

ENDING AN EPIDEMIC: PRIORITIZING PEOPLE WHO INJECT DRUGS IN HCV ELIMINATION EFFORTS

BACKGROUND

Fuelled by political will, resources for cost-effective, evidence-based prevention programmes and revolutionary advances in hepatitis C virus (HCV) treatment, momentum is building towards halting a deadly global epidemic. Worldwide, an estimated 71 million people are living with hepatitis C, a blood-borne virus that infects liver cells [1]. Without treatment, HCV can progress to liver cirrhosis, liver failure and liver cancer. In 2015 alone, 400,000 people died from these complications globally [2].

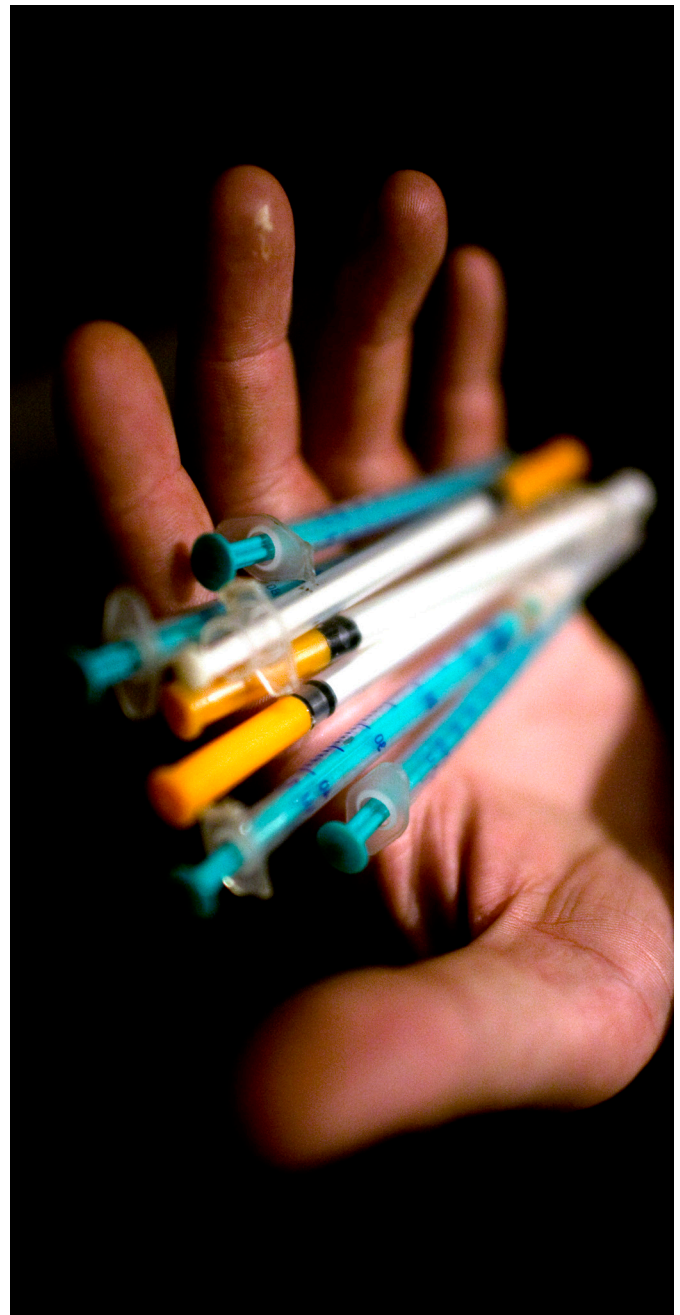
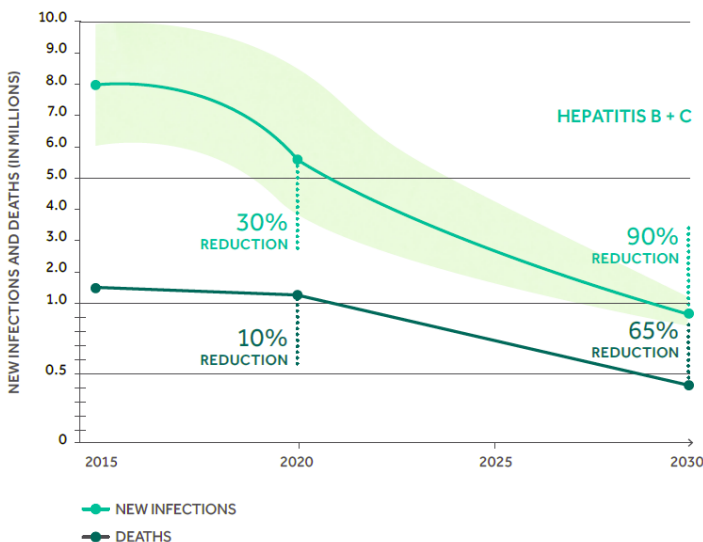
Nearly a quarter of the world’s new HCV infections occur among people who inject drugs (PWID) [2]: lack of access to sterile needles, syringes and other injection equipment renders them highly vulnerable to HCV. Legal and structural barriers also greatly increase HCV risk among PWID. Worldwide, more than 50% of the 15.6 million PWID are HCV antibody positive [3,4]. Without urgent, strategic and measurable action that includes PWID, HCV will continue to inflict a staggering, and increasing, burden of preventable illness and death among families, communities and countries. The World Health Organization (WHO) has described it as a “viral time bomb”.

HIV has demonstrated that effective treatment, while essential, will not conquer an epidemic without a robust community response, resource mobilization and political will. As with HIV, therapeutic advances have created an opportunity to halt and reverse the HCV epidemic. HCV treatment has been transformed by direct-acting antivirals (DAAs), highly effective and tolerable oral drugs that cure more than 95% of people in eight to 12 weeks. Just five years ago, the standard of care was interferon based treatment, which had suboptimal effectiveness, debilitating side-effects, and was unsuitable for scale up in

resource-limited settings. DAAs have made HCV elimination a tangible goal – and the world has signed on to do so. At the World Health Assembly in May 2016, 184 Member States adopted the WHO Global Health Sector Strategy (GHSS) on viral hepatitis [5].

In addition to mortality and incidence reduction targets, the GHSS includes service delivery targets so that countries can monitor their progress and maximize their investment in individual and public health by deploying prevention and treatment – both of which will be required to achieve the WHO 2030 elimination targets.

Figure 1: WHO Global Health Sector Strategy targets for reductions in viral hepatitis incidence and mortality [6]





HARM REDUCTION

“The persistence of unsafe injection-linked HIV and HCV transmission that could be stopped with proven, cost-effective measures remains one of the great failures of the global responses to these diseases.”

Joanne Csete, Adeeba Kamarulzaman, Michel Kazatchkine, et al; Report of the Johns Hopkins – Lancet Commission on Drug Policy and Health. 2016

Ongoing access to HCV prevention is essential to HCV elimination since people become susceptible to HCV re-infection after they have been cured. Despite this, less than 1% of all people who inject drugs live in countries where high coverage of evidence-based harm reduction interventions and programmes are available [7], and access to them is endangered by funding cuts, Global Fund transition plans and other donor withdrawal.

“I don’t see a single drug user anywhere in the world that gets enough syringes. What is one syringe going to stop?”

Loon Gangte, Founder of the Delhi Network of Positive People and Regional Coordinator for South Asia at the International Treatment Preparedness Coalition

High-coverage needle and syringe programmes (NSPs) – defined as 100% of injections with a new needle/syringe – reduce HCV risk by 56%. Combining high-coverage NSPs with high-coverage opioid substitution therapy (OST) [8] – >40 recipients per 100 PWID [9] – reduces the risk for HCV infection by 76% [10].

NSPs are remarkably cost effective, with an annual cost ranging from US\$23 to \$71 per person [1]. A recent study estimated that Australia’s NSPs reduced the incidence of HIV by 34-70%, and HCV by 15-43% between 2000 and 2010, while saving AU\$70-220 million in healthcare costs [12].

TREATMENT AS PREVENTION

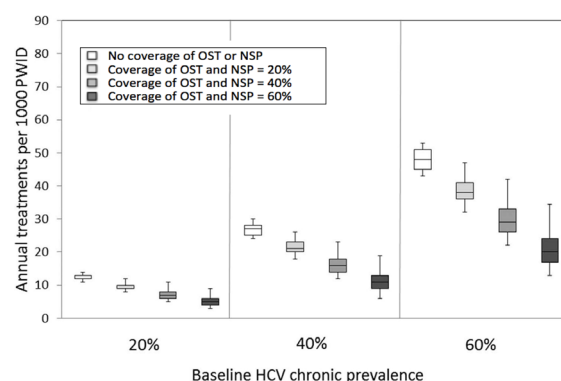
“HCV treatment has the power to cure an individual and break the transmission chain. Providing treatment and harm reduction to PWID is the key to reducing HCV incidence and achieving elimination.”

Natasha Martin, Associate Professor, Division of Infectious Diseases and Global Public Health, Department of Medicine, University of California San Diego

Countries can also deploy HCV treatment as prevention (TasP). The success of TasP among PWID relies on the extent of treatment coverage. Low-level coverage will not reduce prevalence enough to prevent many new infections/re-infections. Higher treatment coverage could dramatically reduce HCV prevalence and, thereby, the incidence of new infections and re-infections [13].

Investment in HCV and population impact can be maximized by countries through combining treatment and prevention interventions (to prevent infection and re-infection). TasP is more effective with high-coverage NSP and OST than by itself, and combination prevention strategies are likely needed in most settings, particularly in areas with high HCV burden among PWID [14].

Figure 2: Combination interventions required to reduce



incidence among PWID by 90%, 2017-2030 [15]

ACCESS BARRIERS

“The data is in, and is conclusive: people who inject drugs adhere to DAA treatment and are cured at extremely high rates. The challenge is to remove drug use-based restrictions on DAA access and to build a harm reduction foundation for engagement with drug users, HCV testing and linkage to care, and reducing risk of HCV re-infection.”

*Greg Dore, Professor and Program Head, Viral Hepatitis Clinical Research Programme,
Kirby Institute, NSW Australia*

The obstacles that limit access to DAAs differ across low-, middle- and high-income settings – except for the arbitrary legal, structural and treatment barriers facing PWID, which exist in all countries. These must be addressed to achieve elimination goals.

High prices are often used as a justification for withholding treatment from PWID, but in countries where they are available, prices for generic DAAs are dropping – and they could be profitably mass produced for less than US\$50 per treatment course [15]. Research on, and implementation of simple and affordable rapid tests and one-step diagnostics, including core antigen testing and finger-stick testing for viral load, could facilitate diagnostic scale up [16,17].

Table 2: HCV treatment access barriers by country income classification [1,18]

INCOME CLASSIFICATION	N (%) OF GLOBAL HCV INFECTIONS	DAA PRICE PER 12 WEEK TREATMENT COURSE	ACCESS STRATEGIES ⁱ	LOW DIAGNOSIS RATES, LIMITED OR NO ACCESS TO FREE SCREENING AND DIAGNOSTICS	LACK OF AND INADEQUATE DOMESTIC FUNDING ⁱⁱ	LEGAL AND STRUCTURAL BARRIERS (INCLUDING IMPLICIT AND EXPLICIT EXCLUSION AND ABSTINENCE CRITERIA)
Low-income	~6.9 million (~10%)	US\$720-780 (Rwanda)	Generic production (where there are no patents); patent opposition or rejection; voluntary licences	~0.5 million people diagnosed (~8%)	X	X
Lower-middle-income	~32.0 million (~47%)			~4.3 million people diagnosed (~13%)	X	X
Upper-middle-income	~17.0 million (~25%)	US\$6,255 (Brazil)	Patent opposition or rejection, compulsory licencing, voluntary licencing, bilateral negotiations with originator companies ⁱⁱⁱ	~3.1 million people diagnosed (~18%)	X	X
High-income	~12.9 million (~19%)	US\$31,500-51,000 (UK)	Patent opposition, non-transparent bilateral negotiations with originator companies	~5.6 million people diagnosed (~43%)	X	X

i. A number of different access strategies to expand access to DAA in low- to high-income settings exist for treatment advocates and countries [19].

ii. This is the case in most, but not all countries. Australia, Brazil, Egypt, Mongolia and Portugal are among the exceptions. Brazil has removed all restrictions to HCV treatment access, and is on track to reach the 2030 elimination targets [1]. Egypt is home to the world's highest HCV prevalence, and one of the most effective HCV treatment programmes. In 2006, Egypt created a National Committee for Control of Viral Hepatitis; between 2007 and 2016, 54 treatment centres were opened across the country. Once DAAs became available, Egypt negotiated with originator pharmaceutical companies to obtain price reductions. Gilead Sciences, the patent holder on sofosbuvir (SOF), lowered the price for a 3-month treatment course from US\$15,000 to \$900; BMS, the patent holder on daclatasvir (DCV), charged US\$750 for a 12-week course of DCV [21]. These prices dropped dramatically as Egypt rejected patents on SOF and DCV; locally produced generic versions are available for US\$150 (SOF) and \$22.50 (DCV) [1]. In 2017, Mongolia announced a plan to eliminate HCV by 2020. Nationwide screening and generic DAAs are available (the lowest price for a 12-week treatment course is US\$585), and treatment uptake has increased from 1,000 people in 2015 to 6,500 in 2016 [1].

iii. Bilateral negotiations with originator pharmaceutical companies are non-transparent, and countries are subject to monopolistic pricing schemes. However, some countries have negotiated deals with originator pharmaceutical companies, allowing them to provide unrestricted treatment access. Australia's government negotiated a risk-sharing agreement so that an uncapped number of people could be treated within five years for AU\$ 1 billion [22]. Portugal made a volume- based agreement, paying only when people are cured, regardless of their treatment duration [23].

BOX 1: COST CALCULATIONS

Affordability is a main concern for policy makers. Tools now exist to help them predict the cost of addressing hepatitis C, allocate adequate resources and assess the impact of these expenditures.

A WHO- and Unitaaid-supported cost-effectiveness calculator has been developed at Harvard's medical school; it is available at <http://tool.hepcccalculator.org/>. Policy makers can select a country and refer to its prices for diagnostics and DAAs. They can look at the economic burden to the healthcare system from HCV at different disease stages, comparing the total costs of treatment versus no treatment, and determine thresholds for cost effectiveness and cost savings.

The Institute of Health Sciences at Portugal's Catholic University has created a policy calculator to assess the outcome of overall and population-specific HCV elimination strategies, using 24 metrics (including civil society involvement, enabling legal frameworks, harm reduction programmes in prisons, screening, linkage to care and treatment, and social services). It is currently being expanded to include more countries. It is available at www.letsendhepc.com.

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Despite the 2016 WHO recommendation to prioritize PWID for HCV treatment [24], there are persistent system-, provider- and patient-level barriers for PWID [1]. A survey of clinicians attending the American Association for the Study of Liver Diseases (AASLD) annual conference reported that only 15% were willing to treat PWID for HCV [25]. Yet in clinical trials and in clinical practice, cure rates among people who used drugs before or during their DAA treatment were comparable to those among non-users [26,27,28]. Similarly, high cure rates among PWID were reported after DAA treatment delivered in a variety of settings, including outpatient multidisciplinary care (>95%) [29], at an NSP (91%) [30] and with OST (100%) [31,32].

The possibility of re-infection – which is often seen as an individual responsibility rather than a public health failure – is also used for justifying treatment rationing or ineligibility for PWID. It is hard to assess re-infection rates as they are directly related to access to NSPs and OST. Once PWID have been cured, they become susceptible to HCV re-infection and should be offered stigma-free access to prevention (which will eliminate any risk of re-infection), continued testing and eventual re-treatment.

BOX 2: HCV AND HIV

Globally, an estimated 2.4% of people living with HIV are HCV co-infected; they are six times more likely to have HCV than HIV-negative people [11]. HCV prevalence is much higher among people living with HIV who have injected drugs; nearly 83% of them are HCV co-infected [33]. HCV treatment is an urgent priority for people living with HIV because HIV increases the risk and rate of liver disease resulting from hepatitis C. People living with HIV/HCV co-infection are also at higher risk for liver-related and non-liver-related death despite use of antiretroviral therapy [34].

DAAs have proven to be safe and effective for people living with HIV; cure rates are comparable to those among people living with HCV alone. Although some countries, such as Thailand, prioritize treatment of HCV co-infection among people living with HIV, they do not always consider PWID as eligible for treatment [35]. A survey conducted by the European Liver Patient's Association (ELPA) in 2016/2017 reported that 13 European countries (Austria, Bulgaria, Croatia, Denmark, Finland, Hungary, Macedonia, Poland, Romania, Slovakia, Spain, Sweden and Ukraine) did not provide HCV treatment to people who are currently injecting drugs [36].

Although treating HCV in people living with HIV will lower HCV-related morbidity and mortality among people living with HIV/HCV co-infection, it will not prevent onward transmission among PWID and will hamper achievement of elimination targets. HCV co-infection among PWID could be eliminated if harm reduction and HCV treatment are brought to scale among both HIV-positive and HIV-negative PWID [11].

COUNTRY SNAPSHOTS

As with HIV, political will and an enabling environment are needed to stop HCV. Unless harsh drug policies change and unless national plans are funded and implemented, many countries will not be able to achieve the 2030 elimination targets, even with access to affordable generic DAAs.

INDIA

India is known as the “pharmacy of the developing world”, and it is indeed one of the main countries where generic DAAs are produced. Combined with its large HCV burden – estimated at approximately 6 million people [37] – India is a country of particular interest in the HCV response. As of 2016, new HCV infections outpaced the treatment rate: approximately 180,000 people were newly infected during that year, while 80,000 were treated and 25,000 people died from HCV complications [36].

India’s strict quantity-based drug sentencing laws reinforce the government’s stance that a narcotics offence is worse than murder since its effect extends beyond one person to society. People have been detained involuntarily for drug treatment, where they are subject to beatings and other human rights violations [39]. NSP coverage is 86 (range: 63-133) syringes per person injecting drugs per year, and OST coverage is three (range 2-4) per 100 PWID [6], but the country’s repressive drug laws make it difficult for PWID to access harm reduction services.

The National Centre for Disease Control has been finalizing an integrated initiative on prevention and control of viral hepatitis, and the National Health Mission is allocating state-by-state funding for a three-year initiative.

Currently, HCV testing and treatment are free of charge in Haryana and Punjab states, where more than 43,000 people, including PWID, have received decentralized care [40]. Cure rates among nearly 20,000 people who have completed it have exceeded 90% [41].

In November 2017, a group of activists, including PWID, people living with HIV, men who have sex with men and sex workers met at a national consultation in Delhi to provide feedback for the government’s prevention and control initiative. Their recommendations included:

- Expanding the National AIDS Control Organization Targeted Intervention programme to include HCV prevention
- Prioritizing community-based harm reduction services for PWID
- Offering voluntary testing, counselling and linkage to HCV care and treatment to key populations
- Treating HCV co-infection within existing ARV centres
- Providing comprehensive HCV prevention, testing and treatment in prisons.



INDIA COUNTRY DATA [4,35]

Estimated number of PWID: 197,000 (127,500-267,000)

Estimated HIV prevalence among PWID: 15.6% (12.9-18.2)

Estimated anti-HCV prevalence among PWID: 40% (33.9-46.1)

National plan: yes

Available treatments: sofosbuvir, daclatasvir, ledipasvir, velpatasvir

Restrictions for the general population: none

Restrictions for PWID: no specific recommendation or restriction in 2016 guidelines

Restrictions for people with HIV/HCV co-infection: no specific recommendation or restriction in 2016 guidelines

MOROCCO

Morocco plans to eliminate HCV by 2030, although implementation remains slow due to insufficient funding. This, with its local generics production due to patents not being filed on SOF and DCV, make it a country of interest [1,42]. Morocco is home to an estimated 300,000 people with HCV; to date, 7,500 people have been treated [1,36]. In 2016, 5,100 people were newly infected and 1,500 died from HCV complications [36].

Currently, there are no national treatment guidelines in Morocco. DAAs are available only through health insurance, although the government plans to offer low-cost care and treatment through its Medical Insurance Plan for the Financially Underprivileged (RAMED) [1,43]. A 12-week course of SOF and DCV is available through the private sector for US\$1,350 [1].

High rates of injecting drug use led Morocco to implement NSP in 2008 and OST in 2010 [44]. NSP coverage in Morocco remains low at eight (range: 5-16) syringes per person injecting drugs per year [7]. OST coverage in Morocco is two (range: 1-5) per 100 PWID. The penalty for drug-related offences in Morocco is imprisonment for up to 30 years, and a fine of up to €60,000 [45]. In 2011, civil society activists launched an ongoing, broad-based campaign to reform national drug policies [40].

THAILAND

With its pioneering HIV policies, universal health care scheme and capacity to produce generic drugs locally, Thailand is a country of particular interest in the HCV response. As of 2016, an estimated 460,000 people were living with hepatitis C; approximately 3,000 of them were treated and 2,100 of them died from HCV complications [36]. New infections surpassed the treatment rate, with more than 10,000 people becoming newly infected during that year.

In 2017, Thai activists from the AIDS Access Foundation filed a patent opposition on SOF. Subsequently, Gilead Sciences, which owns the patent on SOF, expanded the voluntary licence for its DAAs [46] to include Thailand [47].

Thailand is on the path towards HCV elimination; as of 2017, a high-level national committee has been established, elimination targets have been set, and a national plan is currently under development. Despite progress, unless policies on drug use change, it will be difficult for Thailand to achieve its targets.

“Everything is a priority! Last year it was advocacy for HCV testing; this year it is for the medicines. We want DAAs, not interferon.”

*Jirasak Sriparmong, Project Manager,
Thai Treatment Action Group*

Although HCV treatment is available free of charge in Thailand [48], PWID are not eligible, although a handful of doctors will provide treatment to people who promise to stop using drugs immediately [49].

Thailand’s severe anti-drug policies have led to human rights violations, stigma, discrimination and prison being overcrowded,

MOROCCO COUNTRY DATA [4,35]

Estimated number of PWID: 30,500 (15,500-45,500)

Estimated HIV prevalence among PWID: 9.6% (0.0-20.6)

Estimated anti-HCV prevalence among PWID: 53.9 % (33.7-74.0)

National plan: yes

Available treatments: sofosbuvir, daclatasvir and ribavirin

Restrictions for the general population: none known

Restrictions for PWID: none known

Restrictions for people with HIV/HCV co-infection: none known

mostly due to minor offences. This has made it difficult for PWID to access services and healthcare. The country has directed resources towards law enforcement and compulsory treatment rather than harm reduction. For example, NSP coverage in Thailand is 24 (range: 2-46) syringes per person injecting drugs per year [6]. OST with methadone is only available to people who have tried to remain drug free at least three times, and they must pay out of their own pocket [50]. OST coverage in Thailand is seven (range: 7-23) per 100 PWID [6].

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Restrictions for the general population: none known

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Restrictions for people with HIV/HCV co-infection: none known

The time to end HCV as a threat to global public health is upon us. Countries have an unprecedented opportunity to harness the collective power of evidence-based HCV prevention and safe, highly effective treatment. Once they commit to scaling up NSP and OST alongside treatment, they will be able to halt and reverse the HCV epidemic. This will be true if efforts invested in the HCV response are accompanied by progressive evidence-, human rights- and health-based drug policies.

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FOOTNOTES

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ABOUT THE HIV CO-INFECTIONS AND CO-MORBIDITIES INITIATIVE

The International AIDS Society (IAS) HIV Co-Infections and Co-Morbidities initiative aims to remove structural barriers and address human rights violations that inhibit access to and uptake of comprehensive HIV and other health services for vulnerable populations and communities. In particular, people who inject drugs (PWID) are disproportionately affected by HIV and HCV because of limited investments in and hugely restricted access to proven interventions. Even when effective care is available, the combination of punitive laws and experiences of stigma – both within healthcare settings and in the broader community – create barriers to their use. There is a need to support the rationale for inclusive HIV and HCV care policies that use an evidence- and human rights-based approach to drug policies and harm-reduction interventions.

Find more information at <http://www.iasociety.org/HIV-Programmes/Programmes/Co-Infections>.