

Pre-exposure HIV prophylaxis, PrEP - recent Global trials

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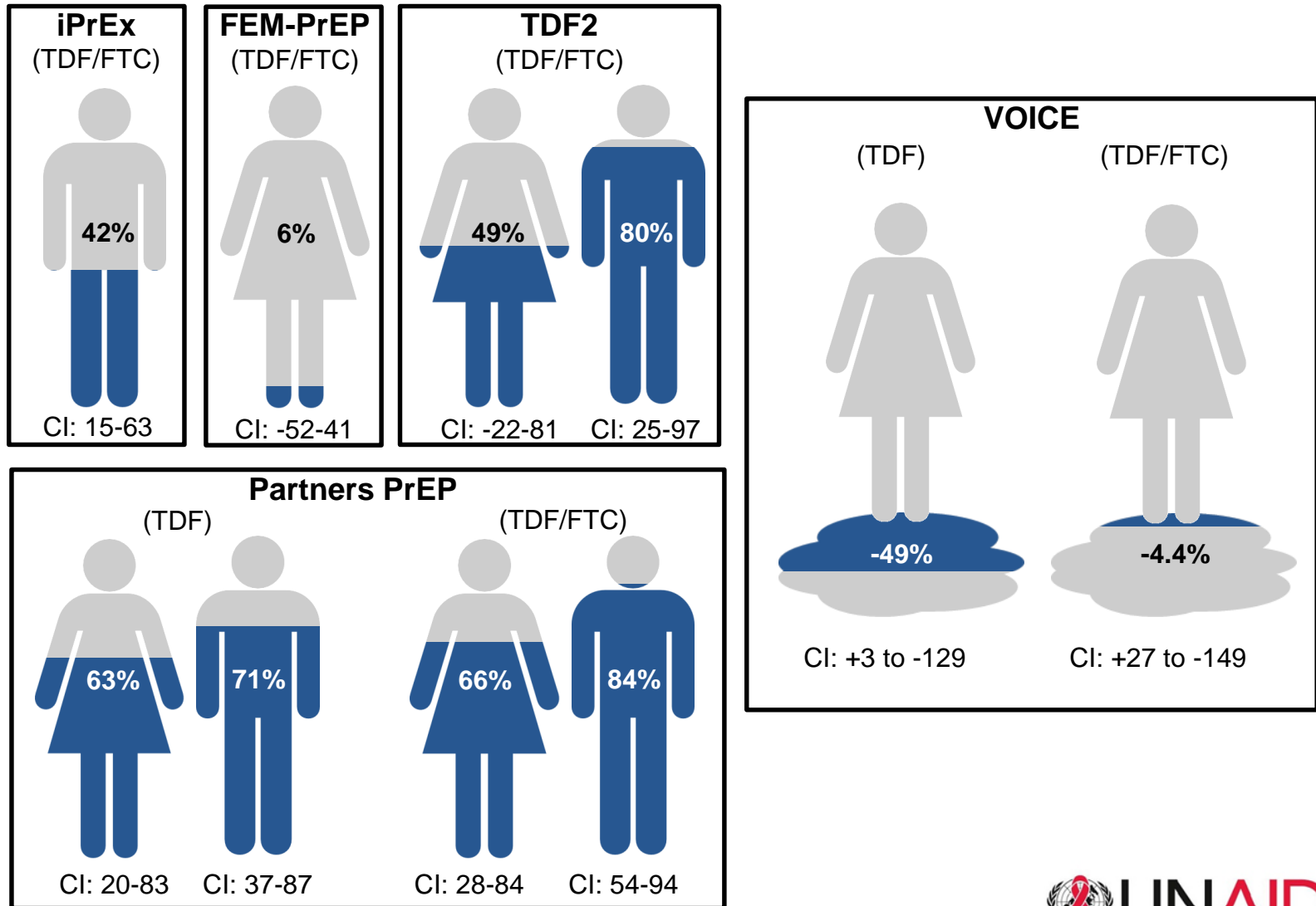
What is PrEP?

PrEP is the use of antiretroviral medication containing tenofovir to prevent HIV infection.

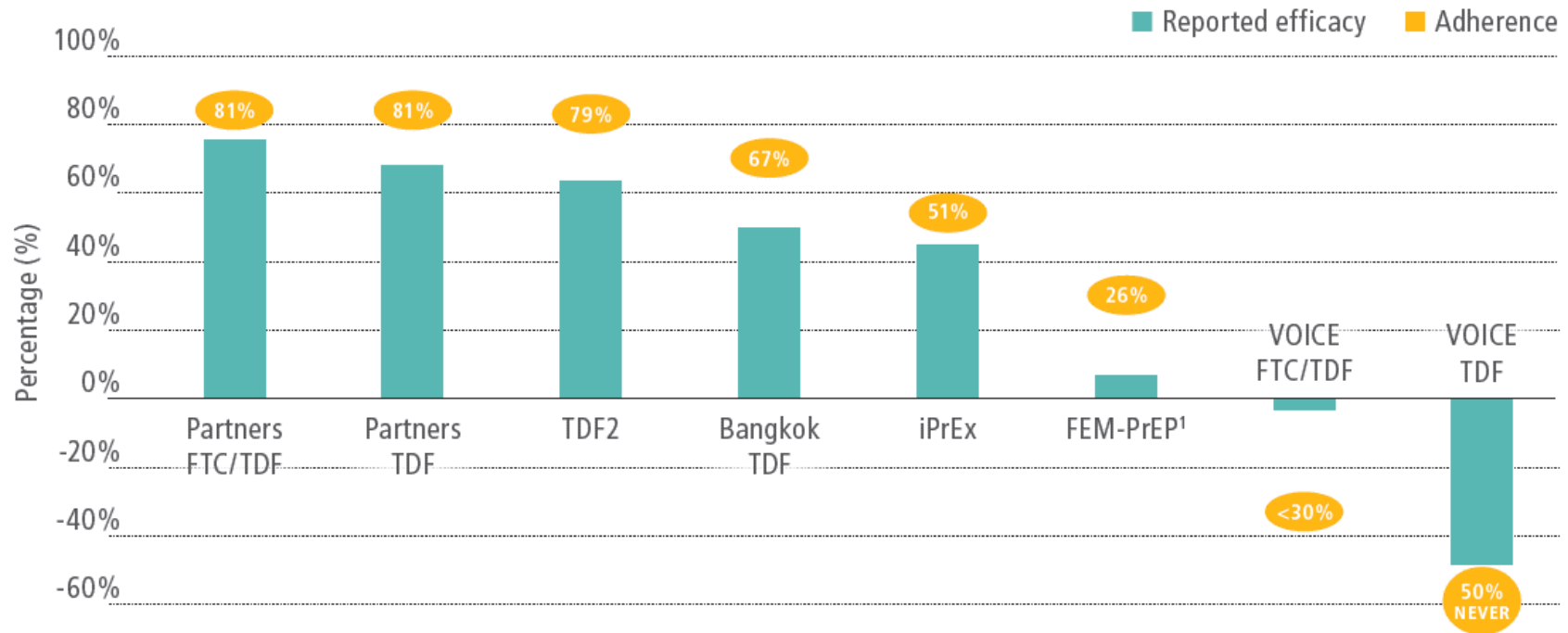
PrEP is for people who are **HIV-negative**, during periods of time when they are **at substantial risk** of HIV exposure and **not consistently using other prevention methods**, such as condoms and lubricants.

PrEP that is being rolled-out now is daily oral tenofovir (TDF 300mg) with or without emtricitabine (FTC 200mg)

Effectiveness in Clinical Trials

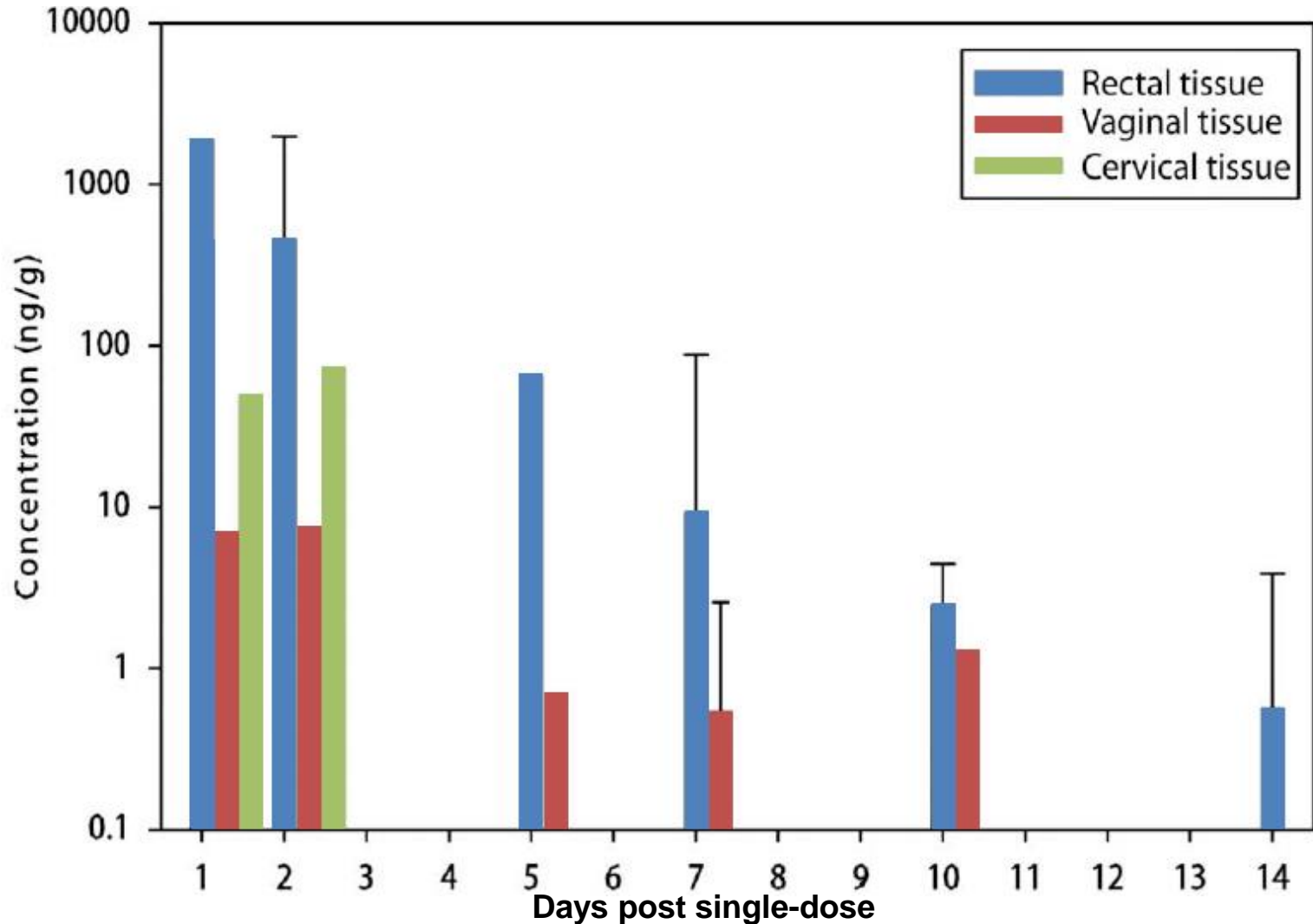


PREP works, if taken!



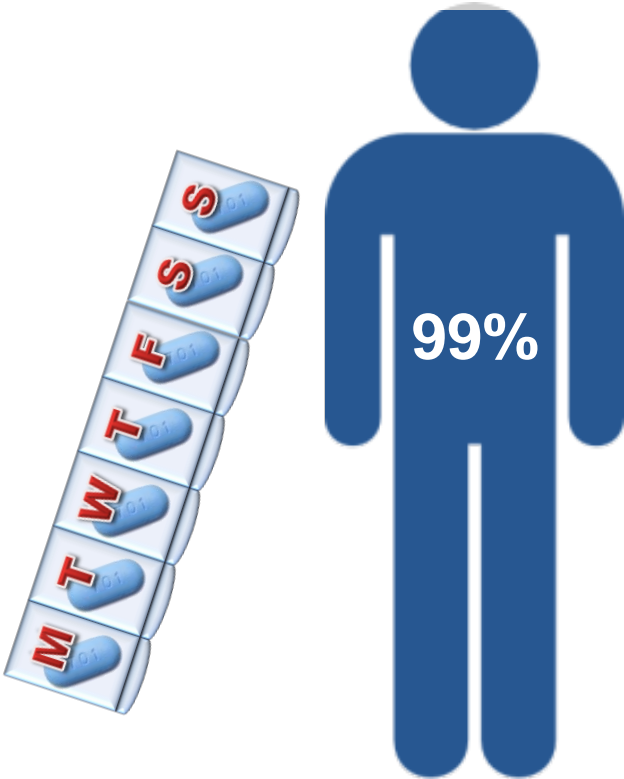
¹ 26% over two visits, 38% maximum at one visit.

TDF Concentrates 10-100x More in Rectal Tissue than in Cervico-vaginal Tissues



Maximizing the Potential Effectiveness

TDF/FTC (7x/week)

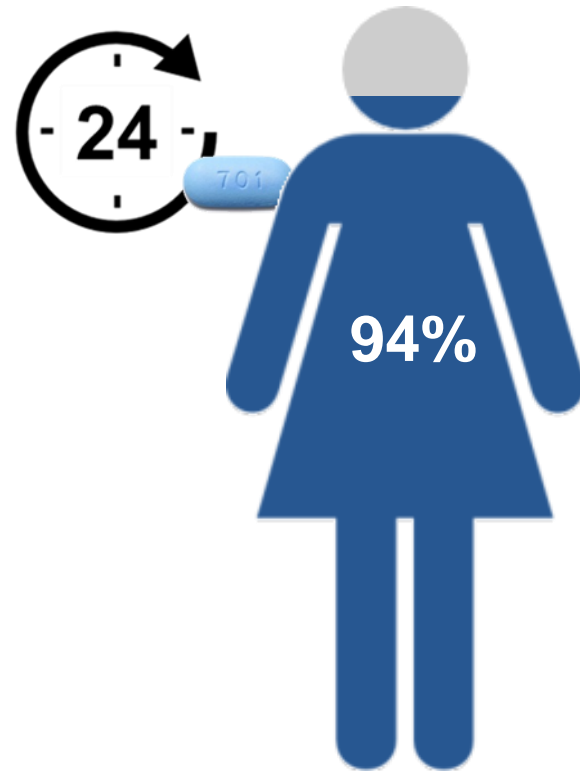


CI: 96 - 99

**Some adherence forgiveness
with retained protection**

Anderson P *et al*, *Sci Transl Med*. 2012.

TDF/FTC (~1x/24^h)



CI: -17 - 100

**6-7 doses per week likely
required**

Donnell D *et al*, *JAIDS*. 2014.
Cottrell ML *et al*, *R4P*, 2014.



ipergay

ANRS

Intervention Préventive
de l'Exposition aux Risques
avec et pour les Gays

www.ipergay.fr

Study Design

Double-Blinded Randomized Placebo-Controlled Trial

- HIV negative high risk MSM
- Condomless anal sex with ≥ 2 partners within 6 m
- eGFR > 60 mL/mn

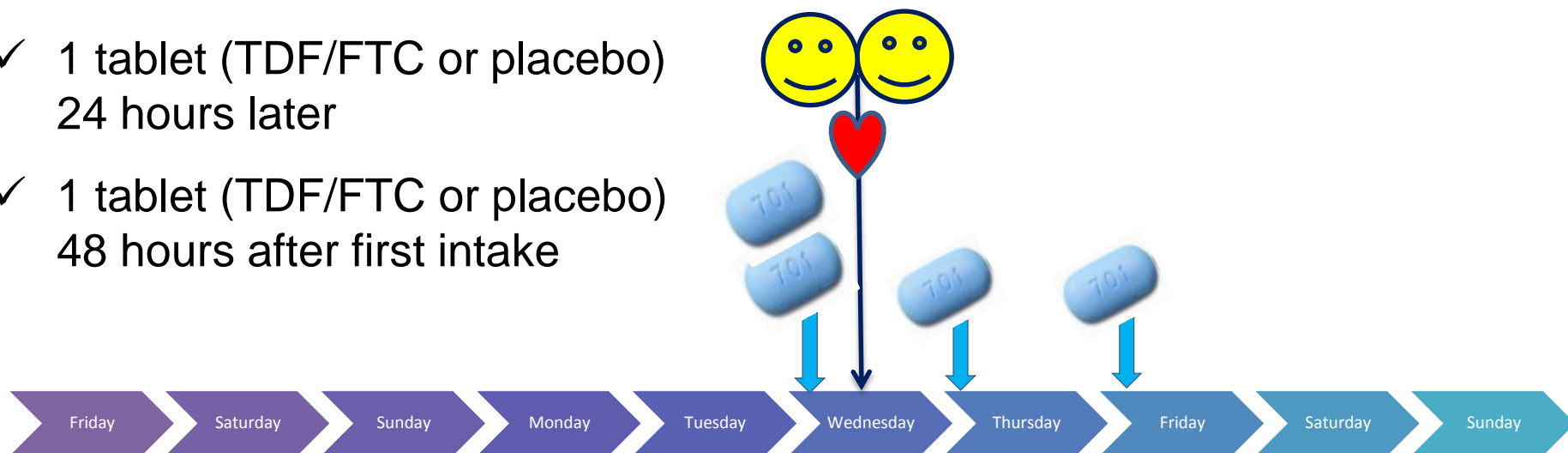
Full prevention services*
TDF/FTC before and after sex

Full prevention services*
Placebo before and after sex

- * Counseling, condoms and gels, testing and treatment for STIs, vaccination for HBV and HAV, PEP
- End-point driven study : with 64 HIV-1 infections, 80% power to detect a 50% relative decrease in HIV-1 incidence with TDF/FTC (expected incidence: 3/100 PY with placebo)
- Follow-up visits: month 1, 2 and every two months thereafter

Ipergay : Event-Driven iPrEP

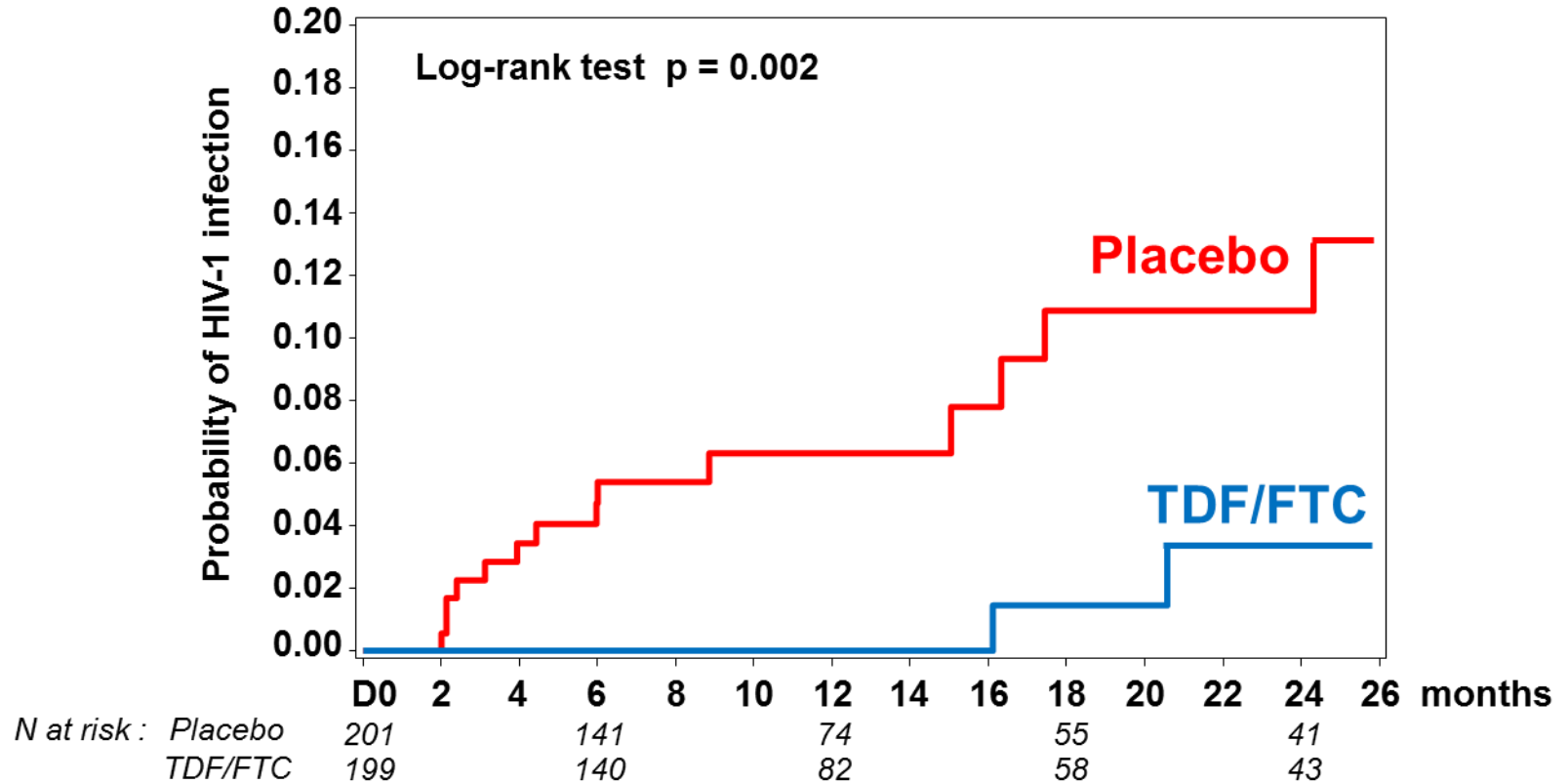
- ✓ 2 tablets (TDF/FTC or placebo)
2-24 hours before sex
- ✓ 1 tablet (TDF/FTC or placebo)
24 hours later
- ✓ 1 tablet (TDF/FTC or placebo)
48 hours after first intake





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KM Estimates of Time to HIV-1 Infection (mITT Population)



Mean follow-up of 13 months: 16 subjects infected

14 in placebo arm (incidence: 6.6 per 100 PY), **2 in TDF/FTC arm** (incidence: 0.94 per 100 PY)

86% relative reduction in the incidence of HIV-1 (95% CI: 40-99, $p=0.002$)

NNT for one year to prevent one infection : 18

PROUD Pilot



GMSM reporting UAI last/next 90days; 18+;
and willing to take a pill every day

Randomize HIV negative MSM
(exclude if treatment for HBV/Truvada contra-indicated)

Risk reduction includes
Truvada **NOW**

Risk reduction includes
Truvada **AFTER 12M**

Follow **3 monthly** for up to 24 months

Main endpoints in Pilot: recruitment and retention
From April 2014: HIV infection in first 12 months

PrEP interruptions for medical event

- **PrEP interrupted** by 28/545 participants (**both groups**) but only **13** had events considered related to drug:
 - nausea alone or with diarrhoea/abdominal pain/aches and fatigue (n=5)
 - decline in creatinine clearance (n=2)
 - headache (n=2)
 - joint pain, with fatigue in one case (n=2)
 - sleep disturbance (n=1)
 - flu-like illness (n=1)
- **PrEP re-started** by 11 of 13 participants above

HIV Incidence

Group	No. of infections	Follow-up (PY)	Incidence (per 100 PY)	90% CI
Overall	22	453	4.9	3.4–6.8
Immediate	3	239	1.3	0.4–3.0
Deferred	19	214	8.9	6.0–12.7

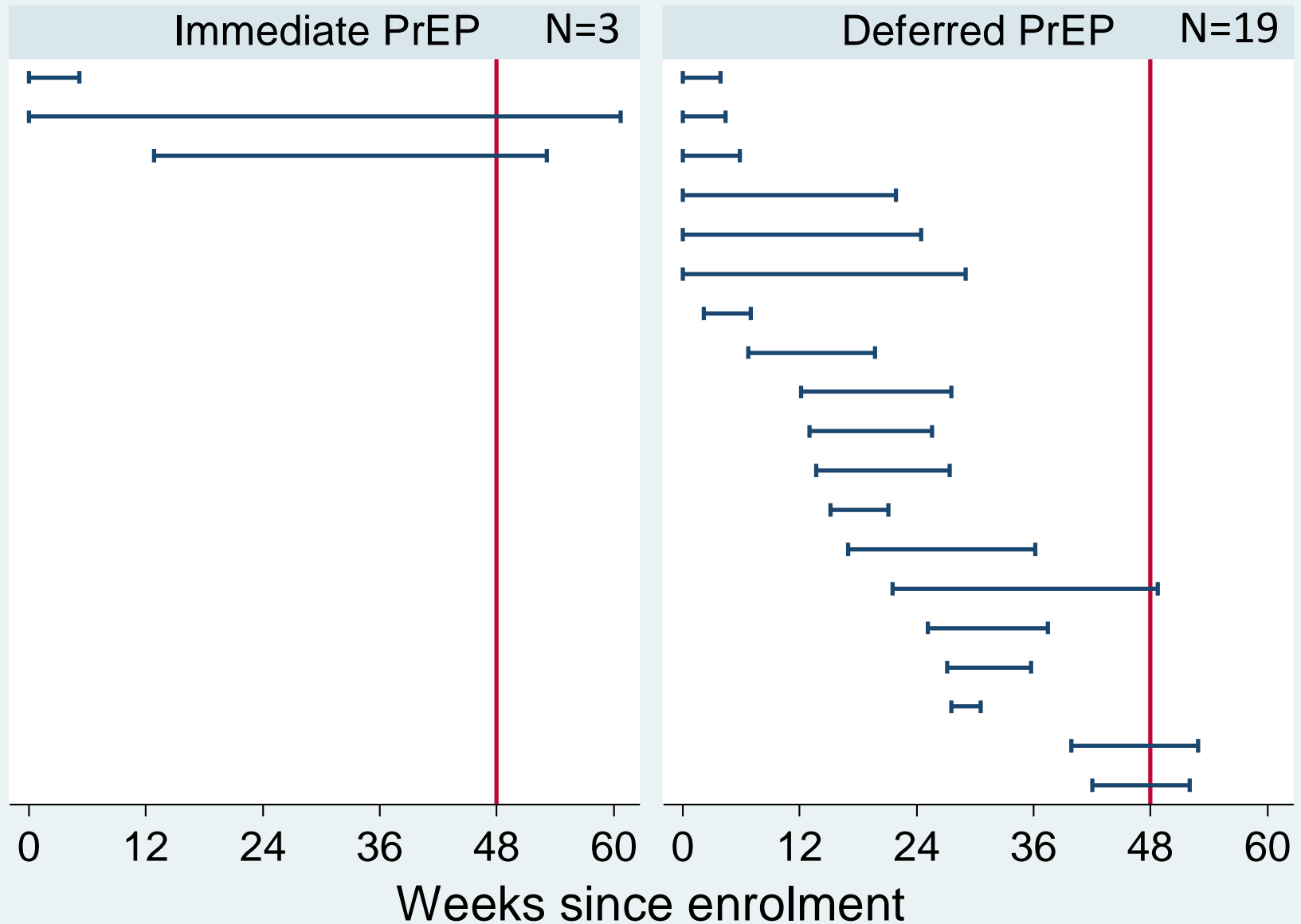
Efficacy =86% (90% CI: 58 – 96%)

P value =0.0002

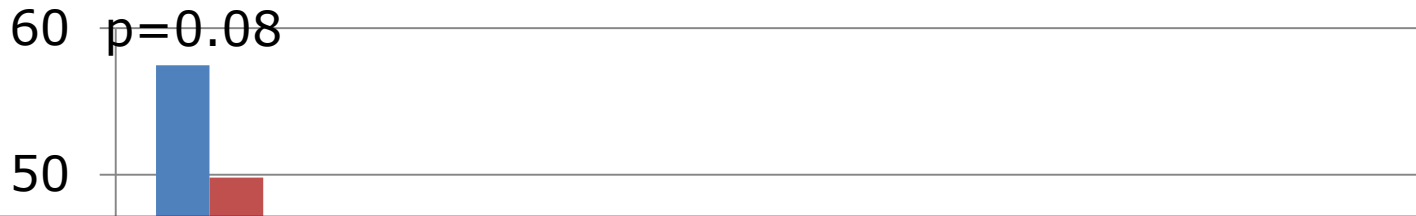
Rate Difference =7.6 (90% CI: 4.1 – 11.2)

Number Needed to Treat =13 (90% CI: 9 – 25)

Individual incident HIV infections

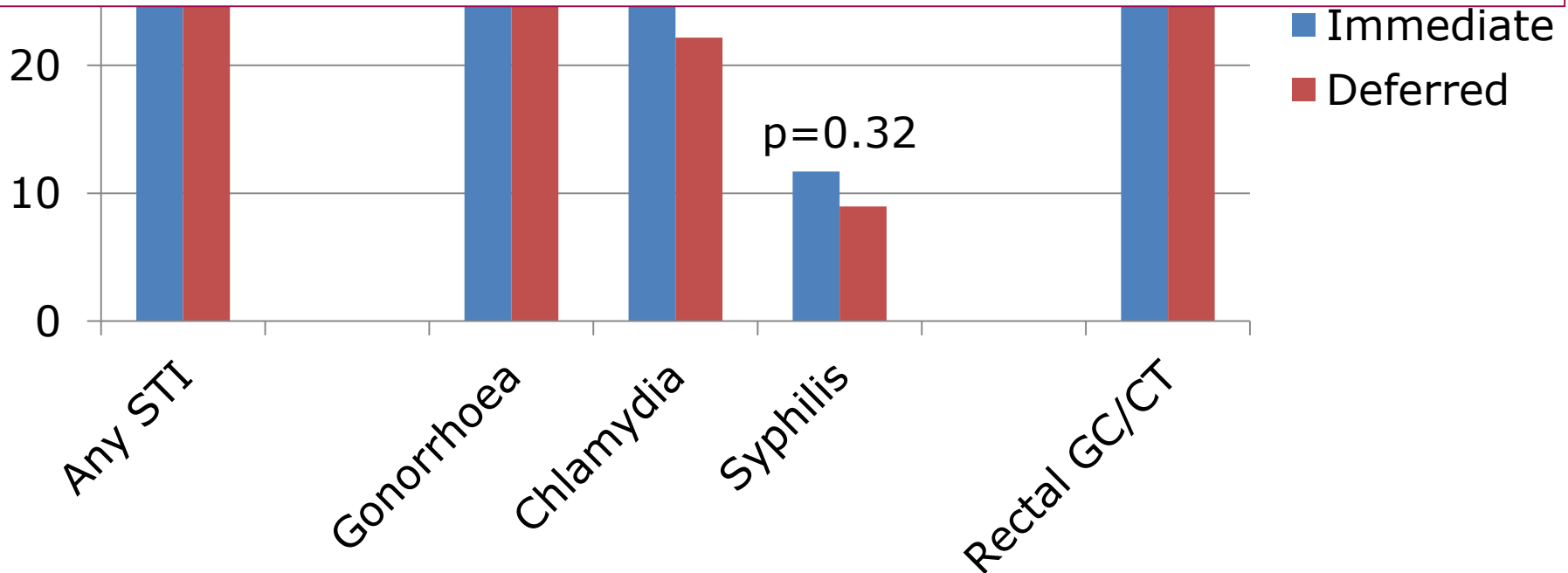


STIs



Caveat

Number of screens differed between the groups:
e.g. Rectal gonorrhoea/chlamydia
974 in the IMM group and 749 in the DEF



Reported sexual behaviour (preliminary)

Anal sex partners in last 90 days

BASELINE n=539

	Immediate Median (IQR)	Deferred Median (IQR)
Total number of partners	10.5 (5-20)	10 (4-20)
Condomless partners, participant receptive	3 (1-5)	2 (1-5)
Condomless partners, participant insertive	2.5 (1-6)	3 (1-7)

Anal sex partners in last 90 days

MONTH 12 n=349

	Immediate Median (IQR)	Deferred Median (IQR)
Total number of partners	10 (3-24)	8 (3-15)
Condomless partners, participant receptive	3 (1-8)	2 (1-5)
Condomless partners, participant insertive	3 (1-8)	3 (1-6)

Safety: Well tolerated

- **Start-up syndrome**
 - 1-18.5% with nausea, vomiting ± dizziness
- **Renal safety**
 - 0.2% Grade 2-4 elevations in creatinine among 5469 participants randomized to TDF/FTC
- **Bone safety**
 - 0.4 to 1.5% loss of BMD across total hip, spine, FN and trochanter
 - Return towards baseline with withdrawal
 - Not associated with increased fracture risk
- Longer term follow-up in diverse populations needed

Grant RM, *et al.* N Engl J Med. 2010.

Baeten JM, *et al.* N Engl J Med. 2012.

Thigpen M, *et al.* N Engl J Med. 2012.

Van Damme L, *et al.* N Engl J Med. 2012.

Marrazzo JM *et al.* N Engl J Med. 2015.

Solomon MM *et al.* AIDS. 2014.

Liu AY *et al.* PLoS One. 2011.

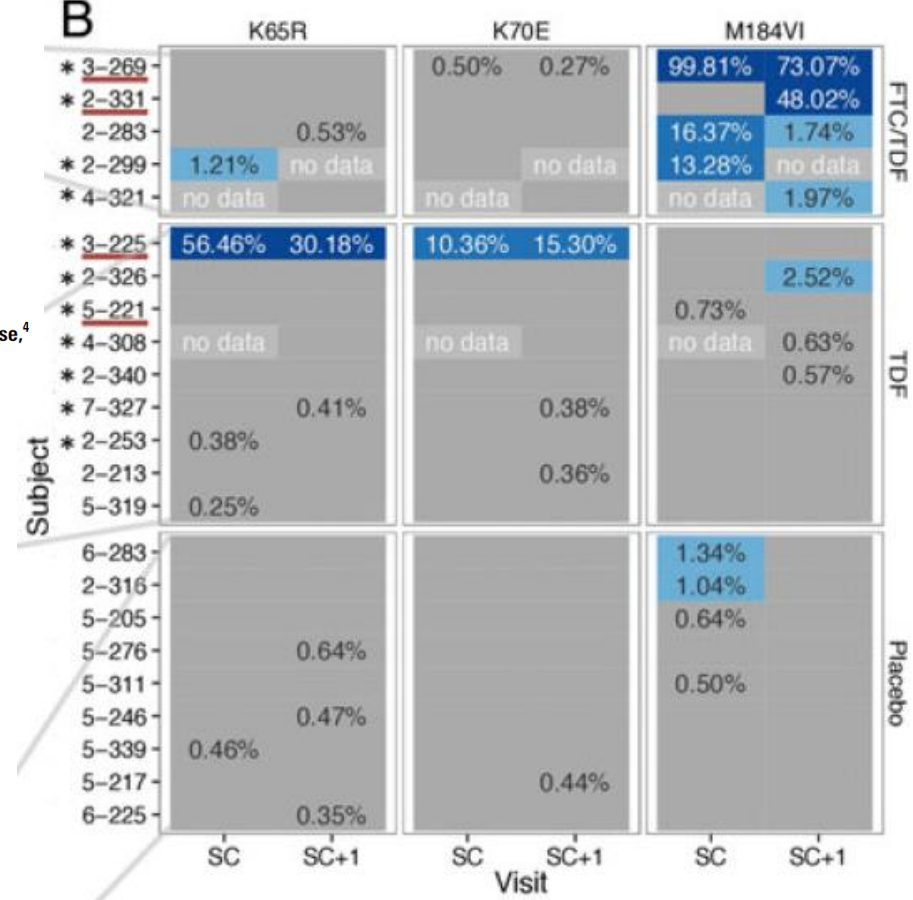
Kasonde M *et al.* PLoS One. 2014.

Risk of Drug Resistance Among Persons Acquiring HIV Within a Randomized Clinical Trial of Single- or Dual-Agent Preexposure Prophylaxis

Journal Inf Dis 2015

Dara A. Lehman,^{1,4} Jared M. Baeten,^{4,5,6} Connor O. McCoy,² Julie F. Weis,¹ Dylan Peterson,¹ Gerald Mbara,^{1,4} Deborah Donnell,^{3,4} Katherine K. Thomas,⁴ Craig W. Hendrix,^{8,9,10} Mark A. Marzinke,^{8,9,10} Lisa Frenkel,⁷ Patrick Ndase,⁴ Nelly R. Mugo,^{4,11} Connie Celum,^{4,5,6} Julie Overbaugh,^{1,2} and Frederick A. Matsen²; the Partners PrEP Study Team^a

- 4747 couples randomised - FTC/TDF:TDF:Placebo
- 122 new HIV infections – 25:39:58
- 9/121 cases with >1% resistance detected (5:2:2)
- 18/122 were RNA +ve at enrollment, 12 on PrEP
- 3/12 were resistant
- 3 other cases of resistance on FTC/TDF and 1 on TDF – probably not related
- Estimated that 74-123 HIV infections averted



- Resistance can occur if HIV infection occurs and levels of PrEP are still high enough (good adherence means no HIV; bad adherence means no PrEP)
- If PrEP is well organised, the prevention of HIV and therefore of resistance will outweigh the risk of resistance due to PrEP
- Better adherence in less controlled trials and demonstration projects is encouraging
- Excluding people who may be acutely infected is challenging but important

PrEP works!

When taken correctly, PrEP prevents more than 90% of new HIV infections.

When PrEP is *chosen* as an HIV prevention strategy adherence is seen to be high.

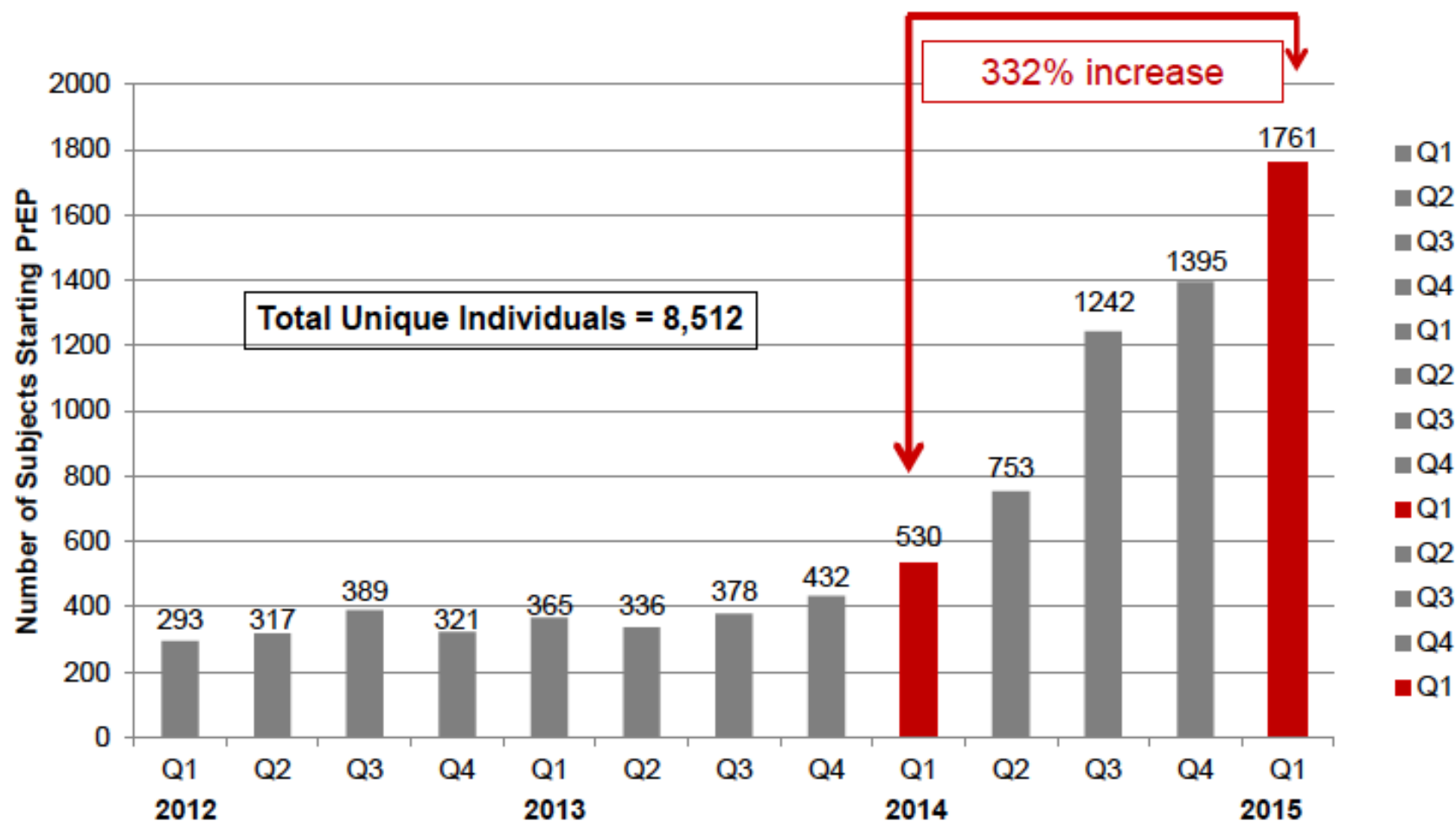
PrEP should always be part of a broader combination prevention discussion that responds to the individual's HIV prevention needs

PrEP is safe and well tolerated. Few drug-drug interactions

No evidence in clinical trials of risk compensation, but good STI services needed by people who are at substantial risk of HIV

PrEP can *reduce* drug resistance

New PrEP Starts per Quarter



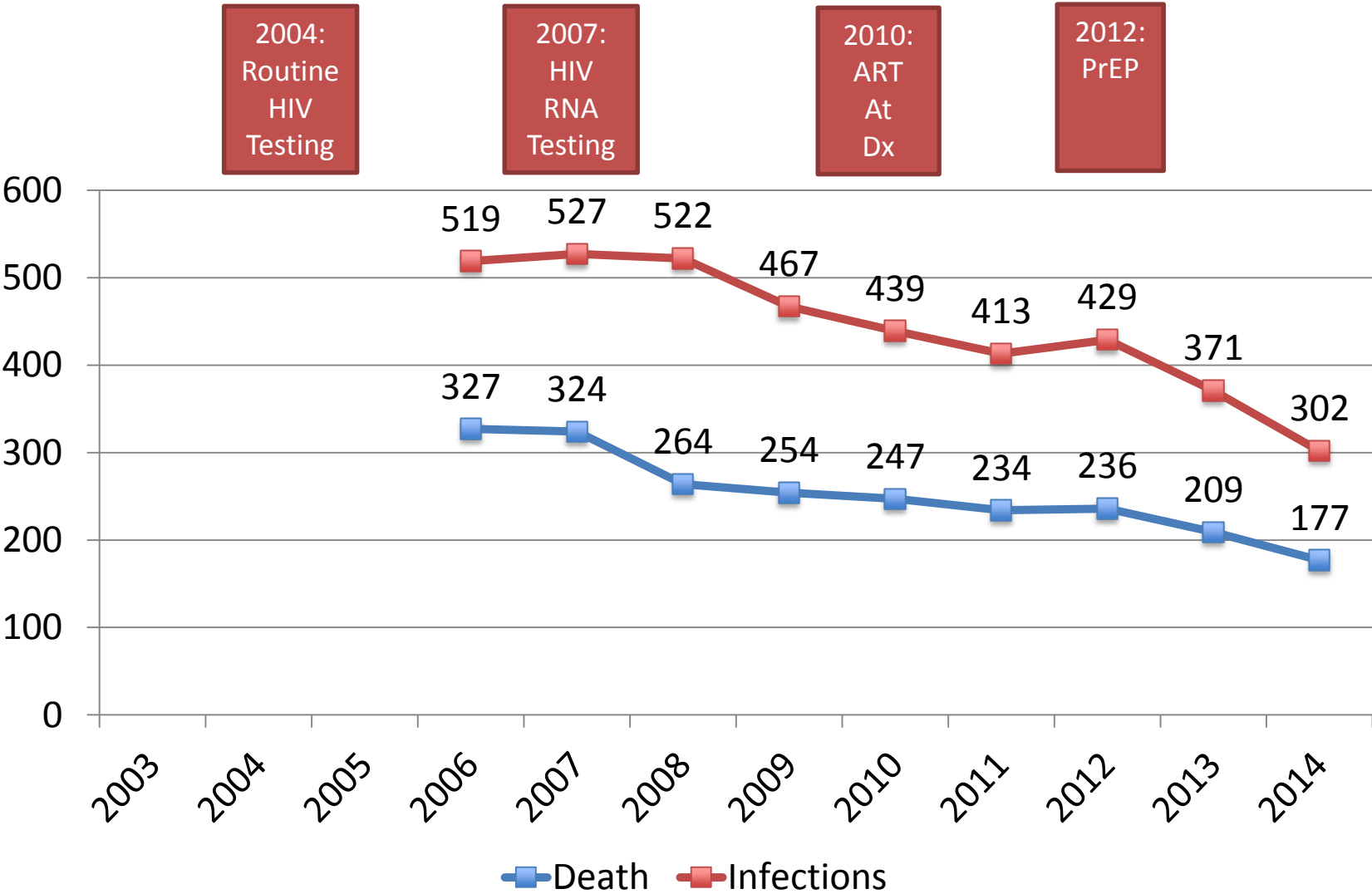
IMS National Prescription Database accounts for approx. 39% of all TVD prescriptions

PrEP Use by Sexual Practices in MSM: San Francisco, 2014

Condomless AI Partners last 6 months	Street Survey (% EVER on PrEP)	NHBS (% ANY PrEP In 12 mos)	SFCC (% CURRENT PrEP Use) ¹
0	9%	3%	8%
1	10%	4%	10%
2	11%	17%	16%
3-5	25%	30% ²	33%
6 or more	63%		46%
% on PREP	15.5%	10.1%	11.2%⁴
No. on PrEP		5,059	

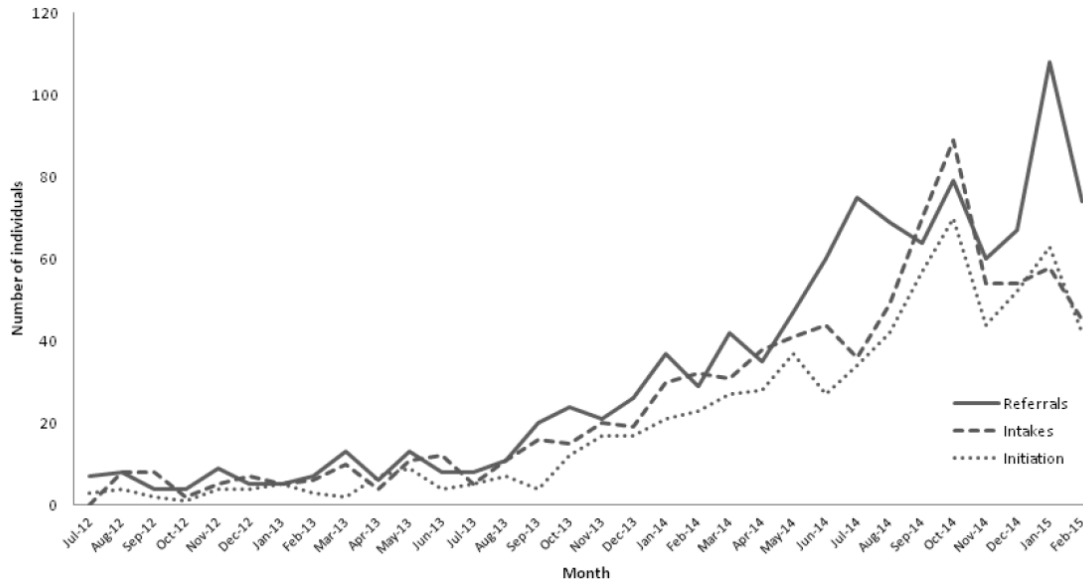
1. SFCC asked specifically about condomless receptive anal intercourse partners.
2. NHBS collected detailed information on no more than 5 partners.
3. Percent using any PrEP in the past 12 months x 50,000 HIV negative population size.
4. Includes clients with missing data regarding ncRAI.

Epidemic Trends in San Francisco



Adapted from SF DPH Health Commission Report, July 7, 2015

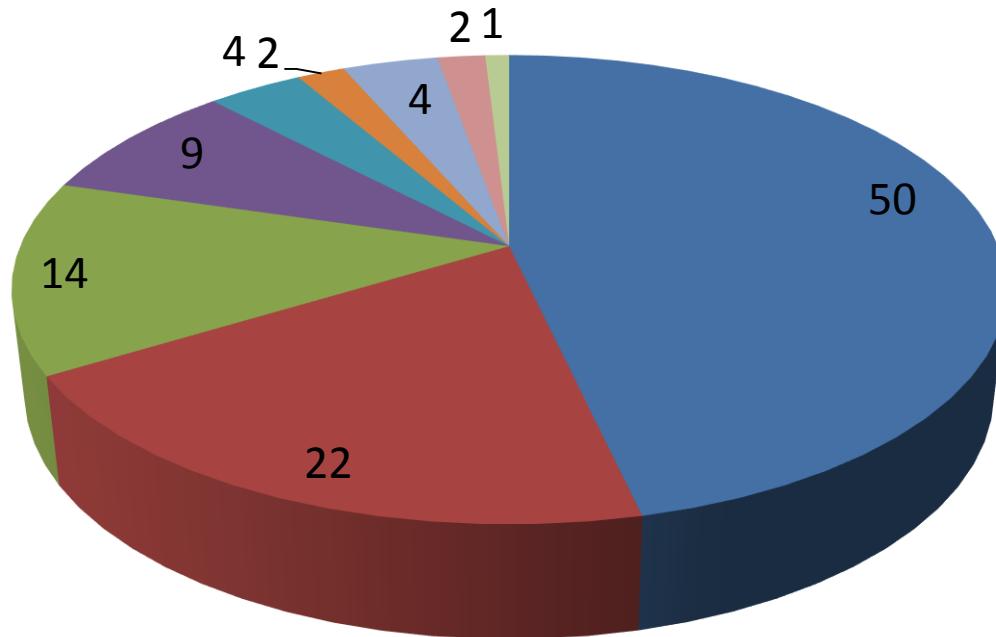
Kaiser Permanente study (Jonathan Volk et al. Clin Inf Dis 2015)



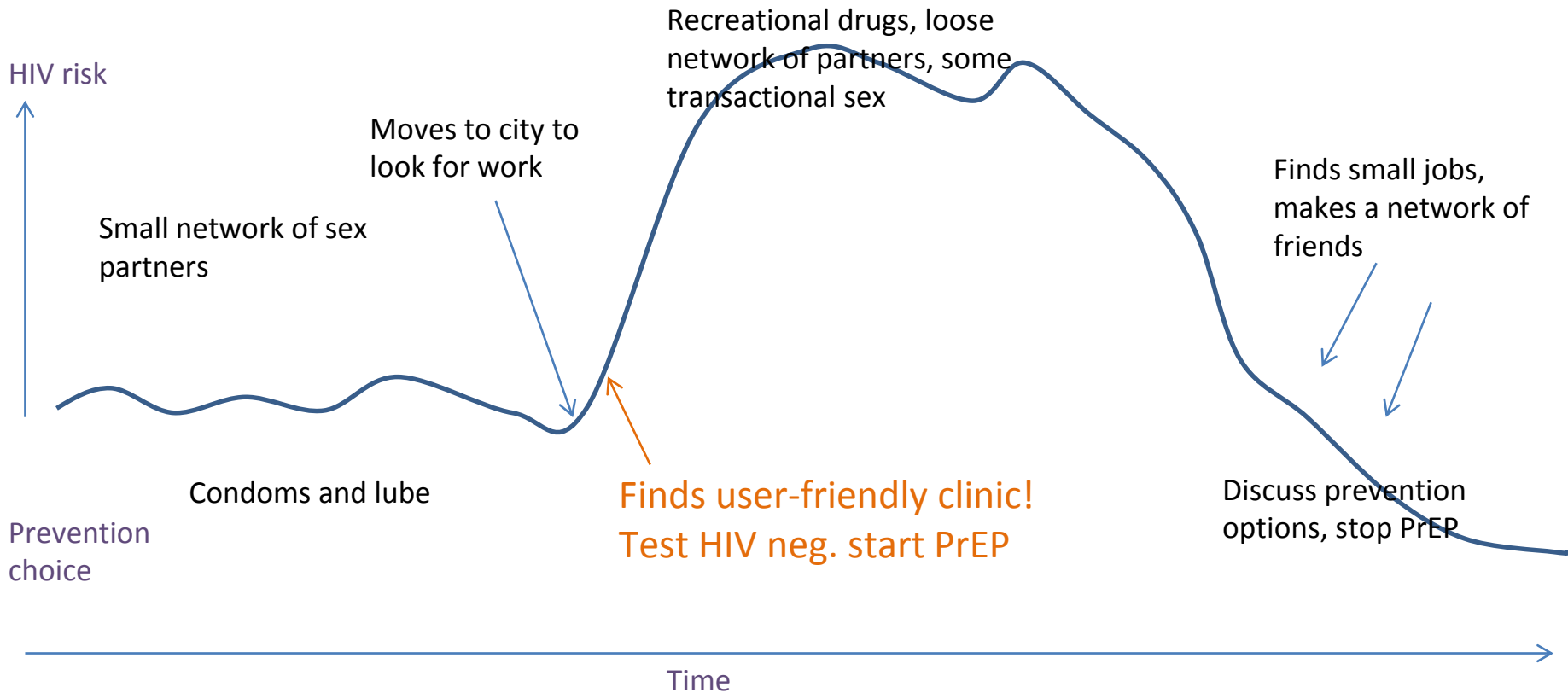
- 801 people seen at clinic
- Of whom, 657 started PrEP and were followed for 388 pyears of follow-up
- Zero new HIV infections!
- STIs were common

Reasons not to start PrEP

- Low HIV risk
- Cost
- Follow-up
- Other prevention strategy
- Worried about side-effects
- Worried about behaviour
- Acute HIV infection
- Renal
- Bone







PrEP is for people at substantial risk of HIV infection and not forever



Predicting peaks in HIV risk

Consider adding PrEP to prevention choice to cover times of increased risk, for example

-  Sexual debut, including 'coming out' or change in sexuality
-  Moving to a place with no social network
-  Relationship breakdown
-  Leaving home

Depends on good information and feedback to those at risk and potentially at risk.

Acknowledgements

- Raphael Landowitz
- Sheena McCormack
- Jean-Michel Molina
- Bob Grant
- Rosalind Coleman
- UNAIDS and WHO PrEP groups

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