkina Faso, [11]Inserm U1058, University of Montpellier, Montpellier, France, [12]Hôpital Universitaire des Enfants Reine Fabiola (HUDERF), Service de pédiatrie, Bruxelles, Belgium, [13]EA 3620, University of Paris-Descartes, Paris, France, [14]Luxembourg Institute of Health, Luxembourg, Luxembourg
Presenting author email: valeriane.leroy@isped.u-bordeaux2.fr

Background: An early antiretroviral therapy (EART)<2 years of age in HIV-infected children virologically supressed after 12/15 months of a lopinavir (LPV)-based therapy could be simplified with an efavirenz-based therapy (EFV).
Methods: The MONOD-ANRS-12026 study is an international, randomized, phase 2-3 non-inferiority trial conducted in Abidjan, Côte d'Ivoire and Ouagadougou, Burkina-Faso (ClinicalTrial.gov registry number: NCT01127204). All HIV-1-infected children, tuberculosis-free, receiving <2 years, a 12-15 month suppressive twice-daily LPV/r based-therapy (undetectable viral load [VL]<500 copies/mL, confirmed) were randomised in two arms: once-daily ABC-3TC-EFV (EFV) therapy versus continuation of the twice-daily LPV therapy (AZT or ABC-3TC-LPV/r). The primary endpoint was the difference in proportion of children virologically suppressed by 12-month post-randomisation, between arms (14% non-inferiority margin), Chi-square-test.
Results: Between 05/2011 and 01/2013, 156 children were included. After 12/15 months on EART, 13 infants have died (8%), 2 were lost-to-follow-up (1%), 3 withdrew (2%), 32 virologically failed (21%) and 106 (68%) were randomized (54 LPV, 52 EFV): 44% male, median age 27 months; 77% Abidjan site; 34% of median CD4%, 54% not exposed to any PMTCT intervention, 8.5% exposed to NVP-single-dose.
At 12-month post-randomization, 46 (85.2%) children under LPV vs. 43 (82.7%) under EFV had VL<500 copies/mL; difference 2.5% (95% Confidence-Interval [CI]:-11.5-16.5); 47 (87.0%) under LPV vs. 47 (86.5%) under EFV had VL<1000 copies/mL; difference 0.5% (95%CI:-12.4-13.4). Adjusted baseline correlates of virological success (< 1000 copies/ml) were Abidjan site (aOR: 0.38;95%CI:0.09-1.59), NVP-single-dose exposure (aOR: 0.18; 95%CI:0.02-1.56) and absence of malnutrition (aOR: 6.87;95%CI:1.34-35.11).
No significant difference in Severe Adverse Events was observed: 3 (5.6%) in LPV vs. 4 (7.7%) in EFV arm (p=0.71). 11/14 children with VL>1000 copies/ml had a genotype (6/7 EFV, 5/7 LPV): 7 had at least one major NNRTI mutations (4 EFV of whom 2 were acquired, 3 LPV none being acquired) at VL failure (K103N; Y181C; P225H) whereas none had LPV/r mutation.
Conclusions: Considering the 1000 copies/mL threshold, the non-inferiority of EFV compared to LPV on VL suppression was shown. Resistance analyses highlight the need to consider the PMTCT-exposure before switching to EFV. This simplified treatment strategy may be interesting in resource-limited settings to improve adherence and spare Protease-Inhibitor-based regimen for future failures.

Track C

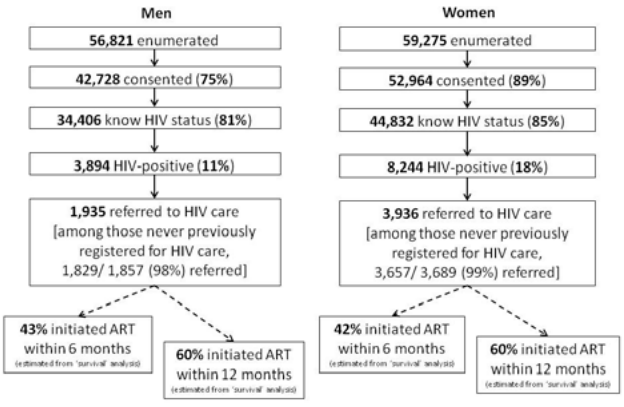
Monday, 20 July 2015

MOLBPE19

HPTN 071 (PopART): Uptake of first year of a combination HIV prevention intervention including universal HIV testing and treatment across 4 communities in Zambia.

R.J. Hayes[1], H. Ayles[2,3], N. Beyers[4], S. Floyd[1], A. Schaap[1,2], K. Shanaube[2], R. Dunbar[4], P. Bock[4], B. Yang[4], M. Limbada[2], S. Griffith[5], K. Sabapathy[1], D. Van Deventer[4], W. El-Sadr[6], S. Fidler[7], on behalf of the HPTN071 (PopART) Study Team
[1]London School of Hygiene & Tropical Medicine, Infectious Disease Epidemiology, London, United Kingdom, [2]Zambia AIDS Related TB Project (Zambart), Lusaka, Zambia, [3]London School of Hygiene & Tropical Medicine, Clinical Research, London, United Kingdom, [4]Desmond Tutu TB Centre, Cape Town, South Africa, [5]FHI360, Durham, United States, [6]Columbia University, New York, United States, [7]Imperial College, London, United Kingdom
Presenting author email: richard.hayes@lshtm.ac.uk

Background: HPTN 071 (PopART) is a 3-arm community-randomised trial in 21 communities in Zambia and South Africa, with adult HIV prevalence of approximately 15% and an adult population of 350,000 across 14 intervention communities. It will test the impact of a combination prevention intervention in Arms A and B, compared with a control arm providing standard-of-care (Arm C), on HIV incidence within a randomly selected population cohort. In arms A and B, the intervention comprises annual rounds of home-based voluntary HIV counselling and testing (HCT) by Community HIV Care Providers (CHiPs), who support referral to, and retention in, HIV care. ART is provided at local clinics, and is offered irrespective of CD4 count in Arm A and according to national guidelines in Arm B.
Methods: The first annual round of intervention occurred between December 2013 and March 2015. Here we summarise data for the four Arm A communities in Zambia. CHiPs record data electronically during household visits, including consent to participate, acceptance of HCT among adults who do not self-report HIV-positive, the HIV test result, and referral to HIV care. CHiPs document clinic linkage to care and ART initiation for all HIV-positive adults.
Results: 46,676 households (~100%) in Arm A communities were visited by CHiPs during the first round. Enumeration of household members was completed in 96% of households. 75% of men and 89% of women consented to participate (Figure), 15% of men and 4% of women were not contacted, and 8% of men and 5% of women refused. Of those enumerated, 81% of men and 85% of women accepted HCT, reported they were HIV-positive, or had tested for HIV in the previous 3 months and were HIV-negative. Among HIV-positive individuals who had never previously registered for HIV care, 99% were referred. Of all those referred, approximately 42% and 60% initiated ART within 6 and 12 months respectively. Among clients offered immediate ART outside national guidelines in Zambia, 99% accepted and started ART.



[Figure. Flow chart of cascade from enumeration through ART initiation]

Conclusions: The intervention was well accepted. The greatest challenges include contacting men in the household, and rapid linkage to care and ART initiation following referral.

MOLBPE20

HIV vertical transmission risks among South African female sex workers

S. Schwartz[1], Z. Kose[2], M. Mcingana[3], C. Holland[1], N. Phaswana-Mafuya[2], A. Lambert[4], S. Sweitzer[1], S. Baral[1]
[1]Johns Hopkins School of Public Health, Epidemiology, Center for Public Health and Human Rights, Baltimore, United States, [2]Human Sciences Research Council, HIV/AIDS, STIs and TB (HAST), Port Elizabeth, South Africa, [3]TB/HIV Care Association, Port Elizabeth, South Africa, [4]TB/HIV Care Association, Cape Town, South Africa
Presenting author email: sschwartz@jhu.edu

Background: The past decade has witnessed significant declines in HIV mother-to-child transmission (MTCT) in South Africa due to scale-up of HIV testing and antiretroviral therapy (ART) for all HIV-positive pregnant women. However, female sex workers (FSW) are disproportionately affected by HIV, have high pregnancy rates, and commonly experience socioeconomic and structural barriers which may limit engagement in PMTCT care.
Methods: Respondent driven sampling (RDS) was used to recruit 410 FSW in Port Elizabeth, South Africa, from October 2014-April 2015. Women ≥18 years were eligible if sex work was their primary source of income. Following consent, all participants completed a questionnaire covering demographics, pregnancy history and engagement in healthcare. Pregnancy, syphilis, and HIV testing were performed on all FSW; viral loads were assessed on all pregnant HIV-positive FSW.
Results: Overall 261/410 FSW (63.7%) had positive HIV tests (RDS-adjusted estimate 63.0%, 95% CI 56.7-69.3]); syphilis prevalence was 20.3% (RDS-adjusted 17.1% [95% CI 12.1-22.1]). Young children were common among FSW, 192/410 (46.8%) had children ≤5 years and 77/410 (18.8%) had a child ≤2 years. Among 192 women with children ≤5 years, 90.0% reported attending antenatal care during their last pregnancy and 82.3% had their infants tested for HIV. Breastfeeding was common (70% of children ≤5 years were breastfed) and only 45.8% of breastfeeding mothers had their infants tested for HIV after breastfeeding. Of the 19 (4.7%) FSW pregnant at the time of the study, 2/18 (11.1%) had untreated syphilis (one sample was lost) and 13/19 (68.4%) were HIV-positive. Among pregnant HIV-positive FSW, 4/13 were on ART and none (0/10) were virally suppressed (3 samples rejected/lost by laboratory). Pregnancy and postnatal HIV exposure and transmission risk was evident as 38% of FSW engaged in sex work during their prior pregnancy (on average for 5 months), and 48% returned to sex work before 6 months postpartum.
Conclusions: These data suggest that MTCT risk is likely not evenly distributed among women in South Africa and FSW represent an underserved and at-risk population for this preventable outcome. Health assessments and family-focused interventions for pregnant FSW and their children are critically needed to reduce MTCT risk and promote early infant HIV diagnosis.

Tuesday, 21 July 2015

TULBPE21

PrEP, sex, and the paradoxes of prevention: qualitative data from New York city participants in HPTN 067

J. Franks[1], Y. Hirsch-Moverman[1,2], A. Loquere[1], K.R. Amico[3], B.J. Dye[4], L. Mckinstry[5], R.M. Grant[6], S. Mannheimer[1,2,7]
[1]ICAP, Columbia University Mailman School of Public Health, New York, United States, [2]ICAP, Columbia University Mailman School of Public Health, Department of Epidemiology, New York, United States, [3]University of Michigan, Department of Health Behavior and Health Education, Ann Arbor, United States, [4]FHI 360, Durham, United States, [5]Fred Hutchinson Cancer Research Center, Seattle, United States, [6]University of California, San Francisco, Gladstone Institutes, San Francisco, United States, [7]Harlem Hospital Center, Department of Medicine, New York, United States
Presenting author email: jf642@cumc.columbia.edu

Background: Daily oral FTC/TDF is effective in preventing HIV infection. HPTN 067 evaluated the feasibility of intermittent dosing strategies for FTC/TDF-based pre-exposure prophylaxis (PrEP). 179 men who have sex with men (MSM) and transgender women enrolled in New York City (NYC) were randomly assigned 1:1:1 to three PrEP dosing regimens over 24 weeks: daily, time-driven (taken twice weekly plus a post-sex dose), or event-driven (pre- and post- sex). Qualitative data was collected to explore PrEP-users experiences and beliefs about HIV prevention.
Methods: Focus groups (FG) and in-depth interviews (IDI) were conducted with a subset of participants within three months of study completion. Stratified convenience sampling was used to enroll two FG and two IDI per PrEP dosing arm (total six FG and six IDI). Semi-structured guides were used to explore experiences and changes in HIV prevention-related attitudes and behavior while taking PrEP. Transcripts were coded and analyzed using the constant comparative method. Critical dimensions of participants' HIV prevention strategies emerged as themes within coded data.

Results: 37 MSM participated in FG and IDI. Participants were 68% Black, 11% White, 8% Asian; 27% Hispanic. Median age was 34 years; 68% were unemployed. Analysis identified critical dimensions of prevention strategies and PrEP adherence, including HIV risk conceptualization; endorsement of combination prevention; HIV-related stigma; and difficulty with sex-dependent doses (Table). These dimensions affected adherence to PrEP in distinct ways. Participants associated HIV risk with partner characteristics and linked motivation to use PrEP with partner risk. Many participants reported adopting additional HIV prevention strategies while on PrEP, including discussing HIV status with partners, reducing partners, and increasing condom use. Participants described HIV-related stigma that made disclosing PrEP use difficult, affecting their ability to adhere to intermittent regimens. Similarly, value placed on sexual spontaneity made adhering to sex-dependent doses in non-daily intermittent regimens challenging.

Dimensions of HIV Prevention	Illustrative Quotes (with codes)
Estimation of partner-related risk	Early in the study I had just two people that I been dealing with for a long time. I knew their status. … It wasn't that important to me to remember the regimen. (Trust in partners) It's really hard to extract the truth when you're in extracurricular relationships. (Limits to disclosure) I'm very optimistic about the pill, because if someone even really truly tested negative that means that he can be in the window period. So it's even more dangerous for you. (Limits to testing technology)
Awareness of behavioral risk	I want to say that I would say no, but when that shit's in front of me, nah, I ain't gonna say no, because that's the way that I am. I am working on my impulsivity. (Impulsivity) Because sometimes I am not able to say no when I need to say no when I know it is the best thing for me to say no. (Can't say no) Condom or no condom, PrEP or no PrEP, people take risks. It's innate behavior. (Human nature)
Endorsement of combination Prevention	PrEP is only one aspect of whole thing. . . . Where you stand in your relationship, your commitment, dedication, behaviors, risk-taking, all go hand-in-hand. (PrEP in combination) Nothing is perfect and a hundred percent accurate. Use both [condoms and pills]. . . . Because you could use a condom and God forbid, he ramming and it break. (PrEP in combination)
Risk reduction	It made me reduce [my partners] by a huge amount- just taking the pills continually reminded me to protect myself from HIV. (Reduce partners) It made me be more conscious of everything. I started wearing condoms even more. I just don't want to catch it from anybody. (More condom use)
Risk amplification	It made me practice safe sex a little bit less than I would normally, I felt kind of impervious to it, to catching HIV, because of the pill. I really had to check myself about that. (Less safe sex) I definitely wasn't as regimented [while on PrEP], like on top of using condoms or making sure I have them available. I just didn't worry about it. (Less regimented)
Dimensions of PrEP Adherence	
HIV-related stigma	AIDS. You telling them you're taking a pill to prevent it; they thinking you taking a pill to stop it. (HIV stigma bleeds onto PrEP) One of my partners was like, "Whoa. What does this mean? What are you doing?" Indicating that taking the pill means that I'm willy-nilly having unprotected sex. (Promiscuity label)
Difficulty forecasting sex	Say [sex] just happened, and I didn't have the pills on me, I was like freaking out. (Spontaneous sex missed pills)
Difficulty dosing during sexual encounters	I didn't want to have them with me where the other person would find it. . . . It was awkward. Somebody did find them and I had to do some explaining. (Awkward to explain) If you'd been partying, and drinking you're not going think about taking a pill. (Partying and pills don't go together) I [would think sex-dependent dosing] may also spoil the mood. (Sex and pill don't go together)

[Dimensions of HIV prevention and PrEP adherence]

Conclusions: Analysis of qualitative data from the NYC HPTN 067 cohort of mostly Black MSM highlights the negative impact of HIV-related stigma on PrEP use and on adherence to sex-dependent doses of intermittent PrEP regimens. Interventions to address stigma in the context of PrEP use are needed for US Black MSM.

TULBPE22

Baseline characteristics of a rectal phase 2 extended safety and acceptability microbicide study of tenofovir reduced-glycerin 1% gel: MTN-017

R. Cranston[1], J. Lama[2], B. Richardson[3], A. Carballo-Diéguez[4], R.P. Kunjara Na Ayudhya[5], B. Galaska[5], C. Jacobson[5], M. Marzinke[6], S. Johnson[7], J. Piper[8], C. Grossman[9], K. Ho[1], T. Holtz[10], S. Chariyalertsak[11], L.-G. Bekker[12], P. Gonzales[2], K. Mayer[13], A. Liu[14], C. Zorrilla[15], I. McGowan[1]

[1]University of Pittsburgh, Pittsburgh, United States, [2]Impacta, Lima, Peru, [3]University of Washington, Seattle, United States, [4]HIV Center for Clinical and Behavioral Studies, New York City, United States, [5]Magee-Womens Research Institute, Pittsburgh, United States, [6]Johns Hopkins University, Baltimore, United States, [7]FHI360, Durham, United States, [8]National Institute of Allergy and Infectious Diseases, Bethesda, United States, [9]National Institute of Mental Health, Bethesda, United States, [10]Thailand MOPH - US CDC Collaboration, Bangkok, Thailand, [11]Chiang Mai University, Chiang Mai, Thailand, [12]Institute of Infectious Disease and Molecular Medicine, Cape Town, South Africa, [13]Fenway Health/The Fenway Institute, Boston, United States, [14]Bridge HIV at the San Franciso Department of Public Health, San Francisco, United States, [15]University of Puerto Rico, San Juan, Puerto Rico
Presenting author email: rdc27@pitt.edu

Background: Men who have sex with men (MSM), and transgender women (TGW), are disproportionately affected by human immunodeficiency virus (HIV) infection worldwide. MTN-007 previously demonstrated that the reduced-glycerin formulation of 1% tenofovir gel (RGT) is safe and acceptable when applied rectally for up to 7 consecutive days. MTN-017 is a Phase-2, 3-period, randomized sequence, open label, expanded safety and acceptability crossover study evaluating RGT when used either daily or before and after receptive anal intercourse (RAI), compared to daily oral emtricitabine/tenofovir disoproxil fumarate (FTC/TDF). Baseline study participant (ppt) characteristics are presented here.
Methods: MTN-017 recruited ppts through social media, online advertising, flyers, community events and engagement, and word of mouth. Healthy HIV-1 uninfected MSM and TGW ≥18 years of age were enrolled at 8 clinical research sites in the United States (4), Peru (1), South Africa (1) and Thailand (2).
Results: Between September 2013 and November 2014, 347 ppts were screened and 195 enrolled. Reasons for screen outs were mostly for laboratory criteria (including sexually transmitted infections) and investigator discretion, with 7 individuals diagnosed as HIV-infected. The mean ppt age was 31.1 years (range 18-64). The race/ethnic composition was predominantly white: 64 (33%), Thai: 54 (28%), or mixed race: 29 (15%). Twenty three ppts (12.1%) self-identified as TGW/women, and 156 (80%) had a college education. At enrollment 29 (15%) and 32 (16%) had a perianal or rectal mucosal abnormality detected, respectively. Of those who reported having RAI in the past 8 weeks, 95% reported some lubricant use. Most ppts (67%) considered themselves at some risk for HIV infection, and nearly half (49%) had condomless RAI within the previous 8 weeks. Only a few ppts said they would be unlikely to use the daily gel (7%) or oral medication (6%), with fewer (3%) unlikely to use gel before and after RAI to prevent HIV were it available and effective.
Conclusions: An international cohort of MSM and TGW at risk for HIV infection and who may potentially benefit from rectal microbicides, if shown to be effective, was successfully engaged into research and enrolled into a Phase 2 rectal microbicide study.

WELBPE23

Facilitators and barriers affecting PrEP adherence among Thai men who have sex with men in the HPTN 067/ADAPT study, a qualitative analysis

T. Chemnasiri[1], A. Varangrat[1], K.R. Amico[2], S. Chaikummao[1], A. Chitwarakorn[3], B.J. Dye[4], R.M. Grant[5], T.H. Holtz[1,6], the HPTN 067/ADAPT Study Team

[1]Thailand MOPH-U.S. CDC Collaboration, HIV/STI Research Program, Nonthaburi, Thailand, [2]University of Michigan, Department of Health Behavior and Health Education, School of Public Health, Ann Arbor, United States, [3]Thailand Ministry of Public Health, Department of Disease Control, Nonthaburi, Thailand, [4]FHI 360, Durham, United States, [5]Gladstone Institutes, University of California, San Francisco, United States, [6]Division of HIV/AIDS Prevention, Centers for Disease Control and Prevention, Atlanta, United States
Presenting author email: hpu4@cdc.gov

Background: The HPTN 067/ADAPT Study sought to evaluate the feasibility, acceptability and patterns of adherence and coverage for three randomly assigned oral FTC/TDF pre-exposure prophylaxis (PrEP) dosing regimens to prevent HIV infection among Thai men who have sex with men (MSM); daily, time-driven (twice a week with a post-sex dose), and event-driven (pre/post-sex dosing). Using qualitative methods we explored the acceptability and perceptions of these PrEP regimens.
Methods: In August 2013 and March 2014, 32 HPTN 067/ADAPT MSM participants joined in six focus-group discussions, and six attended key-informant interviews, two per each study regimen after they completed 34 weeks of study follow-up.

Results: Overall, participants assigned to the three regimens reported that understanding and being assigned a regimen that fit the participant's lifestyle facilitated adherence. Other facilitators were disclosure about study participation and PrEP use to friends/family/partners, believing in PrEP efficacy, and understanding their own risk. Participants in the daily regimen reported it was the easiest regimen for this 34-week study, but it might be difficult to use if sex were infrequent. There were concerns about long-term side effects, fear of being seen as being HIV infected, and affordability. Participants assigned to either the time-driven or event-driven regimens both reported less confusion if sexual acts were infrequent. Preference for fewer doses and being able to choose the day to take pills facilitated adherence. Difficulty in linking routine activity with two pill-taking days in the time-driven regimen was noted. Participants in the event-driven regimen reported that having control over planning for sex facilitated adherence. Regimen confusion, intoxication, and inability to forecast sex were barriers to adherence of the event-driven regimen.
Participants did not completely trust PrEP to be 100% protective and preferred to take PrEP and use condoms together to increase their confidence in HIV protection.
Conclusions: The adaptability of PrEP regimens to participant preference and sexual practices may be a powerful facilitator of adherence. Preferences for regimens varied within each group, highlighting the need for multiple PrEP regimen options for MSM. Disclosure about PrEP use facilitated adherence, so mitigating stigma by disseminating information that PrEP is a responsible choice may foster more effective use.

Wednesday, 22 July 2015

WELBPE24

Role of condyloma acuminata in incident HIV infection: a population-based cohort study in Taiwan 2000-2010

H. Zou[1,2], Y.-C. Chen[2,3], C. Strong[4], C.-Y. Li[4], A. Grulich[1], W.-C. Ko[5,6], N.-Y. Ko[2,5]
[1]University of New South Wales, Kirby Institute, Kensington, Australia, [2]National Cheng Kung University, Department of Nursing, Tainan, Taiwan, Province of China, [3]National Cheng Kung University, Institute of Allied Health Sciences, Tainan, Taiwan, Province of China, [4]National Cheng Kung University, Department of Public Health, Tainan, Taiwan, Province of China, [5]National Cheng Kung University, Department of Internal Medicine, Tainan, Taiwan, Province of China, [6]National Cheng Kung University, College of Medicine, Tainan, Taiwan, Province of China

Background: The role of Condyloma Acuminata (CA) in incident HIV infection has not been well documented. We aimed to elucidate this relationship by analyzing a large national cohort.
Methods: Medical claim records 2000-2010 of 1 million individuals randomly selected from the Taiwan National Health Insurance Research Database (NHIRD, approximately 23 million individuals in total) were retrieved. We included all patients with definite CA diagnosis (those with clinical diagnosis and specific clinical treatment for CA, PDCs) and patients with possible CA diagnosis (those with clinical diagnosis but no specific clinical treatment for CA, PPCs). We matched five patients never clinically diagnosed with CA (PNCs) for every one PDC by year of first CA treatment (PDCs)/first clinical visit (PNCs), gender and age. PDCs, PPCs and PNCs were followed from the date of first CA treatment, first CA screening and first clinical visit, respectively. Endpoint was incident HIV infection. Chi-square test was used to compare socio-demographic characteristics among patients. Characteristics with a *P* value of < 0.1 using univariate Cox regression were entered into a multivariate Cox regression model to calculate adjusted hazard ratio (aHR) of incident HIV infection.
Results: We included 1539 PDCs, 1106 PPCs and 7695 PNCs. HIV incidence among PDCs, PPCs and PNCs was 284.0 (95% confidence interval (CI): 164.9-489.1), 110.6 (95% CI: 41.5-294.7) and 3.8 (95% CI: 0.5-27.2) per 100,000 person-years, respectively. After adjusting for potential confounders, PDCs were more likely to develop incident HIV infection compared to PNCs (adjusted Hazard Ratio (aHR)=23.1, 95% CI: 2.7-195.1). Other variables associated with incident HIV infection were being a male (aHR=14.0, 95% CI: 3.1-63.4), being under 30 years of age (aHR=2.8, 95% CI: 1.0-7.5), having tested HIV once during the year of observation commencement (aHR=9.8, 95% CI: 2.9-33.8) and having tested HIV multiple times during the year of observation commencement (aHR=24.7, 95% CI: 5.7-106.4).
Conclusions: CA seemed to be associated with elevated incident HIV infection. HIV risk reduction interventions and routine HIV screening among patients with CA are warranted.

WELBPE25

Epidemiology of HIV among men who have sex with men: respondent driven survey in Dodoma Tanzania

N.E. Makyao[1], G. Somi[2], A. Leshabari[3], E. John[4], A. Ramadhan[5]
[1]Ministry of Health and Social Welfare, National AIDS Control Programme, Dar es Salaam, Tanzania, United Republic of, [2]National AIDS Control Programme, Epidemiology, Dar es Salaam, Tanzania, United Republic of, [3]Muhimbili Univerisity of Health and Allied Sciencies, Public Health and Social Sciencies, Dar es Salaam, Tanzania, United Republic of, [4]Muhimbili University of Health and Allied Sciencies, Epidemiology and Biostatistics, Dar es Salaam, Tanzania, United Republic of, [5]National AIDS Control Programme, Dar es Salaam, Tanzania, United Republic of
Presenting author email: neemakirei@gmail.com

Background: Tanzania's HIV epidemic has been characterized as a generalized epidemic though there are sub groups in society with high HIV and STIs prevalence. This study aimed at determines the prevalence of HIV, other sexually transmitted infections and risk related behaviours among MSM in Dodoma, Tanzania
Methods: Respondent-driven sampling was used to recruit self identified MSM aged 18+ years living in Dodoma who reported to had anal or oral sex with another man in the last 6 months. Socio-demographic characteristics, HIV/STI knowledge and behavioural profile were collected. Blood samples were tested for HIV, HSV2, Syphilis, Hepatitis B and Hepatitis C. Point estimates and 95% confidence intervals (CI) were adjusted for social network size and recruitment patterns using RDS-A and STATA
Results: From June to August 2014 409 MSM were recruited. Their median age was 27 (ranged 18 - 60). The median age at first anal sex was 15 and the majority (80.4%) were single while 8.1% were married/cohabiting a woman. 37.5% had had receptive anal sex, 47.5% insertive and 15.0% both an insertive and receptive sex during last anal sex. Perceived risk for HIV infection was fairly low in this population and was associated with low condom use during the last sex. The prevalence of HIV, HSV2, Syphilis and Hepatitis B and Hepatitis C infections were 17.4%, 38.5%, 0.2%, 0.54 and 3.4%, respectively. HIV infection was associated with HSV2 (Adjusted Odds Ratio (AOR), 5.0, 95%CI: 3.01, 11.21) and having lived outside Dodoma (AOR, 1.70 95% CI: 1.05, 6.73). Other predictors of HIV infection included ; young age (18-24) (AOR, 2.1, 95% CI: 1.7, 3.65), sexual relationship with a woman (AOR, 5.6, 95% CI: 3.99, 12.8), receptive anal intercourse (AOR, 7.11 95%CI: 4.87, 17.41) and both a receptive and insertive intercourse (AOR, 4.5, 95%CI: 1.90, 11.42) during last anal sex, engaging in group sex (AOR, 3.10, 95%CI: 1.21,6.14), and use of alcohol/drugs (AOR, 3.97, 95%CI: 1.11, 9.15).
Conclusions: HIV prevalence (17.4%) among MSM is five times higher than that of men in the general population in Dodoma (3.7%). These findings cement the plans to mount intensified HIV prevention programs that address key population in Tanzania.

WELBPE26

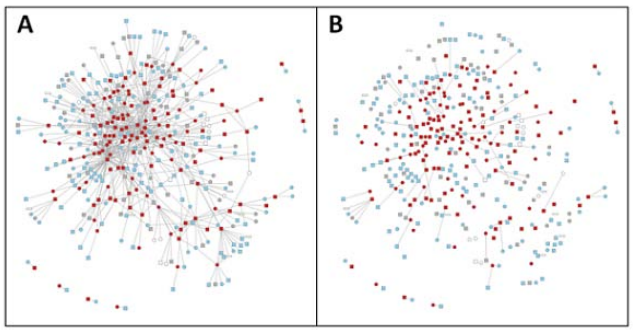
Network analysis of a contact network from an investigation of a community outbreak of HIV infection linked to injection drug use of oxymorphone - Indiana, 2015

M.W. Spiller[1], J. Shields[2], H. Bradley[1], E. Chapman[2], C. Conrad[2], J.M. Duwve[3], D. Hillman[2], B. Hoots[1], A. Perez[2], P. Peters[2], P. Pontones[2], J. Roseberry[2], M. Sandoval[1], J. Walthall[2], D. Waterhouse[2], P. Weidle[2], C. Wejnert[1], D. Broz[1]
[1]U.S. Centers for Disease Control and Prevention, Division of HIV/AIDS Prevention, Atlanta, United States, [2]Indiana State Department of Health, Indianapolis, United States, [3]Indiana State Department of Health and Indiana University Richard M. Fairbanks School of Public Health, Indianapolis, United States
Presenting author email: mspiller@cdc.gov

Background: In January 2015, a cluster of HIV-1 infections was detected in a rural county in southeastern Indiana among persons who reported injection of the prescription opioid oxymorphone. As of May 13, 2015, HIV infection has been diagnosed in 153 individuals. Network analysis was conducted as part of an ongoing outbreak investigation to characterize the outbreak and inform contact tracing efforts.
Methods: Disease Intervention Specialists (DIS) conducted contact tracing for persons diagnosed with HIV after October 1, 2014; risk contacts included sexual or injecting partners (persons with whom they shared injection equipment). All located contacts provided demographic information and were offered HIV testing. If a contact tested positive for HIV infection, DIS requested the name and sex of their contacts. The reported ties among risk contacts were used to create a "risk network" and calculate measures of the network structure that may be related to transmission of HIV infection within this population.
Results: The risk network consisted of 385 persons. Among 815 unique dyads linked by a risk contact, 656 ties were injection-only (80%), 56 were sex-only (7%), and 103 were both sex and injection (13%; Figure 1). Two sex-only and 6 sex and injection ties were between two men. Among ties between persons with known HIV status, 68% of injection-only ties were between two persons with HIV infection (positive concordant). 14% of sex-only ties were positive concordant, and 65% of sex and injection ties were positive concordant. Persons with HIV infection reported a median of 6 risk contacts (IQR: 6.75); persons without HIV infection were named as

a risk contact a median of 1 times (IQR: 1). 78% of risk contacts named by persons with HIV infection tested HIV positive during DIS investigation.

Conclusions: HIV-infected persons in this outbreak had a large number of risk contacts, reflecting a very dense network through which HIV could spread rapidly. A large majority of ties in the risk network were between injection partners, suggesting that HIV infection spread primarily via parenteral transmission due to shared injection equipment. A network-informed analysis of this outbreak investigation provided a method to characterize the outbreak and inform contact tracing efforts.



[Figure 1. Graphical depictions of risk network from the investigation of a community outbreak of HIV in Indiana, US, 2015. Red nodes have HIV infection (N=146); blue nodes do not have HIV infection (N=158); and grey nodes were not tested for HIV infection (N=81). Squares are men (N=218); circles are women (N=159); and rectangles are persons of unknown sex (N=8). Panel A displays all risk ties in the network as grey lines between nodes; panel B displays sex-only risk ties]

Track D

Monday, 20 July 2015

MOLBPE27

Interpreting the UNAIDS 90-90-90 targets in the context of the HIV care continuum in Vancouver, Canada

K. Vasarhelyi[1,2], B.G. Williams[3], L. Ahrenberg[1], B. Ramadanovic[1], A.R. Rutherford[1,4]
[1]Simon Fraser University, IRMACS, Burnaby, Canada, [2]Simon Fraser University, Faculty of Health Sciences, Burnaby, Canada, [3]SACEMA, Stellenbosch, South Africa, [4]Simon Fraser University, Department of Mathematics, Burnaby, Canada
Presenting author email: kvasarhe@sfu.ca

Background: UNAIDS predicts that reaching its 90-90-90 targets by 2020 will substantially reduce the HIV epidemic by 2030. Using an HIV transmission model of the care continuum in Vancouver, we determined HIV incidence in 2030 for various operational strategies for implementing the targets, with or without optimizing allocation of healthcare resources.

Methods: We used our previously developed model which incorporates details of Vancouver´s HIV care continuum, including delays associated with progressing through the healthcare system (doi:10.1007/s10729-014-9312-0). We simulated service-delivery expansion for men who have sex with men (MSM), injection drug users (IDU) and the general population (GP) such that by 2020, 90% of HIV-positive individuals in each population were diagnosed, 90% of them were on antiretroviral therapy, and 90% of those treated were virologically suppressed; these targets were achieved: (1) without optimizing resource allocation; (2) by simultaneously minimizing 2030 HIV incidence through optimized allocation of resources among targeted and routine testing programs (each with its unique combination of per-test cost and diagnostic efficiency); or (3) with optimized testing resource allocation that minimized the cost of reaching 2020 targets.

Results: Total HIV incidence in 2030 varied minimally among strategies (95-97 cases). However, the unoptimized strategy (1) required 7 times more resources than the minimum-cost strategy (3). For MSM, IDU and GP respectively, strategy (1) reduced incidence from 2010 baselines of 122, 41 and 20 cases to 66, 23 and 7 cases (reductions of 46%, 43% and 65%). Applying 95-95-95 targets, incidence was reduced by 76%, 75% and 82% for MSM, IDU and GP, respectively.

Conclusions: All operational paths reduced HIV incidence to comparable levels by 2030. However, costs required to achieve these same outcomes varied widely among strategies. Thus, operational guidance accompanying UNAIDS targets will be critical for ensuring appropriate use of scarce resources. Additionally optimizing allocation of care and treatment service resources promises further benefits. More specific outcome definitions--possibly emphasizing absolute rather than relative incidence reductions--may help better adapt the 90-90-90 strategy to local conditions, which can vary widely in baseline service levels. This will facilitate interpretation of the targets within local contexts and the meaningful evaluation of progress toward ending the HIV epidemic.

MOLBPE28

Economic analysis of HIV self versus facility testing and counselling in the context of a cluster-randomized trial in Blantyre, Malawi

H. Maheswaran[1,2], S. Petrou[1], P. Macpherson[3,4], F. Kumwenda[2], A. Choko[2], A. Clarke[1], E.L. Corbett[2,5]
[1]Warwick Medical School, Division of Health Sciences, Coventry, United Kingdom, [2]Malawi-Liverpool-Wellcome Trust, Blantyre, Malawi, [3]University of Liverpool, Department of Public Health and Policy, Liverpool, United Kingdom, [4]Liverpool School of Tropical Medicine, Department of Clinical Research, Liverpool, United Kingdom, [5]London School of Hygiene and Tropical Medicine, London, United Kingdom
Presenting author email: petermacp@gmail.com

Background: Rates of HIV testing and counseling (HTC) in sub-Saharan Africa remain suboptimal and substantially below target. HIV self-testing (HIVST) is safe, accurate, and can reach high coverage levels among otherwise hard-to-reach groups such as adolescents and men. However, design of affordable and scalable implementation strategies requires the economic impact of HIVST for health providers and users to be known.

Methods: A cross-section of adult (aged≥18 years) participants was recruited from residents of 28 neighborhoods in Blantyre, Malawi, demarcated for a cluster-randomized trial (ISRCTN02004005) investigating health impacts of semi-supervised semi-restricted HIVST. Specifically, a random sample of HIV self-testers was recruited from the trial's quality assurance cohort, along with all cluster residents testing at health facilities (Clinic A; Clinic B) serving the study population. Participants were questioned about direct health care, direct non-medical and indirect costs incurred in accessing either modality of HTC, and their health-related quality of life (HRQoL) measured using EuroQoL EQ-5D. The costs of HTC were estimated from health provider and societal perspectives to estimate costs per individual tested and costs per

HIV positive individual identified. All costs were adjusted to 2014 US and International Dollars.
Results: 1,241 participants underwent either HIVST (n=775) or facility-based HTC (n=446) and completed study questionnaires. Participants receiving HIVST reported better HRQoL, with those testing positive having higher mean EQ-5D utility scores (0.842, 95%CI:0.814-0.870) than those testing positive at health facilities (0.803, 95%CI:0.784-0.822). The mean health provider cost per individual tested through HIVST was comparable (US$8.78) to routine facility-based HTC (US$7.50 & US$10.53), although the mean cost per HIV positive individual identified through HIVST was higher (US$97.50) than for the two health facilities (US$67.07 & US$76.14). Facility testing was associated with higher direct non-medical and indirect costs, and consequently the mean societal cost of HTC was lower for the HIVST group.

	Clinic 1			Clinic 2			HIV Self-testing Service		
	US Dollars (2014)	INT Dollars (2014)	% of Total	US Dollars (2014)	INT Dollars (2014)	% of Total	US Dollars (2014)	INT Dollars (2014)	% of Total
Staff Salaries and Training	7,091	24,997	18.4%	6,963	16,490	12.2%	35,334	113,508	43.3%
Monitoring and Evaluation	1,907	5,298	3.9%	5,594	15,539	11.5%	15,833	54,521	20.8%
Consumables + Equipment	38,453	96,475	71.0%	40,910	94,070	69.8%	82,1330	94,051	35.9%
Capital + Overhead	32,557	9,047	6.7%	3,102	8,618	6.4%	0	0	0%
Total Health Provider Cost	50,709	135,817		56,570	134,718		133,300	262,080	
Health Provider Cost per Individual tested	7.50	20.09		10.53	25.08		8.78	17.25	
Direct non-medical and indirect Cost per Individual tested (Mean/SE)	2.27 (0.64)	6.32 (1.78)		3.74 (1.93)	10.38 (5.37)		0.05 (0.03)	0.15 (0.08)	
Societal Cost per Individual tested (Mean/SE)	9.92 (0.64)	26.10 (1.79)		14.21 (1.93)	35.20 (5.38)		9.22 (0.05)	18.62 (0.14)	

[Costs of facility-HTC and HIV self-testing]

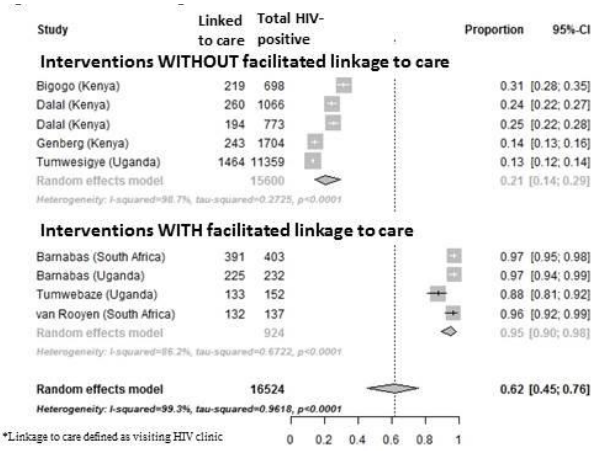
Conclusions: HIVST is associated with reduced direct non-medical and indirect costs, whilst health provider costs of HIVST were comparable to those for facility HTC. The provider cost of HIVST could be substantially lower under less restrictive distribution models, or if costs of oral fluid HIV test kits become comparable to finger-prick kits used in health facilities.

MOLBPE29

Community-based approaches address gaps in HIV testing and linkage: a systematic review and meta-analysis

M. Sharma[1], R. Ying[2], G. Tarr[1], R. Barnabas[1,3,4]
[1]University of Washington, Epidemiology, Seattle, United States, [2]University of Washington, Global Health, Seattle, United States, [3]University of Washington, Department of Global Health, Seattle, United States, [4]Fred Hutchinson Cancer Research Center, Vaccine and Infectious Diseases Division, Seattle, United States
Presenting author email: msharma04@gmail.com

Background: HIV testing and counseling (HTC) is the critical first step for linking to life-saving ART and reducing further transmission. Despite high HIV burden in sub-Saharan Africa, only 50% of HIV-positive persons are aware of their status, with youth and men least likely to be tested. HTC scale-up is urgently needed to reach the UNAIDS target of 90% of persons knowing their HIV status. Community-based HTC (testing not based in health facilities) has the potential to achieve widespread coverage, but whether community testing modalities address gaps in population coverage has not been reviewed.
Methods: Following Cochrane Guidelines, we searched Pubmed, EMBASE, Cochrane Library, Global Health Database, African Index Medicus, and conference abstracts using MeSH terms including "HIV Infections/diagnosis" AND "testing/screening/diagnosis" published from 2000 to 2014. We identified and screened 1,428 abstracts; 122 studies met eligibility criteria for inclusion. We characterized facility and community (home, mobile, index, key populations, workplace and self-testing) testing modalities by population reached, e.g. coverage, first-time testers, men, youth and high-risk groups, as well as HIV-positivity rate, CD4 count at diagnosis, and cost per person tested when available.
Results: Facility HTC achieves limited population coverage, 14% (95% CI: 9-20%), compared with home HTC which achieved 66% coverage (95% CI: 58-74%). Facility HTC also identifies HIV-positive persons later in the course of their disease: 61% of newly diagnosed HIV-positives had a CD4 count < 350 (95% CI: 51-71%), compared to 42% (95% CI: 34-51%) in mobile and 38% (95% CI 36-41%) in home HTC. Mobile testing reached more men (51%, 95% CI: 48-55%) than facility HTC (42%, 95% CI: 38-45%). Among youth, self-testing had the highest uptake (66%, 95% CI 65-67%) compared to all other modalities. Summary facility and community-based HTC costs were comparable (USD 17.35 and 23.92 per person tested, respectively). Community HTC with enhanced linkage to care has the potential to achieve high rates of linkage to care (Figure) similar to rates for facility HTC (68% linkage 95% CI: 57-77%).



[Figure 1. Home HTC: linkage to care]*

Conclusions: Optimizing community-based HTC is essential to achieving high testing coverage among at-risk populations. Enhanced linkage to care is critical to the success of community HTC.

MOLBPE30

Performance characteristics and cost benefit of the SD Bioline Duo HIV/Syphilis in clinics in Zimbabwe

S. Mtapuri-Zinyowera[1], G. Ncube[2], A. Machiha[3], P. Gumbo[1], E. Munemo[1], D. Mangwanya[1], R. Simbi[1], K. Maeka[1], M. Mugabe[1], S. Mupandasekwa[1], T. Sakubani[1]
[1]Ministry of Health and Child Care, Laboratory, Harare, Zimbabwe, [2]Ministry of Health and Child Care, HTC, Harare, Zimbabwe, [3]Ministry of Health and Child Care, STI, Harare, Zimbabwe
Presenting author email: zinyoweras@nmrl.org.zw

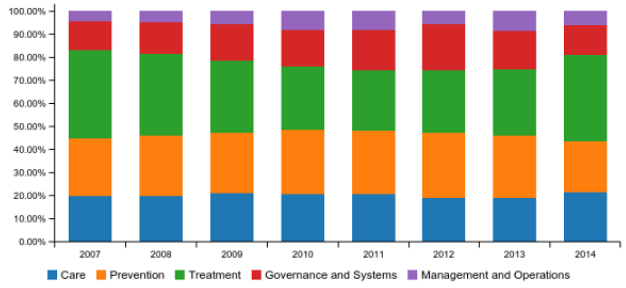
Background: Clinics are having to provide a number of rapid tests because of the increased need at a point-of-care. One such test that can simultaneously detect both HIV and syphilis using a single specimen and a single cartridge is the SD Bioline HIV/Syphilis Duo rapid test kit. Mother-to-child transmission of syphilis and HIV can result in severe adverse pregnancy outcomes and serious illness in infants, including miscarriage, stillbirth, preterm delivery, congenital syphilis, and pediatric HIV infection, hence the need to assess the performance characteristics of this kit.
Methods: Specimens were collected from 321 mothers attending 3 clinics in Harare where the rapid test was carried out by the nurses at sites. Specimens were then tested in the laboratory using EIA assays with the gold standards for HIV being Anilabs (Labsystems Diagnostics Oy, Finland), Vironostika HIV ag/ab (Biomerieux, France) confirming with HIV Blot 2.2 western-blot kit (MP Diagnostics, Singapore). The reference tests for syphilis were the RPR kit (Lab 21 Health Care Ltd, UK) TPHA kit (AMS, UK). For the other 5 clinics that were far from the testing lab, in the Northern part of the country inter-reader variability of the SD color scale was assessed for positive tests from 241 pregnant mothers by 2 nurses reading results independently of each other. The cost benefit of using this single test as compared to using 2 separate tests was also assessed.
Results: For HIV the sensitivity and specificity were 100% (37/37 and 284/284) respectively. For syphilis the sensitivity and specificity were also 100% (4/4 and 290/290) respectively. Concerning the inter-reader variability assessment, 63(26%) were HIV positive and 30(12.4%) were syphilis positive. According to the SD Bioline grading scale there was no reader variability as no results among all readers overlapped to the next category of the 3 grades. The cost of using the SD duo ($1.50/test) compared to the cost of 2 separate kits (HIV $1.00, syphilis $0.75) was cheaper by 14%. Distribution and storage costs were also reduced by half.
Conclusions: Simultaneous testing of two diseases using a single cartridge is cost effective in resource constraint environments as results are also comparable to laboratory results.

MOLBPE31

PEPFAR allocation priorities: an assessment of PEPFAR COP allocations across strategic are and country

G. Millett, B. Honermann, J. Sherwood, J. MacAllister, S. Wijayaratne, K. Lindsey
amfAR, Public Policy Office, Washington, United States
Presenting author email: brian.honermann@amfar.org

Background: Since PEPFAR's inception, the country operational plans (COPs) have been the primary medium through which spending priorities and proposed activities are documented. Increasing pressure on both domestic and international financial resources for HIV requires an increased focus on ensuring priorities are appropriately monitored. amfAR's COP database enables users to view PEPFAR's evolving process of priority setting and decision making within broad strategic areas. We analyze how COPs allocations by strategic area have been changing over time and examine country level variability across these areas for the most recent year.
Methods: Utilizing standard open source tools, amfAR created a navigable database of all allocation data contained in published COPs from 2007 through 2014. Data were entered by host country, year, and strategic area (among other categories). Total allocations to each strategic area (Care, Treatment, Prevention, Governance and Systems, and Management and Operations) were tallied by country and year and graphed proportionally.
Results: PEPFAR allocations to Care reached their highest levels in 2014 (21.35% of all COPs allocations) from a low of 19.02% in 2012. Likewise, allocations for Treatment increased in 2014 to 37.16% from 26.20% in 2011 - though below its highest level of 38.21% in 2007. After peaking at 28.28% in 2012, Prevention spending declined to 22.17% in 2014. Governance and Systems also decreased in 2014 to 13.13%, from 19.72% in 2012. With the growth of the PEPFAR program, management and operations costs increased from 4.57% in 2007 to 8.62% in 2013.
At the country level within 2014, significant variability is apparent. For countries with funded Care programming, allocations ranged from a low of 7.56% (Guyana) to a high of 38.57% (DRC, 2014); Treatment: 0.79% (Caribbean Region) to 47.04% (Uganda); Prevention: 9.86% (Botswana) to 47.05% (South Sudan); Governance and Systems: 5.14% (Zimbabwe) to 48.34% (Ukraine); Management and Operations: 0.6% (Burundi) to 34.40% (Cambodia).



[Figure. Proportionate COP allocations by strategic area by year (2007-2014]

Conclusions: Although PEPFAR COP allocations have varied widely by strategic area depending on the country and context, a strong commitment to Treatment and Care is evident. Civil society groups and PEPFAR should engage each other to identify priorities and needs on the ground.
All data is available at http://copsdata.amfar.org

MOLBPE32

Systematic literature review and network meta-analysis of tenofovir/emtricitabine and abacavir/lamivudine backbone regimens for HIV-1

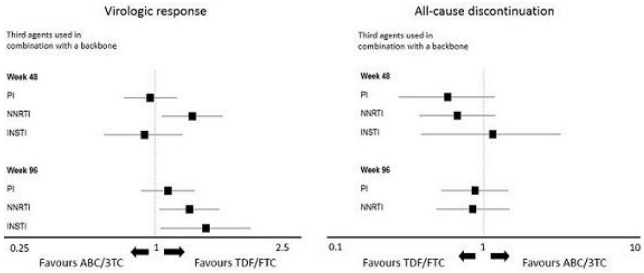
I. Agirrezabal[1], C. Lereun[2], L. Eddowes[1], J. Kusel[1], R. Perard[3]
[1]Costello Medical Consulting Ltd., Cambridge, United Kingdom, [2]Independent biostatistician, Sainte-Anne, Guadeloupe, France, [3]Gilead Sciences Europe Ltd, Uxbridge, United Kingdom
Presenting author email: rodolphe.perard@gilead.com

Background: Recommended treatment regimens for HIV-1-infected patients combine antivirals from different therapeutic classes, usually a two-drug N(t)RTI backbone (tenofovir/emtricitabine [TDF/FTC] or abacavir/lamivudine [ABC/3TC]) with a third agent from another therapeutic class. We sought to understand the clinical evidence differentiating these backbones.
Methods: A systematic literature review (SLR) identified randomised and non-randomised prospective studies of TDF/FTC or ABC/3TC in HIV-1 infection. MEDLINE, EMBASE, and the Cochrane Library were searched in March 2014. Bayesian network meta-analyses (NMA) of randomised controlled trials (RCTs) in treatment-naïve patients were run in WinBUGS for virologic response (VR; viral load < 50 copies/mL) and all-cause discontinuation at 48 and 96 weeks. The treatments evaluated included a backbone plus a third agent, and regimens were grouped by third agent class (protease inhibitors [PI], non-nucleoside reverse transcriptase inhibitors [NNRTI] and integrase strand transfer inhibitors [INSTI]). Inconsistency was assessed using an unrelated mean-effects model. The effects of baseline characteristics (gender, age, viral load, CD4 count and race/ethnicity) were gauged by network meta-regression.
Results: Of 1,093 citations retrieved, 243 citations were included in the SLR, reporting 18 RCTs that were included in at least one network. In the NMA, fixed-effect models represented a better fit for VR data, whereas random-effects models fitted the all-cause discontinuation data best. No significant differences were found between TDF/FTC and ABC/3TC with PIs. With NNRTIs, TDF/FTC was associated with significantly higher odds of VR than ABC/3TC at 48 and 96 weeks (Table, Figure). In combination with INSTIs, TDF/FTC had a significantly higher odds of VR at 96 weeks compared with ABC/3TC (Table, Figure). No statistically significant differences in all-cause discontinuation at 48 and 96 weeks were observed between the backbones when these were combined with the same class of third agent (Table, Figure). Networks showed little inconsistency, and baseline characteristics did not have any significant effect on results.
Conclusions: TDF/FTC was associated with VR benefits compared with ABC/3TC with NNRTIs as the third agent at both 48 and 96 weeks and with INSTIs at 96 weeks, and no statistically significant effect was seen with respect to all-cause discontinuation.

	Virologic response (fixed-effect)	Virologic response (fixed-effect)	All-cause discontinuation (random-effects)	All-cause discontinuation (random-effects)
	48 weeks	96 weeks	48 weeks	96 weeks
TDF/FTC+PI versus ABC/3TC+PI	0.96 (0.79, 1.17)	1.10 (0.90, 1.34)	0.59 (0.29, 1.17)	0.88 (0.54, 1.43)
TDF/FTC+NNRTI versus ABC/3TC+NNRTI	1.32 (1.05, 1.65)*	1.29 (1.03, 1.61)*	0.68 (0.39, 1.18)	0.85 (0.50, 1.46)
TDF/FTC+INSTI versus ABC/3TC+INSTI	0.92 (0.68, 1.22)	1.46 (1.04, 2.04)*	1.14 (0.40, 3.09)	Not available

* Statistically significant, assessed by whether the 95% CrI crosses 1

[Odds ratio and 95% credible interval]



[Forest plot]

MOLBPE33

Artificial Intelligence (AI) accurately predicts HIV treatment response in the setting of treatment failure without resistance testing

B. Larder[1], D. Wang[1], A. Revell[1], C. Hoffmann[2,3], R. Wood[4], C. Morrow[4], H. Tempelman[5], R. Hamers[6], P. Reiss[6,7], M. Nelson[8], C. Smith[9], C. Lane[10], RDI Data and Study Group
[1]RDI, London, United Kingdom, [2]Johns Hopkins University, Baltimore, United States, [3]Aurum Institute, Johannesburg, South Africa, [4]Desmond Tutu HIV Centre, University of Cape Town, Cape Town, South Africa, [5]Ndlovu Care Group, Elandsdoorn, South Africa, [6]Amsterdam Institute for Global Health and Development, Academic Medical Center of the University of Amsterdam, Amsterdam, Netherlands, [7]Stichting HIV Monitoring, Amsterdam, Netherlands, [8]Chelsea and Westminster Hospital, London, United Kingdom, [9]Royal Free Hospital NHS Foundation Trust, London, United Kingdom, [10]National Institute of Allergy and Infectious Diseases, Bethesda, United States
Presenting author email: brendanlarder@hivrdi.org

Background: To date, *Individualised therapy* remains the Standard of Care in high-income countries, with resistance testing used to guide selection of the optimum drug combination following treatment failure. In contrast, a *public health approach* is mostly used in low-middle income countries (LMIC) where genotyping is not available, using treatment guidelines based on the probability of cross-resistance between regimens. Unfortunately high rates of treatment failure are being reported. We evaluated a novel AI approach to predicting virological response to enable individualised therapy in LMIC without a genotype, and compare it to previous models, whose accuracy had plateaued at 75%.

Methods: We trained 'standard' random forest (RF) models to predict virological response (plasma viral load < 50 copies) to a change of therapy using data from 31,274 treatment change episodes including viral load and CD4 count prior to treatment change, drugs in prior and the new regimen and virological response. A novel algorithm was developed to divide these data into similar clusters and new RF models developed from each cluster. For independent test cases, a prediction of treatment response from the standard models was used, together with their historical data, to allocate them to the appropriate 'cluster model' and a refined final prediction obtained from that model.
Results: The new models predicted virological response with accuracy of 91% overall and 93% for 222 test cases from South Africa (vs 73% for standard models). The area under the ROC curve was 0.97 and 0.98 (vs 0.82). Sensitivity and specificity was 91-92% (vs 68-77%). They identified alternative, available regimens that were predicted to be more effective than those used in the clinic for all but one of the South African cases and, for up to 74% of the cases that failed their new regimen in the clinic, alternatives were identified that were predicted to give a full response.
Conclusions: This novel AI approach predicted treatment response highly accurately within the setting of treatment failure, in the absence of resistance testing. This makes it possible to individualise HIV therapy in LMIC and greatly reduce treatment failure, supporting the roll out of ART and the proposed UN 90-90-90 Target implementation.

Tuesday, 21 July 2015

TULBPE34

Mortality among participants in a community-based cohort in Western Kenya, findings of the HIV risk and pregnancy incidence study

A. Odoti[1], J. Kiarie[1], J. Kinuthia[2], C. Farquhar[3], A. Kurth[4], C. Nock[4], I. Irene[5], C. Peter[6], J. Francis[7], A. Wangombe[7], A. Mwaniki[7], F. Abuna[7], N. Ruth[8], O. Alfred[9]
[1]University of Nairobi/University of Washington, Nairobi, Kenya, [2]University of Nairobi/ Kenyatta National Hospital, Obstterics and Gynaecology and Research, Nairobi, Kenya, [3]University of Washington, Epidemiology, Global Health, Medicine, Seattle, United States, [4]New York University, Nursing, New York, United States, [5]Kenyatta National Hospital, Research, Nairobi, Kenya, [6]University of Washington, Global Health, Seattle, United States, [7]University of Nairobi, Nairobi, Kenya, [8]University of Nairobi, Peadiatrics, Nairobi, Kenya, [9]University of Nairobi/University of Washington, Obstetrics and Gynaecology, Nairobi, Kenya
Presenting author email: alfosoti@yahoo.com

Background: Non-facility based strategies that increase HIV counseling and testing may reduce HIV related morbidity and mortality. However, there is paucity of data on mortality following community based HIV counseling and testing. We sought to estimate the rates and determinants of mortality in a community-based cohort.
Methods: This was a prospective community based cohort of heterosexually active couples enrolled in Western Kenya. Eligible households were identified following spatial sampling and eligible enrolled couples were followed up six monthly for a period of two years. At each visit participants underwent individual audio computer assisted self-interviews and home based couple HIV counseling and testing. At each follow-up visits, information on linkage to care was obtained and possible cause of mortalities ascertained from the family through verbal autopsy and where available medical sources. We conducted survival analysis and obtained weighted mortality rates. Univariate and multivariate analysis was conducted to determine the predictors of mortality.
Results: Of the 2593 (1274 male and 1319 female) participants followed up, 79 deaths were reported. The overall mortality rate was 1.55 per 100 person years. There were 29, 14, 17 and 19 deaths at 6, 12, 18 and 24 months respectively. Majority of deaths occurred among men (n=58) compare to women (n=21), giving mortality rates of 2.34 versus 0.80 per 100 person years respectively. The predictors of mortality were male gender (odds ratio [OR] 2.41, 95% Confidence Interval [CI] 1.39-4.19 p=0.002), HIV infection (OR 4.71, 95% CI 2.59-8.59 p< 0.001), partner HIV infection (OR 1.83, 95% CI 1.12-3.02 p=0.02) and polygamy (OR 1.20, 95% CI 1.02-3.99 p=0.049). The weighted mortality rate was 2.8 among HIV infected participants compared to 0.9 among those who were HIV uninfected.
Conclusions: In this low resource and high HIV prevalence setting, there was a higher than base population HIV related mortality despite increased national HIV testing and antiretroviral coverage. Urgent community based interventions are required to address barriers to early diagnosis and linkage to care especially among men and those in polygamous relationships.

TULBPE35

Assess HIV patient pathway and drop-out trends in the healthcare system in Ukraine

N. Avaliani[1], I. Kuzin[2], V. Martsinovskaya[2], O. Iaremenko[1], N. Nizova[2]
[1]Deloitte Consulting LLP, HIV Reform in Action Project, Kiev, Ukraine, [2]Ukraine Center for Control of Socially Dangerous Diseases, Kiev, Ukraine
Presenting author email: navaliani@deloitte.com

Background: Ukraine faces one of the highest burdens of HIV infection in Eastern Europe, the region with the highest increase in prevalence among regional epidemics. The epidemic is mainly concentrated in injecting drug users (IDUs), female sex workers (FSW) and their partners, and men who have sex with men (MSM). The country's public health system faces a challenge to ensure people who test positive for HIV are timely referred for treatment. The purpose of this study is to analyze steps across the cascade of services with the highest impact on patients' loss to follow-up.
Methods: HIV Patient Pathways analyzes six major service entry points - maternal care services, TB/STI/drug rehabilitation clinics, prison services, primary care clinics, volunteer testing (VCT) sites and community outreach points. Patient losses at HIV/AIDS centers were analyzed separately.
Results: Maternal care services have the least patient loss for follow-up at 7%, with coverage of testing among pregnant women at over 95%. Patient loss to follow-up was 14% at VCT clinics, with no difference observed in the referral patterns among general and key affected populations (KAP). Data is limited for TB/STI/drug rehabilitation services, with better coverage of testing observed at TB clinics which showed 52% and 89 % for outpatient and inpatient settings respectively. Non-governmental organizations (NGOs) conduct outreach testing among KAPs and provide data on each step of the service cascade. This analysis shows that 42% of patients tested by NGOs with confirmed diagnosis are not enrolled into care and the highest percentage is observed among IDUs at 45%. Finally 25% of registered HIV patients and 49 % of the estimated amount, are lost for follow up.
Conclusions: HIV Patient Pathways identifies steps in the service cascade with the largest impact on patients' losses to follow-up. Significant gaps were observed in referral of KAPs tested through NGO outreach programs. Immediate action from public health authorities is needed to ensure proper protocols and monitoring of patient referrals across the cascade of services. Public health research should aim to address data limitations.

Wednesday, 22 July 2015

WELBPE36

Unconditional cash transfers not associated with HIV patient outcomes in Uganda: a randomized-controlled trial

E.J. Mills[1,2], J. Bertfelt[3], J.I. Forrest[1,4], E. Druyts[1,4], A. Tusiime[3], K. Holloway[3], S. Okoboi[5], P. Jakiela[6], A. Adhyaryu[7], S. Kanters[1,4], F. Mills[1], J. Jansen[1], K. Thorlund[1], D. Karlan[8], Empowerment for Positive Living Study Group
[1]Global Evaluative Sciences, Vancouver, Canada, [2]University of Ottawa, Faculty of Health Sciences, Ottawa, Canada, [3]Innovations for Poverty Action, Kampala, Uganda, [4]University of British Columbia, Vancouver, Canada, [5]The AIDS Support Organization, Kampala, Uganda, [6]University of Maryland, College Park, United States, [7]University of Michigan, Ann Arbor, United States, [8]Yale University, New Haven, United States
Presenting author email: emills@geshealth.com

Background: There is continued debate about whether cash grants to alleviate poverty may improve HIV-positive patient outcomes. We aimed to investigate the effect of this intervention on adherence to antiretroviral therapy (ART), change in CD4 cell counts, and mortality among people living with HIV in Uganda.
Methods: The Empowerment for Positive Living randomized-controlled trial in Masindi and Soroti, Uganda, completed in April 2015. Participants were randomized to one of four conditions: I) unconditional cash transfers of 350,000 UGX (~$138 USD), II) the same cash transfer with financial planning sessions, III) no cash transfer with expectation of a lottery for the same sum upon trial completion, and IV) no cash transfer control. Surveys were conducted at baseline, and at 3 and 15 months post-randomization. Adherence to ART was self-reported and defined as optimal or sub-optimal (having missed any pills in the three days prior to assessment). Mortality was any death following randomization. Changes in CD4 cell counts between baseline and endline were calculated for all participants. Logistic regression was used to estimate the effect of the treatment groups on adherence and mortality, and linear regression was used to estimate the effect of the interventions on the mean change in CD4 cell counts.
Results: A total of 2,170 patients were randomized and 2,069 completed the study, including 518 in group I, 521 in group II, 529 in group III and 525 to group IV. Retention between baseline and endline was high at 96.5% overall. In total, there were 24 deaths in the study (1.15%), 158 (7.6%) participants reported sub-optimal adherence and overall mean change in CD4 cell count during the study period was 33.18 cells/mm^3. **Table 1** shows the effect of the

randomized groups on each of the three outcomes. Compared to the control group, no condition had an effect on each outcome that was decipherable from chance alone.

Conclusions: We found no effect of cash transfers on mortality, adherence or CD4 cell count change. Although there were few events on which to build a model, sample adherence and mortality do not suggest that the non-significant results are due to low power.

WELBPE37

Cost-effectiveness of the National Mobile Antiretroviral Therapy Services in Zambia: an evaluation study on decentralizing treatment and care program

S. Miyano[1,2], K. Komada[1,2], A. Mwango[2,3]
[1]National Cener for Global Health and Medicine (NCGM), Bureau of International Health Cooperation, Tokyo, Japan, [2]JICA Project for Scaling up of Quality HIV/AIDS Care Service Management, Lusaka, Zambia, [3]Ministry of Health, Republic of Zambia, Department of Clinical Care and Diagnostic Services, National ARV Program, Lusaka, Zambia
Presenting author email: s-miyano@it.ncgm.go.jp

Background: In resource-limited settings with high prevalence of human immunodeficiency virus (HIV) infection such as Zambia, the decentralization of human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) treatment and care services with effective use of these resources serves as a cornerstone for implementing universal treatment and care. Free anti-retroviral therapy (ART) services were introduced at the hospital level in 2005, and further expanded to selected rural health centers (RHCs) in 2007 through the unique national "Mobile ART Services" program in Zambia. Although this program has contributed to decentralizing the ART services to the primary health care level in order to maximize the efficient use of the extremely limited resources, no economic evaluation has been conducted. This research aims to analyse the cost-effectiveness of the program as a means of decentralizing ART services.

Methods: Cost-effectiveness analysis was performed using decision analytic model and simple Markov model to compare the original ART program, 'Hospital-based ART', with the intervention program, Hospital-based plus 'Mobile ART' services, from the perspective of district government health office in Zambia. Total cost of ART services including capital, recurrent and operational costs, quality-adjusted life year (QALY) and incremental cost-effectiveness ratio (ICER) were examined.

Results: The mean annual per-patient costs were 1,259.16 USD for the original program and 2,601.02 USD for the intervention program, while the mean numbers of QALYs were 6.81 for the original and 7.27 for the intervention programs. Although the cost-effectiveness ratio was higher for the intervention program (357.93 USD/QALY) than for the original program (184.78 USD/QALY), the ICER of the intervention program relative to the original program was 2965.17 USD/QALY which was much below the willingness-to-pay (WTP), or three times the GDP per capita (4,224 USD). Even in the sensitivity analysis, the cost-effectiveness of the intervention program was not much affected.

Conclusions: The National Mobile ART Services Program in Zambia could be a cost-effective approach for decentralizing ART services into rural areas in Zambia. It should be expanded to more districts where the program has not yet been introduced in order to improve access to ART services and the health of people living with HIV in rural areas.

Publication Only Abstracts

Track A

PUB001

HIV-induced abnormalities of the B-cell compartment persist in patients on long-term ART and may reflect a state of terminal B-cell exhaustion

L.N. Abudulai[1], S. Fernandez[1], M. Hunter[2,3], J. Post[2,3], M. French[1,4]
[1]The University of Western Australia, School of Pathology and Laboratory Medicine, Perth, Australia, [2]Prince of Wales Hospital, Department of Infectious Diseases, Sydney, Australia, [3]University of New South Wales, Prince of Wales Clinical School, Sydney, Australia, [4]Royal Perth Hospital and PathWest Laboratory Medicine, Department of Clinical Immunology, Perth, Australia
Presenting author email: nabudulai6@yahoo.com

Background: HIV infection induces B-cell activation, which causes abnormalities of circulating B-cell subpopulations and serum immunoglobulin levels. This leads to B-cell exhaustion, characterised by increased proportions of $CD21^{lo/-}$ B-cells. Persistent B-cell activation and/or exhaustion in HIV patients receiving antiretroviral therapy (ART) may contribute to poor pneumococcal vaccine responses and increased risk of invasive pneumococcal disease.
Methods: The effects of long-term ART on B-cell activation and exhaustion were examined in ART-treated (n=30; median years on ART=9.25) and ART-untreated (n=20) HIV patients and non-HIV subjects (n=20). B-cell differentiation was assessed by enumerating naive, early transitional, late transitional, activated mature differentiated, resting memory and exhausted tissue-like B-cell subpopulations. B-cell activation was assessed by expression of TNF-related apoptosis-inducing ligand (TRAIL), B and T lymphocyte attenuator (BTLA) and IL-21 receptor (IL-21R). B-cell exhaustion was assessed by CD21 expression. We also assessed B-cell differentiation and activation by assaying serum levels of IgG subclasses and kappa and lambda immunoglobulin free light chains (FLCs), respectively.
Results: ART-treated patients exhibited increased proportions of $TRAIL^+$ B-cells and $CD21^{lo/-}$ B-cells compared to non-HIV subjects (p=0.03 and p=0.01, respectively). The proportion of $CD21^{lo/-}$ B-cells correlated negatively with $CD4^+$ T-cell counts (R= -0.68; p< 0.0001) but not with $TRAIL^+$ B-cells. Proportions of $BTLA^+$ and $IL\text{-}21R^+$ B-cells did not differ from non-HIV subjects. When ART-treated patients were compared with ART-untreated patients, proportions of $CD21^{lo/-}$ B-cells were lower (p<0.001) but there was no difference in the proportion of $TRAIL^+$ B-cells. Interestingly, in ART-treated patients alone, BTLA expression on all B-cell subpopulations correlated negatively with $CD21^{lo/-}$ B-cells (R≥ -0.35, p≤0.09). Serum FLC levels correlated with proportions of $CD21^{lo/-}$ B-cells in ART-untreated patients (kappa: R=0.65; p=0.002 and lambda: R=0.59; p=0.006) and were substantially lower in ART-treated patients (p<0.0001 for kappa and lambda). In ART-untreated patients, serum FLC levels also correlated with IgG1 (kappa: R=0.75; p=0.0001 and lambda: R=0.74; p=0.0002) but not IgG2.
Conclusions: Although markers of HIV-induced B-cell activation and exhaustion improve on ART, they persist in HIV patients receiving long-term ART. B-cell exhaustion in ART-treated patients is associated with low $CD4^+$ T-cell counts and BTLA expression on B-cells, and may have a common immunological cause.

PUB002

Flow-based differentiation between latently HIV-1-infected single cells expressing Gag mRNA alone or in conjunction with Gag protein following latency reversal

G. Martrus, M. Altfeld
Heinrich-Pette-Institut Leibniz Institute for Experimental Virology, Department of Viral Immunology, Hamburg, Germany
Presenting author email: gloria.martrus@hpi.uni-hamburg.de

Background: Current antiretroviral treatments cannot eradicate HIV-1 infection due to a pool of persisting latently infected cells. Reactivation of the latently infected cells, using for example HDAC inhibitor, has been suggested as an approach to reduce the HIV-1 reservoir. However, it remains unclear in how many latently infected cells reactivation occur, and whether reactivation leads to production of viral RNA alone versus production of viral proteins or viruses. We aimed to develop an approach to evaluate the molecular kinetics of HIV-1 latency reactivation on the single cell level to distinguish cells in which only viral mRNA is expressed from cells in which viral proteins or novel viruses are produced.
Methods: J89 cells were used as a HIV-1 latency reactivation model, and treated with different concentrations of hTNFα cytokine for defined time points ranging from 1 hr to 24 hrs. Combined intracellular staining for p24 Gag protein and Gag mRNA was performed, using a newly established technique that allows for simultaneous detection of mRNA targets and intracellular proteins. HIV-1 p24 Gag protein production and p24 Gag mRNA synthesis was quantified simultaneously on the single cell level using multiparameter flow cytometry.
Results: Following stimulation of J89 cells with 1 ng/mL of hTNFα for 6h, moderate HIV-1 Gag mRNA expression was detected, accompanied with almost no intracellular Gag protein detection. Higher concentrations of hTNFα (10ng/ml) resulted in elevated expression of HIV-1 Gag mRNA as well as intracellular Gag protein synthesis. After 24h stimulation with 10ng/ml of hTNFα, three distinct populations were identifiable by flow cytometry: only HIV-1 Gag mRNA positive cells, HIV-1 Gag mRNA and Gag protein double-positive cells, and cells only expressing Gag protein, but no HIV-1 Gag mRNA anymore.
Conclusions: We here describe a novel method allowing for the first time to simultaneously quantify the kinetics of HIV-1 mRNA and HIV-1 protein synthesis upon latency reactivation. This approach will enable the phenotypic characterization of latently infected cells at different stages of latently reversal and the identification of surface markers that render these cells as targets for innate and adaptive immune responses.

PUB003

Improved assays to measure the inducible latent HIV reservoir

M. Massanella[1], C. Yek[1], S.M. Lada[1], M.C. Strain[1], D.D. Richman[1,2]
[1]UCSD, Pathology, La Jolla, United States, [2]Veterans Affairs San Diego Healthcare System, La Jolla, United States
Presenting author email: mmassanellaluna@ucsd.edu

Background: Precise and practical assays that can reliably measure the impact of a candidate treatment strategy are essential. We improved the standard quantitative viral outgrowth assay (QVOA) and developed a new assay, which promises to be faster, more sensitive, and higher throughput than the standard QVOA.
Methods: Freshly isolated CD4 T cells from 7 ART-suppressed subjects treated during chronic infection were analyzed for total HIV DNA by droplet digital PCR (ddPCR, gag) and our newly developed assays for the inducible HIV reservoir - modified QVOA (mQVOA) and inducible cell-associated RNA expression in dilution (iCARED). For mQVOA, CD4 T-cells in limiting dilution were activated with anti-CD3/CD28 antibodies. After 2 days of culture, MOLT-4/CCR5 cells were added to the culture and cell-free (cf-) RNA was quantified by real-time PCR (Pol) at day 7. Similarly, we used CD3/CD28 co-stimulation for the iCARED assay in the presence of raltegravir. After 3 days of culture, cell-associated (ca-) RNA was quantified by ddPCR (gag and tat-rev). In both cases, we used a magnetic-bead based RNA extraction system (Hologic™) to specifically extract HIV RNA molecules, making it more sensitive than conventional methods and allowing the testing of large volumes of both cells and culture supernatant.
Results: The median for total HIV DNA was 168 [103-332] copies/10^6 PBMCs and for mQVOA was 5 [1.7-7.3] infectious units/10^6 CD4 T cells. There was only a 42-fold difference between the two measures; substantially less than what has been reported previously. In the iCARED assay, the median frequency of cells with inducible ca-RNA was 45 [20-61] cells/10^6 CD4 T cells, which was 10 times more than the median frequency measured by mQVOA and 4 times less than the median frequency given by total HIV DNA. The latently infected cells detected by iCARED assay was highly correlated with quantification by mQVOA (R=0.89, p=0.007) and HIV DNA (R=0.95, p=0.01).
Conclusions: iCARED is a simple method to quantify the transcriptionally competent latent HIV reservoir. Our results suggest that iCARED, which is more rapid (4 days), less expensive, less cell-demanding and hands on time than QVOA, could prove to be a useful tool for clinical investigations.

PUB004

The tip of the iceberg: impact of asymptomatic STI's on immune cells in the male foreskin

A.J. Olivier[1], R. Harryparsad[1], H.B. Jaspan[1], D. Wilson[2], J. Dietrich[3], N. Martinson[3], H. Mukudu[3], N.N. Mkhize[4], R. Durgiah[4], L. Morris[4], G. Cianci[5], M. Dinh[5], T. Hope[5], J.-A.S. Passmore[6,7], C.M. Gray[6,7]
[1]University of Cape Town, Institute of Infectious Disease and Molecular Medicine, Cape Town, South Africa, [2]Edendale Hospital, Medicine, Pietermaritzburg, South Africa, [3]Perinatal HIV Research Unit, Soweto, South Africa, [4]National Institute for Communicable Diseases, Sandringham, South Africa, [5]Northwestern University, Chicago, United States, [6]Institute of Infectious Disease and Molecular Medicine, Cape Town, South Africa, [7]National Health Laboratory Services, Cape Town, South Africa
Presenting author email: abraham.olivier@uct.ac.za

Background: CMedical Male Circumcision (MMC) reduces the risk of HIV acquisition by up to 60%, confirmed in a number of large clinical trials throughout Africa. MMC has also been shown to reduce the prevalence of other sexually transmitted infections (STIs), which in turn may impact HIV acquisition. We hypothesized that the underlying mechanisms for this protection may be removal of potential target cells for HIV infection and altered levels of keratinisation in men after MMC.

Methods: In a longitudinal study involving 2 clinical sites and 150 participants within South Africa, we have characterised Langerhans cells, proliferating and CD4+ T cell densities by immunofluorescent imaging in a subset of 30 HIV negative boys and men (14 - 24 years) undergoing elective MMC at Edendale Hospital in Kwa-Zulu Natal and at the Perinatal HIV Research Unit in Soweto, Johannesburg. CCR5 expression was also investigated in foreskin tissues. In addition we have compared the levels of keratinisation between the inner and outer foreskin and assessed the impact of STIs (*C. trachomatis, N. gonorrhoea, M. genitalium*, *T. vaginalis, HSV-1 & 2*) on HIV target cell density in foreskin tissues. Testosterone levels were measured in all men included in the study.
Results: Immunofluorescent staining for CD4, Ki67 and CD207 to identify proliferating immune cells showed elevated numbers of both CD4+ T and CD207+ Langerhans cells in the foreskin of men with STIs compared to those without an STI. There was a slight yet significant increase in keratin thickness of the stratum corneum of outer compared to inner foreskins.
Conclusions: STI-induced inflammation and recruitment of immune cells to the foreskin, may be elevating the risk of HIV acquisition in uncircumcised men. We conclude that MMC may reduce the risk of HIV infection in this highly susceptible age group of men by removing the potential CD4+ HIV target cells present in foreskins of young uncircumcised men in South Africa.

PUB005

Reversal of HIV-1 latency by activation of patient-derived CD4+T-cells results in clonal expansion and sustained production of infectious virus from a subset of cells

J. Bui[1,2], E. Halvas[1], E. Fyne[1], M. Sobolewski[1], D. Koontz[1], M. Kearney[3], W. Shao[4], F. Hong[1], J.W. Mellors[1]
[1]University of Pittsburgh, Department of Medicine, Pittsburgh, United States, [2]Howard Hughes Medical Institute, Medical Research Fellows Program, Bethesda, United States, [3]National Cancer Institute (NCI), HIV Dynamics and Replication Program, Frederick, United States, [4]Leidos, Advanced Biomedical Computing Center, Frederick, United States
Presenting author email: job74@pitt.edu

Background: The "kick-and-kill" strategy, consisting of latency reversal followed by death of cells with activated proviruses, has been proposed as a means of eliminating the HIV-1 reservoir. However, the most effective latency reversing agents are also potent T-cell activators (Cillo, PNAS 2014). Recent studies show that virus producing cells can persist and expand *in vivo* (Maldarelli, Science 2014). We hypothesized that activation of patient-derived CD4$^+$ T-cells can lead to clonal expansion of proviruses rather than their elimination.
Methods: To study the effects of latency reversal by CD4$^+$ T-cell activation on virus production and cell survival, we established an *ex vivo* cell culture system involving stimulation of patient-derived CD4$^+$ T cells with PMA/ionomycin (day 1-7), followed by rest (day 7-21), and then restimulation (day 21-28) in the presence of raltegravir and efavirenz to block virus spread. Cell-associated HIV-1 DNA and virion RNA in the supernatant were quantified by qPCR at weekly intervals. Single genome sequencing (SGS) was performed to characterize proviruses and virion RNA. Replication-competence of virions produced was determined by co-culture with CD8-depleted blasts from HIV negative donors.
Results: Experiments were performed with purified CD4$^+$ T-cells from 5 consecutive donors who had been suppressed on ART for 2 or more years (median = 13.4 years). In all experiments, HIV-1 RNA levels in supernatant increased following initial stimulation, decreased during the rest period, and increased again with restimulation. Cell-associated HIV-1 DNA levels did not show a consistent pattern of change. SGS revealed several different outcomes of cells containing specific proviruses: 1) virus production following the first but not the second stimulation; 2) virus production only following the second stimulation; 3) virus production following both stimulations; 4) no virus production with either stimulation, 5) proviral expansion without virus production; and importantly 6) proviral expansion with virus production, including replication-competent virus.
Conclusions: These results indicate that reversal of HIV-1 latency by CD4$^+$ T cell activation results in multiple outcomes of proviral-containing cells including clonal expansion of proviruses that can produce infectious virions. These findings underscore the complexity of eliminating HIV reservoirs and the need for strategies to kill virus-producing cells before they can proliferate.

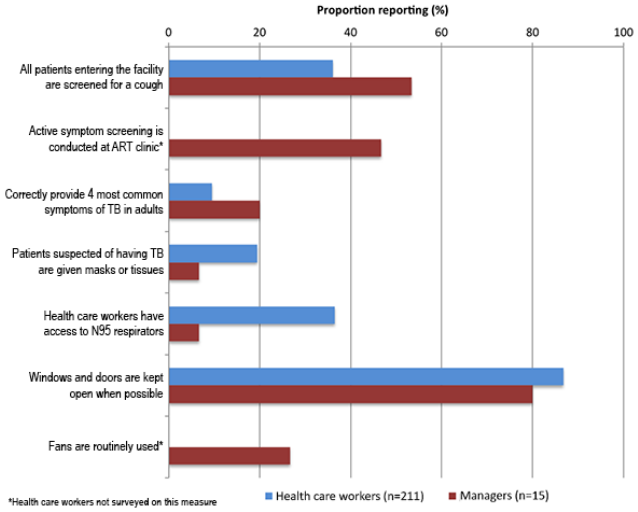
Track B

PUB006

Assessing tuberculosis infection prevention measures and barriers to care for health care workers in public health facilities in Malawi

A. Munthali[1], R. Flick[1,2,3], A. Dimba[4], K. Simon[1,5], M. Kim[1,5], P. Kazembe[1,5], S. Ahmed[1,5]
[1]Baylor College of Medicine-Abbott Fund Children's Clinical Center of Excellence, Lilongwe, Malawi, [2]University of North Carolina Project, Lilongwe, Malawi, [3]University of Colorado School of Medicine, Denver, United States, [4]Malawi National Tuberculosis Control Programme, Lilongwe, Malawi, [5]Baylor International Pediatric AIDS Initiative at Texas Children's Hospital, Baylor College of Medicine, Houston, United States
Presenting author email: adamsonmunthali@gmail.com

Background: Nosocomial transmission of tuberculosis (TB) is an important source of infection for both HIV-infected patients and health care workers (HCWs). In Malawi, guidelines exist for infection prevention and control (IPC) but little is known about their implementation. Our primary objective in this study is to assess the implementation and knowledge of IPC measures aimed at reducing nosocomial transmission of TB in health facilities in Malawi. Our secondary objective is to characterize HCWs´ utilization of TB/HIV services.
Methods: In cooperation with the Malawi National TB Control Programme, we conducted a cross-sectional assessment of IPC measures at seven health facilities supported by the Baylor Tingathe community outreach program in Malawi from September 2014 through January 2015. Three approaches were used: structured interviews with facility managers; completion of an anonymous questionnaire by HCWs; direct observations of pre-selected IPC measures by researchers.
Results: Fifteen manager interviews, 211 HCW questionnaires, and 5 direct observations were analyzed.
Notable findings regarding facility implementation of IPC measures included: 47%(7/15) of managers reported active screening for TB amongst patients receiving antiretroviral therapy (ART); only one site (20%) had separate waiting areas for ART and TB services; no sites were observed to have fans in use (Figure 1).



[Figure 1. Proportion of health care workers and managers reporting on select infection prevention and control measures]

Assessing knowledge among HCWs of IPC measures demonstrated that only 20% of managers and 9% of HCWs correctly provided the most common symptoms of TB in adults (Figure 1); 37% (78/211) of HCWs were able to provide date of their last IPC training (Table 1).

Characteristic	Reported by health care workers (n=211)
Provided date of last IPC training—no. (%)	78 (37)
Median time elapsed since last training (IQR)—yr	1.4 (0.2-2.9)
Provided date they were last screened for TB—no. (%)	21 (10)
Median time elapsed since last screen (IQR)—yr	2.3 (0.6-5.1)
Correctly named four most common symptoms of TB in adults—no. (%)	20 (9)
Know their HIV status—no. (%)	188 (89)
Received an HIV test at the same facility where they work—no. (%)	108 (51)
Would feel comfortable receiving ART at the same facility where they work—no. (%)	119 (56)
Expressed concern that facility layout increases risk of contracting TB from patients—no. (%)	108 (51)

[Table 1. Anonymous responses from HCWs]

Characterization of HCW TB service utilization found that only 10% of HCWs provided a date for their last TB screening, with a median time elapsed of 2.3 years (interquartile range 0.6-5.1); 51% expressed concern that the facility layout might increase their chances of contracting TB; 2(1%) were currently on TB treatment.
Conclusions: Implementation and knowledge regarding IPC guidelines is suboptimal. HIV-infected patients are not routinely screened for TB and knowledge deficits among HCWs may further limit screening effectiveness. Especially given significant well-documented occupational risk in this setting, HCWs are not sufficiently screened for TB. Future work will address effective strategies to implement IPC measures and facilitate HCW access to care.

PUB007

The prevalence of anorectal STI in HIV-positive and negative MSM in Guangzhou, China

X. Ren[1], W. Ke[1,2], S. Huang[1], H. Zheng[1], B. Yang[1]
[1]Guangdong Provincial Centre for Skin Diseases & STI Control and Prevention, Division of STD, Guang Zhou, China, [2]Southern Medical University, Graduate School, Guang Zhou, China
Presenting author email: 173486108@qq.com

Background: There is an increased prevalence of sexually transmitted infections (STIs) in men who have anal sex with men (MSM). The study hypothesis is to compare the rates of anorectal STIs in HIV positive versus HIV negative MSM. We tested the Neisseria gonorrhea, Chlamydia trachomatis, Mycoplasma genitalium, and Human papillomavirus of the anorectal mucosal place in MSM.
Methods: The study conducted in the STD counseling clinic of Lingnan Fellows Health Support Center in Guangzhou, China from January 1 to October 31 2014. We recruited 164 participants who had a history of receptive or had both insertive and receptive anal sex with men by phone. We excluded men who did not have receptive anal sex. Seventy-nine participants were HIV positive and 85 were HIV negative. Using nucleic acid detection methods, we tested for Neisseria gonorrhea, Chlamydia trachomatis, Mycoplasma genitalium, and Human papillomavirus infection by using anorectal swabs. Participants also completed a demographic and sexual history questionnaire.
Results: Compared the demographic and sexual history questionnaire, HIV-positive participants had more homosexual sexual partners (P <0.05) and less knowledge about the regular sexual partner's STIs status (P <0.05) than HIV-negative participants. The infection rates for Neisseria gonorrhea, Chlamydia trachomatis, Mycoplasma genitalium and HPV were 10.4%, 32.3%, 15.2, and 64.0%, respectively. Except for gonococcal infections (P = 0.92), the prevalence of STIs in HIV-positive participants was higher than in HIV-negative participants (P <0.05).
Conclusions: There were high STI infection rates in anorectal sites among this sample of MSM, and a large number of participants were infected with more than one pathogen. Infection rates among HIV-positive individuals were significantly higher than among HIV-negative individuals. Our findings suggest a need to strengthen anorectal mucosal STI screening among MSM populations in order to increase early detection and treatment.

PUB008

Is depression a serious psychosocial problem among men who have sex with men? Evidence from India

S.K. Patel[1], P. Prabhakar[2], N. Saggurti[1]
[1]Population Council, HIV and AIDS Program, New Delhi, India, [2]India HIV/AIDS Alliance, Hyderabad, India
Presenting author email: sangrampatel@gmail.com

Background: Mental health has been a largely neglected issue among men who have sex with men (MSM) across the world and was not given proper attention particularly in developing nations including India. This study examines the prevalence and correlates of mental depression among MSM.
Methods: Data for this study are used from a cross-sectional Behavioural Tracking Survey (BTS- 2012) conducted among 1176 MSM from southern state of India. Besides collecting information on MSM's typology, experience of physical and sexual violence, STI symptoms, self-reported HIV status, mobility, poverty, discrimination and condom use, the mental health status of MSM was assessed using Patient Health Questionnaire-2 depression scale. Descriptive statistics, frequency, bivariate and multivariate logistic regression techniques were used for analysis.
Results: More than one-third of MSMs (35%) in the survey reported to have mental depression. The likelihood of experiencing depression was 5 times higher among MSM who were mobile for sex work outside their place of residence (55% vs 17%, AOR: 5.2, 95% CI: 3.7-7.3) and had experienced physical or sexual violence in past 6 months (82% vs 33%, AOR: 6.0, 95% CI: 2.1-17.4) than their respective counter parts. The probability of reporting mental depression was significantly higher among MSM who had experienced STI symptoms in past 6 months (59%, AOR: 3.1, 95% CI: 1.9-5.0); whose know their HIV positive status (51%, AOR: 2.4, 95% CI: 1.2-4.7); who did not use condoms during anal sex with any clients/partners in past one year (82%, AOR: 2.0, 95% CI: 1.5-2.7); those who used alcohol in past one month (50%, AOR: 2.3, 95% CI: 1.7-3.2) and were under financial debt at the time of survey (41%, AOR: 2.0, 95% CI: 1.4-2.6) than others. Those who were associated with any community groups have 50% less chances of reporting depression.
Conclusions: The study certainly highlighted that the HIV prevention efforts with MSM in India require an integrated approach on addressing the mental health issues. To support this, programs and research based evidence will be highly needed to ensure that mental health issues are properly addressed among MSM and other high risk groups.

PUB009

Early treated HIV-infected children seronegative by ELISA in Cameroon: frequency, factors associated and evolution

M.C. Tejiokem[1], A. Kfutwah[2], F. Ateba Ndongo[3], S. Tetang Ndiang[4], I.C. Penda[5,6], W. Mbanzouen[2], P. Tchendjou Tankam[1], J. Warszawski[7,8], C. Rouzioux[9,10], A. Faye[11,12], ANRS-PEDIACAM Study Group
[1]Centre Pasteur du Cameroun, Service d'Epidémiologie et de Santé Publique, Yaounde, Cameroon, [2]Centre Pasteur du Cameroun, Virology, Yaounde, Cameroon, [3]Centre Mère et Enfant - Fondation Chantal Biya, Unité de Jour, Yaounde, Cameroon, [4]Centre Hospitalier d'Essos, Service de Pédiatrie, Yaounde, Cameroon, [5]Hôpital Laquintinie de Douala, Hôpital de Jour, Douala, Cameroon, [6]Université de Douala, Faculté de Médecine et de Sciences Pharmaceutiques, Douala, Cameroon, [7]INSERM U 1018, Equipe 4, VIH et IST, EPF, Le Kremlin Bicêtre, France, [8]Université de Paris Sud, Paris, France, [9]Assistance Publique Hôpitaux de Paris, Hôpital Necker, Laboratoire de Virologie, Paris, France, [10]Université Paris Descartes, Paris, France, [11]Assistance Publique des Hôpitaux de Paris, Service de Pédiatrie, Paris, France, [12]Université Paris 7 Denis Diderot, Paris, France
Presenting author email: tejiokem@pasteur-yaounde.org

Background: Recent studies have shown that initiation of early antiretroviral therapy (ART) in HIV-infected children may lead to seronegative HIV tests. This could have implications in treatment adherence especially in resource limited settings (RLS) where presumptive diagnosis followed by ART and serological confirmation at 18 months is recommended. We aimed to identify factors associated with the seronegative status in early treated HIV-infected children and describe evolution of serological test results during follow-up.
Methods: .The ANRS-Pediacam is an ongoing prospective cohort which enrolled HIV-infected children identified during the first week of life or not but diagnosed later and before 7 months of age in three urban referral hospitals in Yaounde and Douala. Systematic ART was offered at inclusion and visits planned every 3 months till 2 years of age, and every 6 months thereafter. Frequency and factors associated with seronegative status defined as any negative HIV ELISA test result during follow-up were studied using uni and multivariables logistic regression.
Results: From 2007 to 2011, 210 HIV-infected children were included. Among them, 147 that initiated ART at 4.2 months (IQR: 3.2-5.7) were serologically tested at a median age of 20.2 months [IQR:18.2-22.5], 28 (19.1%) of them were negative. HIV seronegative status were associated with initiation of ART at age ≤3 months (aOR: 2.9, 95%CI[1.1-7.6]), female gender (aOR:3.2, 95%CI[1.2-8.2]) and WHO clinical stage 1 or 2 at ART initiation (aOR:2.9, 95%CI[1.0-8.6]). No association was found with ART protocol between lopinavir/ritonavir and nevirapine based regimens. Almost all seronegative treated HIV-infected infants were virally suppressed (VL< 1000 copies/ml) around the serological test period (96.4% vs 65.6%, p=.001). Of the 28 seronegative infants, 24 did at least two serological tests in a median follow-up period of 33.3 months (IQR:18.2-39.1), sixteen remained negative, five became positive and three indeterminate due to viral load rebound.
Conclusions: Early initiation of ART in HIV-infected children with clinically satisfactory health conditions may lead to seronegative HIV test results. The evolution of this seronegative status is variable depending on the efficacy of ART. Health care personnel especially in RLS need to be trained on the interpretation and relevance of such serological tests.

PUB010

Drug resistance mutations 2 years after delivery in HIV+ pregnant women who have discontinued antiretroviral drugs 6 months postpartum

M. Giuliano[1], C. Galluzzo[1], G. Liotta[2], M. Andreotti[1], H. Jere[3], R. Luhanga[3], R. Amici[1], M.C. Marazzi[4], L. Palombi[2], S. Vella[1], S. Mancinelli[2]
[1]Istituto Superiore di Sanità, Rome, Italy, [2]University of Rome Tor Vergata, Rome, Italy, [3]Community of S.Egidio, Blantyre, Malawi, [4]LUMSA University, Rome, Italy
Presenting author email: marina.giuliano@iss.it

Background: One of the possible drawbacks associated to the Option B strategy for the prevention of HIV mother-to-child transmission (the administration of triple combination therapy until the risk of transmission has ceased) is the emergence of drug resistance as a consequence of drug interruption. In this study we aimed to determine 2 years after delivery the rate of drug resistance in HIV-infected pregnant women who have discontinued drugs 6 months

postpartum and to assess a possible correlation with baseline resistance. Since in the absence of drug pressure mutations may quickly be no longer detectable in plasma, we evaluated the presence of resistance in HIV-DNA.

Methods: Study population included treatment-naïve (with the exception of single-dose nevirapine) HIV-infected Malawian pregnant women receiving a nevirapine-based triple antiretroviral regimen from week 25 of gestational age until six months of breastfeeding. Drug resistance was assessed in HIV-DNA extracted by whole blood samples 24 months postpartum. In patients with resistance the presence of mutations was also evaluated in HIV-DNA at baseline.

Results: A total of 42 women were studied. Their baseline CD4+ count was 503/mm^3 and their baseline HIV-RNA level was 3.4 $\log_{10}$ copies/ml. Six months postpartum 79% of them had HIV-RNA <50 copies/ml. At month 24 their CD4+ count was 603/mm^3 and their HIV-RNA level was 3.5 $\log_{10}$ copies/ml. Seven out of 42 women (16.6%) had archived drug resistance at Month 24 [in 6 cases there were non-nucleoside reverse transcriptase inhibitors (NNRTI) associated mutations and in 2 cases the M184I mutation was present]. In 4 cases resistance mutations were already present at baseline (all NNRTI mutations). In 3 cases there was emergence of "new" resistance (1 K103N mutation and 2 M184I mutations).

Conclusions: Among women who had discontinued drugs 6 months postpartum only 3/42 (7.1%) had accumulated, 2 years after delivery, new resistance mutations in HIV-DNA, possibly affecting response to treatment re-initiation. This is re-assuring in terms of the safety of the Option B strategy for the prevention of HIV mother-to-child transmission.

PUB011

Routine cryptococcal antigen screening before ART initiation: a study from an ART center of Eastern India

S. Kamal Guha[1], R. De[1], M. Mukherjee[2], N. Dutta[1], M. Mondal[1], D. Modak[1], S. Basak[3], B.B. Rewari[4]
[1]Calcutta School of Tropical Medicine, Kolkata, India, [2]National Institute of Technology, Durgapur, India, [3]Burdwan Medical College, Burdwan, India, [4]National AIDS Control Organization, Delhi, India
Presenting author email: drskguha@gmail.com

Background: Cryptococcal disease, particularly meningitis, is a major cause of morbidity and mortality among HIV-infected subjects. The WHO advocates the routine screening of cryptococcal antigen in serum/plasma in ART-naïve patients with low CD4 count (< 100 cells/mm^3) in settings where the burden of cryptococcal disease is high. Retrospective analysis of the Program data from 114 ART centres across India, the prevalence of cryptococcal meningitis (CM) was found to be about 3% in PLHIV with CD4 < 100 cells/mm^3 in 2013. We conducted a prospective study on prevalence of cryptococcal infection in ART-naïve patients from an ART Center of eastern India.

Methods: Approved by the Clinical Research Ethics Committee of Calcutta School of Tropical Medicine, India, this was conducted at the ART Center of the Institute during 18th December 2013 - 4th December 2014**.** Following written & informed consent, 200 consecutive ART-naïve subjects were screened for serum cryptococcal antigen (CRAG) by Latex Agglutination test, irrespective of their symptomatic status. Patients, already diagnosed as CM, were excluded from enrollment.

Results: The median age of the 200 enrolled participants (male - 160, female - 40) was 38 (32-45) years. The cases were distributed in WHO Clinical stage of 1 (41), 2 (20), 3 (91) and 4 (48) respectively. The median CD4 count was 78 cells/mm^3 (range 2 -198, IQR 41 - 121). Overall serum CRAG positivity was 11.5% (23/200) while in subjects with CD4 < 100 cells/mm^3 the prevalence was 14.06% (18/128). CRAG titer varied from 1:32 to 1:1024 with a median titer of 1:128. CRAG positive cases (male - 18, female - 5) had median age of 40 years (IQR 34 - 45), were mostly in clinical stage 3 or 4 (17/23; 73.9%) and febrile (82.6%; 19/23) at presentation. The median CD4 count of the CRAG positive cases was 73 cells/mm^3 (IQR 35 - 100).

	CD4 value 0 - 100 cells/mm3 (n = 128)	CD4 value 101 - 200 cells/mm3 (n = 72)	CD4 value 0 - 200 cells/mm3 (n = 200)
Male, %	103 (80.4%)	57 (79.1%)	160 (80.0%)
Female,%	25 (19.6%)	15 (20.9%)	40 (20.0%)
Age (years), Median (range)	38.50 (18-75)	38 (17-55)	38 (17-75)
CD4 Count (cells/mm3), median (range)	50 (2-100)	149.50 (101-198)	78 (2-198)
CRAG* Reactive	18	05	23
Male, %	15 (83.3%)	03 (60%)	18 (78.3%)
Female,%	03 (16.7%)	02 (40%)	05 (21.7%)
Age (years),median (range)	39.50 (32-70)	40 (32-45)	40 (32-70)
CD4 Count (cells/mm3), median (range)	50 (11-100)	164 (108-189)	73 (11-189)

[Sociodemography, clinico-immune status and cryptoc]

Conclusions: In eastern India, the seroprevalence of CRAG is high among HIV-infected subjects with advanced immunosuppression. Before ART initiation, mandatory screening for serum CRAG will help identify subjects requiring systemic anti-fungal therapy. Adoption of this strategy in the National ART Program will reduce the incidence of cryptococcal IRIS and consequent mortality.

PUB012

Utility of mobile communication devices as a tool to improve adherence to antiretroviral treatment in HIV-infected children and adolescents in Argentina

E. Stankievich, I. Firadori, A. Malanca, S. Ivalo, M. Losso
Hospital General de agudos JM Ramos Mejia, Buenos Aires, Argentina
Presenting author email: estankievich@hivramos.org.ar

Background: Optimal adherence is critical to achieve the benefits of the antiretroviral (ARV) treatment and minimize the risk of ARV resistance. Multiple aspects are involved in adherence in children and adolescents. Although, published evidence about strategies to improve it is scarce in our setting.

The aim of this study is to evaluate the effects on adherence to ARV treatment using mobile devices as a communication strategy to improve it.

Methods: A prospective study was conducted in a cohort of HIV+ patients less than 25 years old. Patients taking ARV were evaluated to establish suboptimal adherence (SOA). Inclusion criteria: HIV infected, taking ARV, viral load (VL)>1000 copies/ml, SOA, use of mobile devise. The intervention was based on mobile generic contact twice a month through any of the applications the patient chose (Whats app, Facebook, text message etc.) during an 8 month period. If the patient or parent required additional information a feedback phone calls were generated. VL was performed before and after the intervention as an outcome measure of adherence.

Results: 25/47 patients identified as SOA were able to be contacted. One refused to participate and 2 have no mobile. 22 patients were enrolled. Median age was 17.2 years old (range: 6-25); 15(68%) were female; median baseline VL was 25,100copies/ml (range: 500,000-1,020copies/ml), median log was 4.3 log (Range: 3-5.7log). Seven/22 were contacted through their parents. 10 (45%) preferred to be contacted by Whatsapp, 8(36 %) by text message, 4(18 %) by Facebook and others. Each participant received a total of 16 contacts, 84%(296) were answered by the patient. 65%(189) of the contacts generated additional requests (about medications, appointments or symptoms). After eight month of strategy implementation 20/22 VL results were available. 13/20 (65%) were undetectable, 14/20 (70%) had VL <1000 copies/ml. 6/20 (30%) VL had no changes.

Conclusions: The use of mobile technology improved adherence to treatment evaluated through VL measurement. The strategy is feasible in our setting. The reminder messages trigger additional contacts between patients and provider and may lead to better engagement with HIV care. Longer follow up time is needed to evaluate the effects of this intervention in the long term.

PUB013

Factors associated with depression among adolescents living with HIV in Malawi: a strong association with bullying victimization

M.H. Kim[1,2], A.C. Mazenga[2], X. Yu[3], A. Devendra[2,4], C. Nguyen[3], S. Ahmed[1,2], C. Sharp[5], J.K. Mhango[2], M. Bvumbwe[2], M. Machika[2], W. Kamuyango[2], A. Munthali[2], P.N. Kazembe[2]
[1]Baylor College of Medicine, Department of Retrovirology, Houston, United States, [2]Baylor College of Medicine - Abbot Fund Children's Center of Excellence, Lilongwe, Malawi, [3]Baylor College of Medicine, Department of Paediatrics, Epidemiology Center, Houston, United States, [4]Baylor College of Medicine, Department of Paediatrics, Houston, United States, [5]University of Houston, Department of Psychology, Houston, United States
Presenting author email: mariakim01@gmail.com

Background: There is a high estimated prevalence of depression amongst HIV-infected youth with data suggesting a detrimental impact on treatment outcomes. Associated risk factors and correlates of depression amongst HIV-infected youth in sub-Saharan Africa have been poorly examined.

This study aimed to identify contributory/protective factors associated with depression in Malawian adolescents living with HIV.

Methods: This was a cross-sectional study assessing factors associated with depression amongst a convenience sample of HIV-infected Malawians 12-18 years old. Depression was measured by a Chichewa version of the Beck's Depression Inventory version II (BDI-II) and the Children's Depression Rating Scale-Revised (CDRS-R). Data on >70 variables were collected including: socio-demographics, past traumatic events/stressors, behavioural factors/social support and bio-clinical parameters. Chi-square test or two sample t-test was used to explore associations between factors and depression. A second round of screening utilized linear/logistic regression, adjusting for age and sex and identified 18 candidate variables (p< 0.1). Final regression models included variables with significant main effects and interactions.

Results: Of the 562 participants enrolled (mean age 14.5 years (SD 2.0), and 56.1% female) the prevalence of depression as measured by the CDRS-R was 18.9% (106/562). In multivariate linear regression (Table 1) the variables significantly associated with higher BDI-II score were female gender, fewer years of schooling, death in the family/household, failing a school term/class, not disclosed or not having shared one's HIV status with someone else, lower level of immunosuppression, and being bullied for taking medications. Bullying victimization was reported by 11.6% of respondents. We found significant interactions: older participants with

lower height-for-age z-scores and dissatisfied with their physical appearance had higher BDI-II scores (Table 1). In multivariate logistic regression: older age OR 1.23 [95% CI 1.07-1.42], fewer years of schooling OR 3.30 [95% CI 1.54-7.05], and being bullied for taking medications OR 4.20 [95% CI 2.29-7.69] were significantly associated with depression.

Variable	Beta Coefficient [95% CI]	p-value
Female	2.13 [0.82, 3.43]	0.0015
Grade- Not in school/Junior Primary School	3.84 [1.71, 5.98]	0.0005
Nobody in my family has died	-1.77 [-3.15, -0.39]	0.0122
Did not fail school term/class	-1.46 [-2.76, -0.17]	0.0268
Bullied for taking medication	5.31 [3.19, 7.43]	<0.0001
Disclosed HIV status and have shared with someone	-1.83 [-3.79, 0.13]	0.0188
Level of Immunosuppression (None or not significant)	-2.58 [-4.29, -0.87]	0.0009
Age* satisfaction with physical appearance interaction	-0.93 [-1.74, -0.11]	0.0259
Age* Height for age z-score interaction	-0.39 [-0.68, -0.11]	0.0072

[Table 1: Multivariate Linear Regression Model of f]

Conclusions: Fewer years of schooling and being bullied for taking medications were most clearly associated with depression. Programs to support the mental health needs of HIV-infected adolescents that address issues such as disclosure, educational support, and most notably bullying may improve treatment outcomes.

PUB014

Cost-effectiveness analysis of early access to medical and social care for migrants living with HIV in France

M. Guillon[1], M. Celse[2], P.-Y. Geoffard[1]
[1]Paris School of Economics, Paris, France, [2]Conseil National du Sida, Paris, France
Presenting author email: marleneguillon88@gmail.com

Background: In 2011, migrants accounted for 47% of newly diagnosed cases of HIV infection in
France, including 70% from Sub-Saharan Africa. These populations meet with specific obstacles leading to late diagnosis and access to medical and social care. Reducing these delays has a proven benefit to patients´ health and contributes to a better control of the epidemic by preventing secondary infections.
Methods: The objective of this study is to assess the cost-effectiveness impact of an early access to care (ATC) for migrant people living with HIV (PLHIV) in France. The model compares "early" vs. "late" ATC for migrant PLHIV in France, defined by an entry into care with a CD4 cell count of 350 and 100/mm3 respectively. The model integrates the collective benefit, or positive externality, of ARV treatments on prevention of secondary infections. Moreover, existing estimates of incidence and size of hidden prevalence among migrants in France were corrected to take into account the specificity of the epidemics among this population which is partly imported.
Results: Early ATC strategy proved cost-saving, or cost-effective in the worst case scenario. In the most favorable scenario, early ATC generated an average net saving of €198,000 per patient, and prevented 0.542 secondary infection. In the worst case scenario, early ATC strategy generated an average cost of €28,000, a cost-effectiveness ratio of €133,000 per averted infection and prevented 0.211 secondary infection. If a decrease in risk behaviors is assumed after diagnosis, these results remain robust when late treatment is defined as an entry into care at 200 CD4, or when more pessimistic values of the key model parameters are assumed.
Conclusions: In addition to individual health benefit, improving early ATC for migrant PLHIV proves an efficient strategy in terms of public health and economics. These results stress out the benefit of ensuring ATC for all individuals living with HIV in France. Future research should focus on ways to improve access to care for migrants in France.

Track C

PUB015

Understanding behavioural and psychosocial factors influencing use of female condoms among female out-of-school adolescents in urban Cameroon

E.E. Tarkang
HIV/AIDS Prevention Research Network, NGO for HIV Prevention through Formalised Education, Kumba, Cameroon
Presenting author email: ebeyang1@yahoo.com

Background: The female condom is a proven effective female controlled HIV prevention device in Cameroon, which is relatively new, compared to the male condom. A major challenge facing HIV prevention efforts among out-of-school adolescents aged 15-24 in Cameroon is inadequate research on factors influencing use of female condoms. This study is aimed at understanding the behavioural and psychosocial factors influencing use of female condoms among female out-of-school adolescents aged 15-24 years in an urban area of Cameroon, using the Health Belief Model (HBM) as the behavioural change model.
Methods: A cross-sectional design was adopted and carried out in the month of November 2014, on a multistage probability sample of 340 consenting female out-of-school adolescents aged 15-24 years in Kumba, the Southwest region of Cameroon, collecting data through self-administered, pretested questionnaires in English. Data were analysed using Statistical Package for Social Sciences (SPSS) version 20 software program. Binomial logistic regressions analyses were conducted at the 0.05 significance level.
Results: Majority, 241 (70.9%) were sexually experienced, of whom only 53 (22.0%) reported ever using the female condom. Up to 94 (39.0%) reported having multiple concurrent sexual partners during the period of this study. Perceived susceptibility, severity, benefit, self-efficacy and perception of HIV risk were low, while perceived barrier was high. Behavioural and modifying factors significantly influenced the use of female condoms: respondents who had multiple concurrent sexual partners were 2.07
(95% CI 1.12-3.84, p=0.021) times more likely to use the female condom during sex; increasing age was associated with a reduction in the likelihood of using the female condom, OR=0.46 (95% CI 0.21-1.01, p=0.05); lack of HIV/AIDS knowledge was associated with a reduced likelihood of using the female condom, OR=0.50 (95% CI 0.26-0.97, p=0.039). None of the perception components of the HBM was statistically associated with use of female condom.
Conclusions: Interventions to increase the perception of risk of contracting HIV, and the knowledge level regarding HIV/AIDS among female out-of-school adolescents aged 15-24 years in urban Cameroon, and strategies to empower them with female condom negotiation skills and to overcome tangible and psychosocial barriers to female condom use are highly recommended.

PUB016

Modeling cost-effectiveness of HIV counseling and testing modalities in Tanzania

T. Mnzava
Center for Diseases Control and Prevention, Science, Dar es Salaam, Tanzania, United Republic of
Presenting author email: thommzava@gmail.com

Background: HIV counselling and testing (HCT) is a key HIV/AIDS control intervention. Several modalities have been developed for expanding HCT coverage in developing countries. Thus the objective of the study was to compare per client tested cost across four modalities which existing in Tanzania's HCT services.
Methods: A retrospective study was conducted in four districts in to two regions. The modalities assessed were Co-located or Integrated Client-Initiated HCT (CICT/VCT), Mobile or Outreach HCT (Mobile CICT), Facility-based Provider-Initiated HCT (PITC), Home-based HCT (door-to-door and client index approaches) (HBCT). Client's demographics and program costs incurred from January to December 2012 were collected. Client characteristics were extracted from National AIDS Control Program (NACP) monitoring systems register. Costing data was abstracted from site specific programme accounts, supply and inventories. Moreover, Cost and effectiveness were measured and compared across HCT modalities by taking a ratio of total cost per modality per clients tested. PITC modality was a baseline modality on cost effectiveness analysis.
Results: Overall, 16,561 records were extracted from the HCT registers. The majority of the clients were aged between 25 and 34 (36.3%), mean (SD) age of clients was 31.8(11.2) years. More female accessed HCT services 51.23% and had a higher HIV prevalence of 8.89% compared to male (48.77% and 5.49%).
Voluntary Counselling Testing (VCT) was found to be a leading modality in detecting HIV positive clients with a HIV prevalence of 9.1% and the least was Door-to-door reported 2.7%. PITC modality reached the largest proportion of previously untested individuals 92.9%. Costs per client (for 2012 in USD) were $17.45 for PITC, $19.92 for VCT, $25.88 for mobile and $21.59 for door-to-door.

When compared to baseline, incremental cost across all modalities increased by 1.5 folds for mobile, 1.1 times for VCT and 1.2 folds for door-to-door. PITC was having least unit cost across HCT modalities.
Conclusions: PITC was most cost effective modality across HCT modalities in Tanzania however multiple HCT modalities is an important components for HCT coverage expansion.

PUB017

Level of adherence to antiretroviral therapy and its determinants among people living with HIV/AIDS in SNNP Region, Ethiopia

M. Belayneh
Hawassa University, School of Public and Environmental Health, Hawassa, Ethiopia
Presenting author email: dinagemehretu@yahoo.com

Background: Recently more than 9.7 million people living with HIV were receiving antiretroviral therapy (ART) in low- and middle-income countries. However, the information related to adherence has been documented only in limited studies which are based in hospitals and there is a need to have regional estimates of these major indicators in Ethiopia.
Methods: Facility based cross-sectional study design using quantitative methods supplemented with qualitative methods was conducted from June to July, 2014. For quantitative part, questionnaire was used to collect the data from a total of 1320 population from twenty different public health institution (12 hospitals and 8 health centers). The data was analyzed using SPSS version 16.0 for windows. Univariate and multivariate logistic regression with 95% confidence interval was carried out.
Results: *According to this study,* The level of complete adherence as of patient report over four days was found to be 87.2%. Being away from home (11.9%), simply forget (8.1%), busy with other things (6.3%) and ran out of pills (5.4%) were major reasons among others for missing doses. Factors associated with non-adherence after multivariate analyses were educational level, religion, distance to clinic, drinking alcohol, attitude towards HIV/AIDS treatment and other predictor variables. According to ART supporters interviewed, though there is adherence counseling and defaulter tracing mechanism (phone call and/or home visit), the tracing mechanism was highly challenged by shortage of financial support, incomplete and fake patients address and name during intake registration.
Conclusions: Adherence level was still below the recommended WHO early warning indicators for HIV drug resistance. Clinicians and adherence supporters should reinforce counseling on adherence and pay attention for those who attend formal education.
Regional health bureau should take responsibility of making and following stock to make interrupted supply chain, supporting tracing mechanism by human and financial resource and assessing work load of clinicians and adherence supporters especially at hospital level.

PUB018

Impact of Option B+ implementation in HIV-positive pregnant/breastfeeding women in Bafoussam: a cross-sectional study

A. Francis Njukeng[1], N. Wouembe Blandine[1], K. Kouam Mermoz[1], F. Tama Gerard[1], J.B. Guiard-Schmid[2]
[1]Regional Hospital, HIV Approved Treatment Centre, Bafoussam, Cameroon, [2]Initiatives Conseil International - Santé, Ouagadougou, Burkina Faso
Presenting author email: atemnkeng_f@yahoo.com

Background: More than 90% of HIV infection in children is as a result of mother to child transmission. Elimination of mother-to-child transmission aims at reducing the transmission rate to <5%. To attain this objective, in 2013, WHO recommended placing every HIV positive pregnant/breastfeeding woman on long term antiretroviral therapy (ART) no matter their CD4 count- Option B+. Does the implementation of this recommendation greatly increase the number of pregnant/breastfeeding mothers not included in the previous recommendations?
Methods: A cross-sectional study was carried out from January to October 2014 involving HIV positive pregnant and breastfeeding women newly placed on option B+ at the Bafoussam Regional Hospital. Anthropometric, clinical and immunologic (CD4 count) parameters were collected. Descriptive statistics were performed to analyse data.
Results: A total of 47 HIV positive pregnant /breastfeeding (39/8) women newly placed on treatment were recruited with an average age of 28.3 years; 27.7% were single, 29.8% were cohabiting, 25.5% and 14.9% in monogamous and polygamous marriages respectively. As a whole, 26 (55.3%) of subjects received treatment >3months after knowing their status. 44 (93.6%) were classified stage 1 according to the WHO classification, 2(4.3%) stage 2 and 1(2.1%) stage 3. The average CD4 count at start of treatment was 463 (19 - 1,366) cells/mm3. Using to the 2010 WHO recommendations (using CD4 count<350 and clinical staging), only 18/47 (38.3%) would have been on ART. Using just the CD4 count <500, and the clinical classifications for eligibility to ART in the 2013 WHO recommendations, 30/47 (63.8%) would have been on treatment. But with option B+ an additional 36.2% received ART.
Conclusions: Option B + increases considerately the percentage of HIV positive pregnant/breastfeeding women benefit from ART as we struggle to attain elimination of mother to child transmission at the Bafoussam Regional Hospital.
Further research should be carried out to verify the impact in mother of Option B+ in preventing new infections in children at the Bafoussam Regional Hospital.

PUB019

Factors affecting contraceptive uptake among female sex workers (FSWs) in Sex Workers Outreach Program (SWOP) in Nairobi, Kenya

J.P. Sore Inyama[1], J. Kimani[2], Z. Ng'ang'a[3], C. Mbakaya[4], G. Gakii[2]
[1]Kenya AIDS Control Project, Sex Workers Outreach Program, Nairobi, Kenya, [2]Kenya AIDS Control Project, Nairobi, Kenya, [3]Jomo Kenyatta University of Agriculture and Technology, College of Health Sciences, Nairobi, Kenya, [4]Kenya Medical Research Institute, Nairobi, Kenya
Presenting author email: sorep2006@gmail.com

Background: Female sex workers (FSWs) are often targeted by public health interventions designed to prevent sexually transmitted infections including HIV. However, such targeted programs sometimes overlook the broader reproductive health needs of these women. This study was conducted to determine contraceptive prevalence among FSWs in SWOP.
Methods: This was a descriptive cross-sectional study which utilized both quantitative and qualitative methods. Systematic random sampling was used to select 385 participants to whom questionnaires were administered. 36 were randomly selected from the 385 for the 3 FGDs. Quantitative data was analyzed using SPSS with qualitative data being manually analyzed according to thematic areas of study.
Results: Most of the respondents were aged between 25-34 years (49.1%), with the highest proportion having been in the program 25 months or more. Almost all the respondents (93.8%) had attained some formal education. Majority were divorced/widowed/separated/cohabiting (68.8%) with a small proportion (7.0%) being married. Majority (75.8%) indicated having a regular sexual partner with (82.3%) reporting having had multiple pregnancies. 73.8% were currently using a contraceptive method with the most reported methods being; condom (61.3%) and injection (21.3%). The main source of the contraceptives was SWOP (50.9%), followed by other hospitals/clinics (30.4%). Having been in the program for 13-24 months or more was significantly associated with increased contraceptive use (74.7%) compared to being in the program for 12 months or less (54.7%), (OR=2.45; 95% CI: 1.27 - 4.72; p=0.007). Assessment of attitude towards contraceptive use revealed that appropriate attitude was significantly associated with increased contraceptive use (87.0%) compared to inappropriate attitude (3.3%), (OR=198.07; 95% CI: 46.65-841.03;p< 0.001). In one of the FGDs, asked what an FSW would have done to prevent an unplanned pregnancy, one said: "She should have used family planning or consistently used condom." FSW, FGD 2.
Conclusions: The level of contraception use was generally high. However, condom was the most utilized contraceptive method. A lot has to be put to ensure increased use of modern contraceptives in combination with condoms to enhance dual protection.

PUB020

Mixed method approach for determining the factors associated with late presentation to HIV/AIDS care in Southern India

U.N. Yadav
Manipal University, Department of Public Health, Manipal, India
Presenting author email: joriens_sm485@yahoo.com

Background: Early diagnosis and treatment of Human Immunodeficiency virus (HIV) is not only beneficial for the people living with HIV/AIDS(PLHA) but for the public and society as well. Delays in HIV care are common and the factors that contribute to delay in seeking treatment are not fully understood. The aim of the study present study was to identify factors associated with late presentation to HIV/AIDS care.
Methods: A facility- based unmatched case-control (1:1) study along with in-depth qualitative assessment was conducted at the ART Plus center in Udupi district, Southern India. A sample of 320 HIV patients (160 cases and 160 controls) was selected randomly between February and July, 2014. Information was collected using interviewer administered semi-structured questionnaire. The qualitative component was assessed by in-depth interviews of four health professionals and 12 HIV positive patients who were late for HIV care**.** The quantitative data was analyzed using SPSS version 15.0. Thematic analysis was adopted for analysis of qualitative data. Ethical approval was obtained from the Institutional Ethics Committee (IEC: 75/2014), of a tertiary care hospital.
Results: HIV positive individuals who lived with families[OR=5.11, 95% CI: 1.90-13.77], patients having non- AIDS co-morbidities[OR= 2.19, 95% CI: 1.09-4.40], who perceived fear of losing family[OR= 5.00, 95% CI: 2.17-11.49], who perceived fear that their status will be ruined in the community[OR= 2.00, 95% CI: 1.01-3.97], who perceived fear with side effects of ART medications[OR=4.3,95% CI:2.65-11.33)], who perceived fear of losing confidentiality[OR=4.94, 95% CI:2.54-9.59], those who lack information available on government services[OR=4.12, 95% CI: 2.127-8.005] and those who consumed alcohol [OR= 3.52, 95% CI:1.83-6.77)] were found to be independently associated with late presentation to HIV/AIDS care after adjusting for all known confounders in multivariable analysis. The qualitative sum-

mary showed perceived HIV stigma, inadequate health education, lack of awareness on available government services, psychological problems, alcohol use, asymptomatic conditions and financial problems were major barriers to access care early for the late presenters.
Conclusions: The identified factors can be utilised for the formulation of policies and interventions by promoting early diagnosis and addressing special concerns such as stigma, disclosure, health education and awareness.

PUB021

Sexual and status disclosure challenges among HIV-positive adolescents receiving care at TASO Entebbe

J. Mwebe
The AIDS Support Organization, Medical Department, Kampala, Uganda
Presenting author email: josephm169@gmail.com

Background: Many HIV positive children and adolescents on ART are developing into adults**.** This paradigm requires that their caretakers understand social requirements of such individuals. One of the decisive development tasks for adolescents and young adults is to explore and establish relationship with the opposite sex. Recent literature has documented sexual behaviors, and unplanned pregnancies among HIV positive adolescents. However their challenges in establishing healthy sexual relationships and disclosure of their HIV status to their partners before are not yet known. The study objective was to asses the key sexual and status disclosure challenges faced by HIV positive adolescents.
Methods: Well thought out interviews were carried out with 30 adolescents during the facility's HIV positive adolescent clinic. Most respondents were females (n=19, 63%), and males were 11 (37%).The mean age was 17.5 (range 15- 20 years). The focus of the interview was on their view point on having a sexual partner(s), sexual activity, Status disclosure, as well as contraceptive use. Quantitative and qualitative analysis of findings was done.
Results: Findings showed that majority of the respondents (22, 73%) are sexually active and find it easier to relate with individuals who are not of the same status. 18 (60%) of these had never disclosed their HIV status to their current dating partners. The major reported barrier to disclosure was fear of relationship cessation (n=16, 53%), and social discrimination. A few respondents (n=3) reported a positive out outcome with supported disclosure. 21 (95%) of sexually active participants reported ever use of condoms but only 10 (45%) reported consistent condom use. None of the respondents had ever used any other type of contraceptive methods.
Conclusions: Status disclosure is a crucial and pertinent factor in prevention with positives among HIV positive adolescents. HIV counseling information to adolescents should centre on how to instigate a healthy sexual relationship, prevention with positives and contraceptive use.

PUB022

Addressing the dual epidemic of HIV and gender-based violence: results from a systematic review of evaluated gender-integrated programs in low- and middle-income countries

E. Rottach[1], S. Pappa[1], A. Muralidharan[2], M. Mandal[3], J. Fehringer[3], M. Das[4], R. Dayal[2]
[1]Futures Group, Washington, United States, [2]Public Health Foundation of India, Gurgaon, India, [3]MEASURE Evaluation, University of North Carolina, Chapel Hill, United States, [4]International Center for Research on Women, New Delhi, India
Presenting author email: erottach@futuresgroup.com

Background: The links between gender-based violence (GBV) and HIV are well documented; however, there is still a pressing need to identify effective strategies for addressing this dual epidemic. Drawing from a systematic review of evaluated gender-integrated health programs in low- and middle-income countries, undertaken by the USAID-funded Health Policy Project, in collaboration with MEASURE Evaluation, Public Health Foundation of India and the International Center for Research on Women, this study highlights effective and promising gender strategies that have been used to improve GBV and HIV outcomes. It also examines regional differences between sub-Saharan Africa and South Asia.
Methods: The search was based on scientific and grey literature published between January 2008 and June 2013. Relevant publications were abstracted to identify strategies for integrating GBV into HIV prevention programs, and were rated on level of effectiveness. A thematic analysis of abstracted data was conducted.
Results: The review found 22 evaluated gender-integrated interventions that collectively addressed GBV and HIV prevention. Among the effective gender strategies used for GBV and HIV prevention, the most commonly used strategies included challenging gender norms through social and behavior change communication and fostering critical reflection on gender norms. Regional differences were identified, reflecting the nature of the epidemic in the two regions: In sub-Saharan Africa, programs often worked with men to mitigate risky behaviors and reduce violence against their female partners, while in South Asia, program efforts focused on collectivizing and empowering key populations, such as female sex workers, and undertaking advocacy efforts with relevant stakeholders like the police and brothel owners. Out of the 22 programs, 18 demonstrated changes in HIV prevention behaviors, such as safer sex practices, consistent condom use, and increased HIV testing. Three programs demonstrated changes in health status, such as decreased sexually transmitted infection prevalence. Thirteen programs demonstrated changes in violence-related outcomes, such as decreased report of GBV perpetration and attitudes toward violence.
Conclusions: These findings provide evidence that gender-integrated programs can improve GBV and HIV outcomes, documenting the importance of integrated GBV and HIV prevention programs. GBV prevention strategies should be tailored to the HIV epidemic in which the programs operate.

PUB023

National size estimation of people who use drugs using capture-recapture method in nine provinces of Cambodia

S. Tuot[1], C. Chhea[2], S. Heng[2], B. Keo[3], S. Yi[4,5]
[1]KHANA, Research Department, Phnom Penh, Cambodia, [2]National Institute of Public Health, Phnom Penh, Cambodia, [3]National Authority for Combating Drug, Phnom Penh, Cambodia, [4]KHANA, Phnom Penh, Cambodia, [5]Touro University, Vallejo, United States
Presenting author email: tsovannary@khana.org.kh

Background: A reliable estimate of national population size of people who use drugs (PWUD) is critically important for better advocacy, resource mobilization, program planning, management of effective targeted health programming, and better HIV projection. This study describes capture-recapture method, a direct technique of estimation of PWUD size in nine provinces of Cambodia.
Methods: The study was carried out in late 2012. We used Respondent Driven Sampling (RDS) to recruit the sample groups of PWUD. A person who had used any illicit drug, as defined by the Cambodia Drug Control Law, by any route of administration in the past 12 months was invited to participate in the study. After receiving consent, the research team ,tagged' study participants by giving the token. The same recruitment method was used to recruit PWUD from the same geographic location at the recapture stage. The protocol was approved by the National Ethic Committee for Health Research.
Results: Of the total sample (n=1,626), 82.2% were male, and 17.8% were female with a mean age of 25 years. Approximately, 52% were single at the time of the survey, while 31% were married. About 50% of them reported currently living with their parents. A total of 1,262 PWUD were tagged at the capture stage, and 314 of the previously tagged PWUD were recaptured. The calculation of the numbers of PWUD was the product of the number of PWUD met in the capture divided by the % of the tagged PWUD who were re-contacted at the recapture stage. Based on this method, the estimated size of PWUD population in the nine provinces were 9,221 (low estimate of 8,666 and high estimate of 9,777). Proportion of PWUD from the nine provinces contributed to the total of 75% of the total number of PWUD in the whole country. Thus, the average number of PWUD for all 24 provinces of the country was 12,296 (low estimate of 11,555 and high estimate of 13,037).
Conclusions: Capture-recapture seems to be a feasible and robust method among the most direct techniques, which can be applied to estimate PWUD population using RDS, where reliable size estimation of PWUD population is lacking

Track D

PUB024

Provider attitudes about childbearing and knowledge of safer conception at two HIV clinics in Malawi

P. Kawale[1], D. Mindry[2], A. Phoya[3], P. Jensen[4], R.M. Hoffman[5]
[1]Nkhoma Hospital, Public Health Department, Lilongwe, Malawi, [2]University of California, Center for Culture and Health, Los Angeles, United States, [3]Ministry of Health, Sector Wide Approach, Lilongwe, Malawi, [4]Partners in Hope Medical Centre, Lilongwe, Malawi, [5]University of California, Division of Infectious Diseases,David Geffen School of Medicine, Los Angeles, United States
Presenting author email: paul.kawale@gmail.com

Background: There is limited understanding of health care providers' attitudes towards HIV-infected individuals´ reproductive choices, as well as knowledge about safer conception. Our study objective was to explore provider-level factors that serve as barriers and/or facilitators to the provision of reproductive and safer conception services for men and women living with HIV.
Methods: Twenty-five providers were interviewed in four focus group discussions about their attitudes regarding childbearing by HIV-infected clients, reproductive health and HIV knowledge, and views and knowledge of safer conception.

Results: Providers reported ambivalence about supporting childbearing among their clients with HIV. They raised concerns about HIV-infected individuals having children, and in certain cases expressed judgment that people with HIV should not have children because of these concerns. Providers lack specific knowledge about safer conception strategies and have low level of knowledge of reproductive health, the efficacy of PMTCT, and the risks of pregnancy for HIV-infected women.
Conclusions: Providers in our setting have complex attitudes about HIV-infected clients having children and lack knowledge to appropriately counsel clients about reproductive health and safer conception. Our findings highlight need for further research in this area as well as the need for provider training in reproductive health and safer conception.

PUB025

Examining health and health service utilization of heterosexual men with HIV: a scoping review

N. Kou, J. Bertrand Nguemo Djiometio, A. Agha, A.-M. Tynan, T. Antoniou
St Michael's Hospital, Centre for Research on Inner City Health, Toronto, Canada

Background: The prevalence of HIV infection among heterosexual men has increased over the past two decades. Consequently, the need for health and support services for this group is likely to increase. The purpose of this scoping review is to provide an overview of the evidence related to the health and health service use of heterosexual men with HIV related to domains of interest identified by the community.
Methods: We searched 6 databases from inception to August 2014. We included all English-language qualitative and quantitative studies examining the health and health service use of heterosexual men with HIV. Two reviewers independently screened titles and abstracts for inclusion in the review, and disagreements were settled by a third reviewer. We extracted data regarding study characteristics (i.e. country of study, design, participant demographics, comparison groups, main findings, and limitations), and used content and thematic analysis to summarize the findings.
Results: Our search strategy yielded 2344 references, of which 87 were included in the scoping review. We summarized the research into the following domains: treatment of HIV and its complications (n = 7), health and social support services utilization (n = 20), social determinants of health (n = 8), prevention (n = 17), family planning (n = 8), and psychosocial research (n = 29). Key findings include difficulties accessing care, poor mental health-related well-being and self-reported functional health, over-representation among ‚late presenters' to care, greater fear of disclosure relative to gay men, being recast as violent and monstrous by mainstream media, and a lack of support regarding family planning and fatherhood.
Conclusions: This is the first comprehensive review of the literature regarding heterosexual men with HIV. The review supports the need for multi-sector collaboration (medical and community) to develop programming and support for these patients.

PUB026

Effects of a cognitive-behavioral intervention on condom use and serostatus disclosure in Mexicans living with HIV

N.P. Caballero Suárez[1], E. Rodríguez Estrada[1], M.C. Iglesias Chiesa[1], J.M. Menez Díaz[2], A. Riveros Rosas[3], G. Reyes Terán[1]
[1]Center for Research in Infectious Diseases (CIENI), Mexico City, Mexico, [2]National University of Mexico, UNAM, School of Psychology, Mexico City, Mexico, [3]National University of Mexico, UNAM, School of Business Administration, Mexico City, Mexico
Presenting author email: nancy.caballero@cieni.org.mx

Background: Serostatus disclosure to sexual partners and condom use are relevant variables for prevention of HIV transmission. Few studies assess interventions promoting disclosure, and fewer still assess both disclosure and condom use. We designed and evaluated an evidence-based, modular, cognitive-behavioral intervention aimed at improving consistent and correct condom use and facilitate serostatus disclosure in people living with HIV (PLWHIV).
Methods: In a single case experimental design (n=1), outpatient PLWHIV of the Center for Research in Infections Diseases in Mexico City, who were under antiretroviral treatment and had moderate to severe levels of anxiety and/or depression were invited to participate between June 2013 and March 2014. Participants received 10 individual weekly cognitive-behavioral sessions, consisting of 6 modules: emotional regulation, serostatus disclosure, quality of sexual life/ couple life, triggers of sexual risk behaviors, correct and consistent condom use and sex negotiation. Depression and Anxiety were measured weekly using Beck Inventories; basal, end of intervention and 3-month follow up measures also included questionnaires on pattern of sexual behaviors, quality of sexual life/quality of couple life, and antiretroviral treatment adherence. Data were analyzed using Wilcoxon or Friedman tests, effect size was obtained through Cohen's d index, and the Jacobson-Truax method was used for clinical significance.
Results: Eleven PLWHIV completed the intervention, 10 were men, mean age was 39.8 (SD=9.0) years old. All participants were able to establish their rule of disclosure (to disclose before sexual activity or not to disclose but to use condom). Skills on correct condom increased from 52.68% to 98.21% in the mean correct score (x^2=26.33,df=4,p< 0.001), showing also large effect sizes, but frequency of self-reported condom use did not change (x^2=2.00,df=2,p=0.368). Symptoms of depression (x^2=83.75,df=13,p<0.001) and anxiety (x^2=102.40,df=13,p<0.001) showed significant reductions, and the size of the effects was large for both variables. Quality of sexual life also improved (x^2=10.10,df=3,p=0.018). No changes in treatment adherence were found.
Conclusions: Results show positive, large and clinical effects of the intervention on correct condom use, levels of emotional distress, and quality of sexual life. This suggests that cognitive-behavior interventions can make key contributions to secondary prevention of HIV transmission and improve the well-being of PLWIHV.

PUB027

Delay in early infant diagnosis and high loss to follow-up among infant born to HIV-infected women in Ethiopia

B. Kebede[1], A. Gebeyehu[2], S. Jain[3], S. Sun[4], R. Haubrich[5]
[1]University of Gondar, Public Health, Gondar, Ethiopia, [2]Institute of Public Health, University of Gondar, Gondar, Ethiopia, Gondar, Ethiopia, [3]University of California San Diego, Department of Family and Preventive Medicine, Division of Biostatistics and Bioinformatics, San Diego, United States, [4]University of California San Diego, Department of Family and Preventive Medicine, Division of Biostatistics and Bioinformatics,, San Diego, United States, [5]University of California San Diego, School of Medicine, San Diego, United States
Presenting author email: bekanasiif@gmail.com

Background: Many HIV-infected infants and children die from HIV related causes without their HIV status being known or receiving HIV care. All HIV exposed infants should be tested by Dried Blood Spots (DBS)-PCR before or at 6 weeks of age.In order to facilitate ART or prophylaxis initiation as soon as possible, the WHO recommends HIV diagnostic testing for all HIV-exposed infants at 4 - 6 weeks of age and to initiate therapy soon thereafter. Testing is a crucial step to facilitate early access to antiretroviral treatment (ART) and then functional cure. However, studies that assess the level of use and implementation of HIV DNA testing in Ethiopia are lacking.
Methods: A multicentre cohort study was conducted in three public hospitals and three health centers. Mother-infant pairs were followed from delivery until the time of the infant HIV diagnostic test. Data were captured using standardized forms. The time-to-diagnostic test was estimated using Kaplan-Meier estimators. Factors associated with Early Infant Diagnosis(EID) were evaluated using logistic regression.
Results: Out of the 266 HIV-exposed infants, 59% had no early infant diagnosis(DNA-PCR tests). The median age at the time of HIV diagnostic testing was 60 days (95% CI: 47 - 73 days), and the median turnaround time between blood draw for DNA-PCR testing to delivery of a test result to the respective health facility was 36 days (95% CI: 33 - 40 days). A total of 35 (13.2%) infants were diagnosed with HIV infection. The predictors of EID were the mother having prenatal care, maternal receipt of ART during pregnancy and place of birth.
Conclusions: Three out of five HIV-infected women did not bring their infant for early HIV testing, during the recommended interval after birth.This would endanger a chance of the exposed or infected infant to initiate ART treatment and other prevention services to facilitate cure.Special attention is required for infants born to HIV-infected women who did not receive ART or delivered at home or a private health facility to ensure early infant diagnosis, reduce loss to follow-up and prevent late initiation of ART for HIV-infected infants.

PUB028

Patients' rights in China and implications for adult HIV disclosure

J.-B. Nie[1], S. Walker[2], S. Qiao[3], J. Tucker[4], X. Li[3]
[1]University of Otago, Bioethics Centre, Dunedin, New Zealand, [2]University of Otago, Dunedin, New Zealand, [3]Wayne State University, Detroit, United States, [4]University of North Carolina, Chapel Hill, United States
Presenting author email: jing-bao.nie@otago.ac.nz

Background: The question of whether it is ethically required to disclose a diagnosis of HIV positive to a third party, such as sexual partners or family members, is a universal challenge for healthcare professionals. Patients' rights are central in today's legislation and social policies related to healthcare, including HIV care, in not only Western countries but around the world. However, given obvious socio-cultural differences it is often asked how or to what extent patients' rights should be respected in non-Western societies such as China.
Methods: Philosophical analysis and an interdisciplinary literature review of the current Chinese practices of HIV disclosure and the historical and philosophical exploration on human rights in China were conducted to investigate the relevance of respecting patients' rights in addressing the challenge of adult HIV disclosure in the Chinese context.
Results: It has been found that human rights are recognized and valued in Chinese traditions, and that respect for patients' rights is essential for developing adequate HIV care in China. These ethical arguments have a series of practical implications for the role of medical professionals regarding HIV disclosure, *viz.* that health providers have a duty to disclose truthfully the diagnosis and prognosis to their patients, that the Chinese cultural practice of involving families in care should - with consent from the patient - be promoted out of respect for patients'

rights and well-being, and that healthcare providers should be prepared but not obliged to address the issue of disclosing a patient's HIV status to sexual partner(s).
Conclusions: The ethical framework of patient's rights can serve as a meaningful guide for medical professionals in addressing the ethical challenges of HIV disclosure in the Chinese socio-cultural context. There is a need for healthcare providers to receive training in ethics and disclosure skills. Also, post-disclosure counseling or psychological support should be in place to address the concerns of potentially adverse consequences of provider-initiated disclosure and to maximize the psychosocial and medical benefits of the disclosure. Some recommendations for improving the centerpiece Chinese legislation, State Council's "Regulations on AIDS Prevention and Control" (2006), are made to further safeguard the rights and well-being of HIV patients.

PUB029

Progress made to enhance understanding of clinical trials by the media: following inaccurate reporting of clinical trials in Zimbabwe in 2011

M. Kanengoni[1], M.E. Shana[2], F.L. Tarumbiswa[2], S. Ruzario[2], P. Ndebele[2]
[1]Medical Research Council of Zimbabwe, Chitungwiza, Zimbabwe, [2]Medical Research Council of Zimbabwe, Harare, Zimbabwe
Presenting author email: muchineripikanengoni@yahoo.com

Background: Following the inaccurate reporting that 127 HIV negative women had tested HIV positive after the VOICE trial in November 2011 in Zimbabwe, Zimbabwean stakeholders in health research have realised the need to actively engage the media and improve their research literacy to guard against potentially harming misconceptions being relayed to the public. The main objectives of this paper are to note the progress made so far in engaging and enhancing comprehension of the media and to determine whether these efforts have resulted in changes in the nature of reporting.
Methods: The project being reported was conducted between November 2011 and December 2014. The project activities included making use of observations of the magnitude of media engagement and level of media coverage of clinical trials since the publishing of an inaccurate report in November 2011. Efforts to engage the media by various stakeholders in the conduct of clinical trials were initiated and also monitored.
Results: There has been an increase in the engagement of the media throughout the process of clinical trials research. "ASPIRE" study researchers in Zimbabwe now engage the media in radio shows where listeners also phone to ask questions. Throughout the project duration, a number of newspaper articles were written updating readers of the ASPIRE Dapivirine vaginal ring study. There is now better coverage of events like Research and Intellectual Expos, Annual Health Research Ethics Forum and Research Symposiums hosted by regulators and research institutions. Medical Research Council of Zimbabwe has written articles published in local magazines explaining its role in medical research.
Conclusions: There is growing engagement between the media and clinical trials conduct stakeholders. Researchers in particular now go the extra mile to engage the media so that accurate information is relayed to the public. Regulators and universities have also been making efforts to reach out to the media. However, more could be done to enhance clinical trials literacy among media personnel as some articles they write still have some minor mistakes which could be rectified by better understanding. There is thus need to hold seminars for media practitioners for them to better understand HIV prevention and treatment trials.

PUB030

Outcome evaluation of the *Safe Love* campaign in Zambia using propensity score matching: positive effects on condom use and HIV testing behaviors

A.C. Franca-Koh[1], S. Herrera[1], J. Manda[2], K. Chilemu[2], K. Unfried[1], M. Elkasabi[1], A. Chipukuma[2], E. Maliwa[2], C. Wakefield[2], J. Simbaya[3], H. Fumpa[3], M. Nyamazana[3], N. Sachingogu[3], M. Aguilar[1], R. Bishwakarma[1], T. Croft[1], T. Hai[1], L. Moonzwe[1], G. Temsah[1], N. Vincent[1], W. Wang[1], A. Weisser[1], J. Yourkavitch[1], M. Do[4]
[1]ICF International, International Health Division, Rockville, United States, [2]Communications Support for Health, Lusaka, Zambia, [3]INESOR, Lusaka, Zambia, [4]Tulane University, New Orleans, United States
Presenting author email: ana.franca-koh@icfi.com

Background: The *Safe Love* campaign was a three-year comprehensive HIV prevention behavior change communication (BCC) initiative that was implemented between 2011 and 2014 in Zambia. An outcome evaluation was conducted to assess the effects of the campaign on behavioral and intermediate outcomes related to condom use, HIV testing, multiple concurrent partnerships (MCP), and voluntary medical male circumcision (VMMC), and to determine if the effects differed by area of residence, sex, and level of recall.
Methods: The evaluation used a one-group post-test-only design with propensity score matching to determine the effects of the campaign. A representative household survey of nine districts where all components of the campaign were implemented was conducted between June and August 2014. A total of 1,993 men and 2,121 women aged 15-49 completed the survey.
Results: The campaign had positive effects on all four condom use behavior outcomes among males and females, but only in urban areas. Consistent condom use in the past six months increased significantly by 8 percentage points among urban respondents who were able to recall spontaneously any campaign elements and by 13 percentage points among those with higher levels of recall. In terms of HIV testing, the campaign had a significant effect on one of the behavior outcomes examined among rural respondents with higher levels of recall: There was a 22.5 percentage point increase in partners getting tested for HIV in the past six months. No campaign effects were detected on MCP-related behaviors or intention. For VMMC, campaign effects on the behavior outcomes examined were inconclusive; however, there was a strong effect on uncircumcised males' intention to get circumcised in the next six months.
Conclusions: The outcome evaluation of the *Safe Love* campaign found that the campaign had a significant effect on increasing key HIV preventive behaviors—in particular, the acquisition and use of condoms in urban areas and HIV testing among partners in rural areas. Overall, the outcome evaluation adds evidence to the BCC literature of the importance of communication campaigns to change HIV preventive behaviors and also provides practical lessons learned and recommendations for future programming in Zambia and beyond.

PUB031

Need for improved testing: HIV testing patterns among female sex workers in Ukraine

A. Tokar[1], I. Sazonova[1], M. Becker[2], P. Smyrnov[1]
[1]ICF, International HIV/AIDS Alliance in Ukraine, Kyiv, Ukraine, [2]University of Manitoba, Centre for Gobal Public Health, Winnipeg, Canada
Presenting author email: annatokar@yandex.ru

Background: Ukraine has been experiencing one of the fastest growing HIV epidemics in Europe, with current estimates of HIV prevalence in the general population at 0.78%. Since 2008, the primary mode of HIV transmission evolved from concentrated within networks of people who inject drugs (PWID) to spread through unprotected heterosexual contact. Expansion of high-risk sexual networks, in combination with continued spread in networks of PWID, currently fuels the HIV epidemic.
Beginning in 2007, as a part of comprehensive response, rapid HIV testing was introduced across Ukraine. By 2013 13,763 female sex workers (FSWs) were reached, however this represents only 17% of the estimated number of FSWs. This paper explores the HIV testing patterns and risk factors among FSWs in Ukraine.
Methods: Integrated biological and behavioural surveys (IBBS) were conducted among FSWs in all regions of Ukraine in 2013 (n=4,806) using time location sampling (TLS) and respondent driven sampling (RDS). FSWs were defined as those providing sexual services for remuneration (money or goods or other services) within the last 6 month. Logistic regression analysis was performed to define factors associated with willingness to undertake HIV testing.
Results: FSWs aged 18 years old or less reported higher willingness to undergo HIV testing (OR=8.7 (3.127-24.21).Still more vulnerable women working on the streets (OR=.182 (.054-.610), highways (OR=.131(0.38-.448)), brothels (OR=.108(.032-.357)) and who use drugs (OR=.504(.326-.779)) less likely to pass HIV testing. HIV positivity was associated more frequently with being victims of violence (OR=1.39 (1.02-1.89)), longer duration in SW (more than 10 years) (OR=2.14 (1.16-3.96)), lack of consistent condom use during last month (OR=1.68 (1.05-2.69)), and injection drug use
(OR=6.77 (3.742-12.31).
Conclusions: FSWs, including those who are street based, victims of violence, and inject drugs have significantly greater risk of HIV infection, yet are less likely to undertake HIV testing. This has important programmatic implications. HIV testing approaches targeting the most vulnerable FSWs should be introduced, with comprehensive prevention interventions to address their prevention and care needs.

PUB032

Outcome of introduction of antiretroviral therapy among HIV (+) people who inject drugs in Bangladesh

Z. Shams, L. Rahman, S. Islam
Save the Children, HIV/AIDS, Dhaka, Bangladesh
Presenting author email: z.shams01@gmail.com

Background: The prevalence of HIV in Bangladesh is less than 0.1% in the general population and has remained less than 1% over the years. HIV infection rate is increasing among key affected population (KAP) particularly among PWID from 1.4% in 1999 to 5.3% in 2011 in Dhaka which put the country into the category of having a "concentrated epidemic". There are 6 ART centers to deliver ART in addition to their medical and psyco-social consultation. National AIDS/STD Program (NASP) has endorsed National guidelines for antiretroviral therapy (ART) in Bangladesh (2011). A study was necessary to measure of outcome with or without ART administration among HIV (+) people who inject drugs.

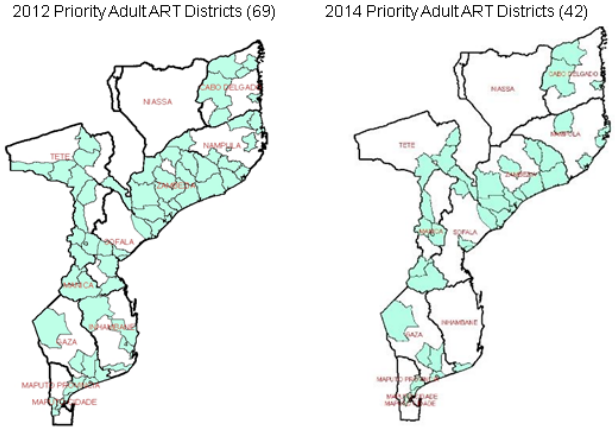
Methods: This was a retrospective cohort study with routinely collected medical data of HIV (+) people who inject drugs from an exclusive ART center based in Dhaka, Bangladesh. The register had data of about 200 cases from December, 2009 to December, 2013. Paramedic and counsellors extracted data. But consistent outcome data were found for 135 case which was analyzed here using established MS Excel based database.
Results: Age ranged from 20-62 years. Majority were male and only 9% of them were female. About half (47%) of them had primary education or below. Among the study participants, 40% (53) are still on ART, 36 % (49) died, 23% (31) were stopped treatment, only 1 was lost, 1 transfer out to another center. Significant proportion of them (71%) had history of taking Co-trimoxazole (CTX) Prophylaxis. Among the death cases, about 70 %(34) had co-infection. It was observed that more than 80% of both death cases along with interrupted treatment cases had history of not taking ART. Usually they came late under treatment and care.
Conclusions: It is assumed that treatment with ART could retain the patients in the program. Their physical and social well-being were dependent on it. For that HIV case detection and linked to continuum of care is vital to revert morbidity & mortality. Early diagnosis and eligibility for ART, efficiently medico-social management can motivate patients to receive treatment and followed up. Smooth distribution of ART from Government authority need to be ensured.

PUB033

Estimating district-level adult unmet need for ART in Mozambique 2012-2014

J. Lara[1,2,3], A. Couto[1], V. Macome[4], I. Wanyeki[5], N. do Nascimento[6]
[1]Ministry of Health, Direcção Nacional da Assistência Médica (DNAM), Maputo, Mozambique, [2]Abt Associates, Maputo, Mozambique, [3]University of Washington, Seattle, United States, [4]Ministry of Health, Direcção Nacional da Assistência Médica, Maputo, Mozambique, [5]Health Policy Project/Futures Group, Nairobi, Kenya, [6]Health Policy Project/Futures Group, Maputo, Mozambique
Presenting author email: joseph.lara@gmail.com

Background: In 2013 Mozambique launched its Acceleration Plan for Combatting HIV, which aimed to increase the percentage of ART eligible persons in treatment to 80% by 2015. To support the strategic allocation of resources and maximize intervention impact at a district level, a methodology utilizing demographic and epidemiologic inputs was developed by the Ministry of Health and CDC to identify priority districts based on estimated unmet need for adult ART. From January 2013 to June 2014 prioritized districts with more than 1,000 adults in need of ART received enhanced support for HIV service scale-up and quality improvement. The unmet need analysis was repeated by the USAID- and PEPFAR-funded Health Policy Project in July 2014 using updated model inputs to determine changes to prioritization results. A description of the methodology and a comparison between the two analyses is presented.
Methods: Regional Spectrum results for adult ART eligibility were disaggregated provincially through application of a relative weighting system generated via census projections and HIV prevalence estimates from the most recent AIS. Eligibility was further disaggregated to the district level by applying a similar weighting system using ANC HIV prevalence available via routine program data. Program records pertaining to adults active in ART were compared with district eligibility to estimate unmet need.
Results: Priority districts with adult unmet need >1,000 were targeted for intensified intervention as part of the national Acceleration Plan. The original 2012 analysis detected 69 priority districts while the follow-up analysis in 2014 found 42—a decrease of 39.1%. Eight of the districts prioritized in the follow-up analysis were new and only three remained in the top ten in both analyses.



[ART Scale Up Priority Districts, 2012 & 2014]

Conclusions: Absolute unmet need for adult ART decreased between 2013 and 2014, suggesting that district prioritization and strategic resource allocation may be an effective approach to continued ART scale-up. More research and policy analysis are required to determine what factors contributed to the reduction in unmet need in the districts not prioritized in the follow-up analysis. Finally, the identification of eight new priority districts in the follow-up analysis highlights the need for a better understanding of prioritization effects in non-priority districts.

PUB034

Highlighting the burden of data capture and reporting associated with provision of HIV/AIDS health services in Uganda

R. Baryamutuma[1], C. Kyomugisha[1], E. Kansiime[2], I. Ssebuliba[2], S. Muhumuza[2], E. Akello[2], R. King[3], K. Lindan[3], W. Bazeyo[4]
[1]Makerere University, College of Health Sciences, School of Public Health, EPI and BIO, Kampala, Uganda, [2]Makerere University, College of Health Sciences, School of Public Health, Kampala, Uganda, [3]University of California San Fransisco, San Fransisco, United States, [4]Makerere University, College of Health Sciences, Kampala, Uganda
Presenting author email: kabacwezi@yahoo.com

Background: Access to quality data is important for the successful implementation of HIV/AIDS programs. Nonetheless, the burden of data capture and reporting associated with the provision of HIV services is not known. We present the total number of tools, indicators, reports and data sources for the HIV/AIDS program in Uganda and their implications.
Methods: We conducted a desk review of the National Management Information System in April 2015 to establish the total number of registers used to capture routine data for HIV/AIDS programs and counted the reports, frequency of reporting, indicators and data sources for HIV related data
Results: In total there are 26 registers/tools used to collect routine data at health facilities for different HIV/AIDS programs, as follows; HIV counselling and testing: 4 (HCT client card, HCT register, HIV test kits, Daily consumption log and triplicate referral booklet), Pre-ART and ART: 5 (HIV care/ART card, Pre-ART register, ART register, Appointment book and the integrated Nutrition register), Safe male circumcision: 3 (safe male circumcision card, safe male circumcision client form and safe male circumcision register). Early Infant diagnosis: 2 (Exposed infant card and register), Medicines and supplies: 2 (ARV dispensing log and stock card) and laboratory monitoring: 2 (laboratory test register and EID dispatch booklet). Other registers where HIV data is collected include; Maternity, ANC, post-natal, TB, post exposure prophylaxis and OVC. Although the registers are longitudinal in nature, a new patient not yet on ART or transferring in from another clinic, health workers fill an average of 120 fields at first visit. Regarding reporting and indicators, there are three main reports: weekly report with 9 indicators from one data source, monthly report with 55 indicators from 10 data sources and the Quarterly report with 71 indicators from 7 data sources.
Conclusions: There are many data collection tools, variables, reports, indicators and data sources that health workers have to work with. This increases workload for health workers with implications not only on quality of data but also services provided. The MOH should reduce the number of tools and indicators reported through merging and getting some data through evaluations.

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