International Journal of Drug Policy 26 (2015) S5–S11

Contents lists available at ScienceDirect

International Journal of Drug Policy

journal homepage: www.elsevier.com/locate/drugpo

Commentary

The cost-effectiveness of harm reduction

David P. Wilson[a,*], Braedon Donald[a], Andrew J. Shattock[a], David Wilson[b], Nicole Fraser-Hurt[b]

[a] The Kirby Institute, UNSW Australia, Australia
[b] Global HIV/AIDS Program, World Bank, United States

ARTICLE INFO

Article history:
Received 10 September 2014
Received in revised form
11 November 2014
Accepted 11 November 2014

Keywords:
Cost-effectiveness
HIV
Harm reduction
People who inject drugs

ABSTRACT

HIV prevalence worldwide among people who inject drugs (PWID) is around 19%. Harm reduction for PWID includes needle-syringe programs (NSPs) and opioid substitution therapy (OST) but often coupled with antiretroviral therapy (ART) for people living with HIV. Numerous studies have examined the effectiveness of each harm reduction strategy. This commentary discusses the evidence of effectiveness of the packages of harm reduction services and their cost-effectiveness with respect to HIV-related outcomes as well as estimate resources required to meet global and regional coverage targets. NSPs have been shown to be safe and very effective in reducing HIV transmission in diverse settings; there are many historical and very recent examples in diverse settings where the absence of, or reduction in, NSPs have resulted in exploding HIV epidemics compared to controlled epidemics with NSP implementation. NSPs are relatively inexpensive to implement and highly cost-effective according to commonly used willingness-to-pay thresholds. There is strong evidence that substitution therapy is effective, reducing the risk of HIV acquisition by 54% on average among PWID. OST is relatively expensive to implement when only HIV outcomes are considered; other societal benefits substantially improve the cost-effectiveness ratios to be highly favourable. Many studies have shown that ART is cost-effective for keeping people alive but there is only weak supportive, but growing evidence, of the additional effectiveness and cost-effectiveness of ART as prevention among PWID. Packages of combined harm reduction approaches are highly likely to be more effective and cost-effective than partial approaches. The coverage of harm reduction programs remains extremely low across the world. The total annual costs of scaling up each of the harm reduction strategies from current coverage levels, by region, to meet WHO guideline coverage targets are high with ART greatest, followed by OST and then NSPs. But scale-up of all three approaches is essential. These interventions can be cost-effective by most thresholds in the short-term and cost-saving in the long-term.

Introduction

HIV prevalence worldwide among people who inject drugs (PWID) is around 19% (World Health Organization, 2013) and almost one-third of HIV incident cases outside sub-Saharan Africa are related to injecting drug use (Open Society Institute, 2004). Injecting drug use is estimated to be responsible for around 10% of all HIV infections worldwide (UNAIDS, 2012). The spread of HIV among PWID has particularly driven epidemics throughout regions of Eastern Europe, and Central and Southeast Asia (Bridge, Lazarus, & Atun, 2010; El-Bassel et al., 2014; Wu, Shi, & Detels, 2013). Indeed, in Eastern Europe and Central Asia the majority of HIV infections have been attributed to injecting drug use and this is the region of the world currently with the largest increase in HIV epidemics (UNAIDS, 2012). Some countries in the Middle East and North Africa region have also been experiencing rapidly emerging HIV epidemics among PWID (Mumtaz et al., 2014).

Many countries in Asia and Eastern Europe have responded to injecting drug use through law enforcement measures and compulsory detention (Wu, 2013). There is no evidence to suggest that compulsory detention of people who use drugs is effective in reducing drug dependency or rehabilitative, as most detained people return to drug dependency after release (Hall et al., 2012; WHO, 2009a). An alternate approach is harm reduction, which refers to methods of reducing health risks when eliminating them may not be possible. Harm reduction can also reduce social and economic

* Corresponding author at: The Kirby Institute, University of New South Wales, Level 6, Wallace Wurth Building, Kensington, Sydney NSW 2052, Australia. Tel.: +61 2 9385 0959.
E-mail address: dwilson@unsw.edu.au (D.P. Wilson).

http://dx.doi.org/10.1016/j.drugpo.2014.11.007

harms that individuals experience as a result of engaging in risky activities. In the context of HIV prevention and injecting drug use, harm reduction generally includes needle-syringe programs and opioid substitution therapy. Provision of antiretroviral therapy is also considered to be within a comprehensive package of HIV-related services for PWID. Harm reduction approaches were first introduced in the Netherlands, United Kingdom and Australia in the mid-1980s in response to AIDS epidemics (Stimson, 1989). We now have three decades of data to assess the evidence of effectiveness and cost-effectiveness of these approaches. In this commentary, we discuss the cost-effectiveness of harm reduction with respect to HIV-related outcomes. We refer the reader to a complementary commentary in this issue by Bruggman and Grebely which addresses harm reduction and hepatitis C virus (HCV) epidemics, including the large opportunity to incorporate new paradigm-shifting HCV treatments into harm reduction packages (Bruggmann & Grebely, 2015).

Although they do not necessarily reduce drug dependency, needle-syringe programs (NSPs) are public health measures which aim to reduce the spread of blood-borne infections, including HIV and HCV, among PWID through the distribution of sterile injecting equipment. NSPs operate in many different modes in different contexts and they may provide a range of services that include the provision of injecting equipment, education and information on reduction of drug-related harms, referral to drug treatment, medical care and legal and social services (Heimer, 1998; Kidorf & King, 2008). Another harm reduction strategy, opioid substitution therapy (OST), has a dualistic aim of firstly reducing drug dependency among PWID, but secondly and subsequently reducing the frequency of injection and unsafe injecting practices which thereby reduces blood-borne viral transmission via injecting drug use. Methadone or other opioid substitutes are prescribed to dependent users to diminish the use and effects of opiates. The provision of ART has also become an ethically-sound and pragmatic intervention for PWID who are also living with HIV, as it reverses disease progression to increase the length and quality of life (Lohse et al., 2007). ART also reduces viral load which is expected to also decrease the likelihood of onward HIV transmission (Cohen et al., 2011; Wilson et al., 2008). These three harm reduction strategies also comprise the main elements of a nine-component comprehensive package, endorsed by the WHO, UNODC and UNAIDS (WHO, 2009b).

Numerous studies have examined the effectiveness of each harm reduction strategy. Each approach has clear evidence of impact on reducing drug dependency or reducing risk behaviours and ultimately averting HIV transmission (among other important benefits). A recent systematic review of HIV prevention programs through Asia and Eastern Europe found that interventions targeted at specific population groups, including harm reduction programs for PWID, demonstrated evidence of effectiveness and cost-effectiveness when compared to non-targeted other HIV interventions aimed at the general populations (Craig, 2014). This commentary assesses NSPs, OST and ART in isolation and then broadly the evidence of them in combination. The amount of money which society, governments and other funders are willing to pay for health and societal benefits is substantially different between settings, interventions and populations. We do not define a specific willingness-to-pay threshold for harm reduction; rather, we comment on general conclusions from studies on the cost-effectiveness ratios calculated.

Effectiveness and cost-effectiveness of NSPs

NSPs have been shown to be safe and effective in reducing HIV transmission in diverse settings (Bastos & Strathdee, 2000; Jenkins et al., 2001; Kwon et al., 2009; Vickerman et al., 2006; Wodak, 2006). A recent review of reviews found sufficient evidence of NSPs to reduce self-reported risky injecting behavior and tentative evidence of effectiveness of NSPs to reduce HIV transmission (Palmateer et al., 2010). Two recent comprehensive reviews found compelling evidence that NSPs are associated with favorable outcomes for PWID (Gibson, Flynn, & Perales, 2001; Wodak & Cooney, 2005) with the more recent review finding that increasing the availability of sterile injecting equipment to PWID reduces HIV infection; 23 of 33 studies reviewed found positive outcomes on HIV risk behavior, with one finding negative outcomes, 5 having indeterminate outcomes, and 6 investigating a variety of other outcomes with either positive or indeterminate results (Wodak & Cooney, 2005). Further, a review of ecological data from 81 cities across Europe, Asia and North America found that HIV prevalence increased by an average of 5.9% per year in the 52 cities without NSPs but HIV prevalence decreased by 5.8% per year in the 29 cities with NSPs (Hurley, Jolley, & Kaldor, 1997); note that mortality rates at the time of this study may have influenced prevalence trends. A particularly notable example of impact was demonstrated in New York, where the introduction of NSPs was associated with a sharp decrease of HIV incidence in the early 1990s from 4% per year to 1% (Des Jarlais et al., 1996, 2005). There are many examples where the lack of NSPs has led to large increases in HIV incidence. For example, HIV prevalence in Cebu, Philippines recently escalated drastically from 0.5% in 2009 to 53% in 2011; similarly rapidly exploding epidemics have been observed in Sargodha (Pakistan), Bangkok (Thailand) and Manipur (India) where HIV prevalence increased from near zero within a few months to reach levels of 20–50% (Choopanya et al., 1991; Emmanuel et al., 2009; Sarkar et al., 1993). NSPs reduce the probability of transmission of HIV and other blood-borne diseases by lowering the rates of sharing of injecting equipment among PWID. Surveillance in Victoria and Vancouver, Canada found that there were similar behaviors in the two cities with NSPs but subsequent to the closure of needle-exchange clinics in Victoria, needle sharing became significantly more prevalent (23%) in Victoria compared to Vancouver (8%) where needle exchange clinics remained open (Ivsins et al., 2010).

NSPs are relatively inexpensive to implement. The average cost of NSP provision has been estimated by UNAIDS to be US$23–71 per person per year (Wilson & Nicole, 2013) depending on region of the world and delivery system (pharmacies, specialist programme sites, vending machines, mobile outreach vehicles) (Schwartlander et al., 2011). Given their relatively low costs and evidence of effectiveness, NSPs are recognized as one of the most cost-effective public health interventions ever funded (International, 2012). Studies in numerous countries have repeatedly provided compelling evidence that NSPs are cost-effective both from societal and health sector perspectives (Vickerman, Miners, & Williams, 2008; Wodak & Maher, 2010). A systematic review found that all 12 included studies that examined the impact of NSPs on HIV infection found that NSPs were cost-effective according to the studies' defined willingness-to-pay thresholds (Jones, Pickering, Sumnall, McVeigh, & Bellis, 2008). Increasingly, evidence has found net financial benefits of NSPs across all regions and in high- and low-income settings (Belani Hrishikesh & Muennig, 2008; Guinness et al., 2010; Ni et al., 2012). For example, NSPs are cost saving when compared to the lifetime costs of HIV/AIDS antiretroviral treatment (Jones et al., 2008) and a recent study estimated that not only did NSPs reduce the incidence of HIV by up to 74% over a 10 year period in Australia but found that they were cost savings and had a return on investment of between $1.3 and $5.5 for every $1 invested (Kwon et al., 2012). Table 1 illustrates the cost-effectiveness ratios of NSPs in Eastern Europe and Central Asia where injecting drug use is prevalent.

Table 1
Illustrative examples of cost-effectiveness of NSP in Eastern Europe and Central Asia (implemented 2000–2010).

Country	QALYs gained	ICER (US $ per QALY gained)
Armenia	223–251	Return ~ investment
Belarus	1310–1642	$1405–1896
Estonia	41–53	$102,375–132,374
Georgia	41–56	$19,811–27,633
Kazakhstan	2364–2518	$5758–6256
Moldova	559–1026	$1882–3640
Tajikistan	909–1283	$2104–3024
Ukraine	3903–7949	$867–2540

Source: Wilson et al. (2014).

Effectiveness and cost-effectiveness of OST

There is evidence that substitution therapy for heroin and other opiates is effective in reducing drug use and behavior related to transmission of blood-borne viruses, including complete cessation of injecting drug use (Ball et al., 1988; Hubbard et al., 1988; OECD et al., 2014; Yancovitz et al., 1991). A recent meta-analysis of studies conducted in North America, Europe and Asia found that OST using methadone maintenance treatment was associated with a 54% reduction in risk of having HIV infection among PWID (rate ratio of 0.46, 0.32–0.67 95%CI) (MacArthur et al., 2012). Numerous Cochrane reviews have been conducted on OST with respect to their effectiveness in treating opioid dependence, psychosocial and other outcomes; one of these reviews addressed the evidence of OST for prevention of HIV infection (Gowing et al., 2011). It found that OST reduces drug-related behaviours with a high risk of HIV transmission, but has less effect on sex-related risk behaviours, and that the lack of data from randomised controlled studies limits the strength of the evidence. It is unethical to design a randomised controlled study and thus difficult to obtain stronger evidence than exists on the effectiveness of OST.

OST is more expensive than NSPs at US$363–1057 per patient per year for 80 mg methadone and US$1236–3167 per patient per year for buprenorphine (Schwartlander et al., 2011). Despite the higher costs, modelling studies have estimated that OST is a marginally-to-reasonably cost-effective strategy when compared to current practice and considering HIV benefits only (Degenhardt et al., 2010), ranging from a cost of US$3324 per HIV infection averted (as indicated by a study in Vietnam) (Tran et al., 2012) to approximately US$7000 per HIV infection averted (as demonstrated by a study of HIV prevention in a high prevalence Indonesian setting) (Wammes et al., 2012). However, the largest benefits of OST are related to wider psychosocial and social benefits including reduction in the number and severity of relapses due to opiate use, and reduced rates of criminal activity and incarceration for drug-related crimes. If these factors are also included in economic analyses, OST is substantially more cost-effective. Furthermore, OST has wider quality of life and economic benefits (Hammett, 2014). For example, a recent study found that methadone maintenance therapy is associated with large reductions in health care service utilization, reduced out-of-pocket costs by HIV-positive people who use drugs and could likely reduce the economic vulnerability of households affected by injecting drug use (TRan & Nguyen, 2013).

In terms of comprehensive HIV responses, OST programs fall into the category of structural interventions, which addresses multisectoral, distal drivers of HIV infection. In implementing these interventions as part of a repertoire of HIV interventions, the policy environment recognizes the reality that these types of programs have multiple health-related and other benefits. Such structural HIV interventions call for cross-sector financing models, which distribute the costs in accordance with the benefits (Remme et al., 2012). If a cross-sector cost-benefit analysis is applied to cost-effectiveness analyses of OST (e.g., by replicating the method used by Remme et al. when examining structural interventions such as cash transfers to young women (Remme et al., 2012, 2014)) then the overall cost-effectiveness ratios of OST would improve by a factor of around 10–20-fold (results not shown). OST is thus highly cost-effective according to almost any willingness-to-pay thresholds.

Effectiveness and cost-effectiveness of ART

There is strong evidence, including from a randomised controlled trial, that ART reduces infectivity among HIV-positive heterosexuals (Anglemyer et al., 2011; Attia et al., 2009; Cohen et al., 2011; Quinn et al., 2000). Currently, there is little evidence that treatment as prevention is as effective for MSM and for PWID although it is highly plausible that this strategy is likely to reduce transmission rates substantially among these groups (Kelley et al., 2011; Wilson, 2010). Additionally, ART may also be given to HIV-negative individuals as pre-exposure prophylaxis (PrEP). PrEP has now been shown to reduce transmission among PWID by 48.9% in the Bangkok Tenofovir Study (BTS) (Choopanya et al., 2013); however, we note that this trial was undertaken in an environment where other harm reduction approaches are highly restricted and illegal.

While UNAIDS estimated that the minimum cost of providing ART to be US$176 per person per year in 2010 and project this cost to decline to USD $125 by 2020, studies have indicated that the average annual costs of treating an HIV-positive PWID per year can be anywhere between US$1000 and US$2000 in low- and middle-income countries (Wilson & Nicole, 2013).

Many studies have shown that ART is cost-effective not only for the purpose of keeping people alive but also because of its prevention benefits (Kahn et al., 2011; Loubiere et al., 2010; Wilson et al., 2014). Considering the prevention and treatment benefits, ART is a highly favourable intervention. However, there is relatively little evidence of cost-effectiveness of ART specifically targeted to PWID. A study in Russia estimated that ART would cost around US$1501 per QALY gained when targeted to PWID which is considered good value for money (Long et al., 2006). The cost-effectiveness of PrEP for PWID will vary according to HIV incidence among the PWID targeted and with the cost of PrEP. Assuming that the measured efficacy of PrEP among PWID in the BTS (of 48.9%) is maintained with broader scale-up outside of a trial setting, cost-effectiveness ratios can be estimated. In high-income countries, the cost per HIV infection averted would range between US$25,000–1.8 million; the cost per infection averted would be US$4200–75,000 when discounted tenofovir is available and US$1200–18,000 where generic tenofovir is available (Craig et al., 2013). These ranges suggest that PrEP may not be cost-effective in all settings compared with commonly funded health interventions.

It is important to note that coverage of ART among HIV-positive PWID is less than 1% in many countries (Mathers et al., 2010). It would be expected that coverage of antiretrovirals among HIV-negative PWID would be substantially lower. Therefore, due to expected low coverage and unimpressive cost-effectiveness ratios, we believe that PrEP is unlikely to be largely utilised for HIV prevention among PWID. However, ART for people living with HIV would be very cost-effective.

Effectiveness and cost-effectiveness of combination strategies

No single harm reduction approach is sufficient. The evidence suggests that comprehensive prevention strategies are synergistic (Beyrer et al., 2010; Lert & Kazatchkine, 2007; Strathdee et al., 2012; Wood et al., 2002). Modelling for Eastern Europe and Central Asia has shown that NSPs alone have small effect unless they

Table 2
Estimated annual cost of scaling up harm reduction by region.

Region	Harm reduction strategy (current coverage)[a]	Annual cost (USD) of scale up to reach 'Mid coverage targets' (%)[b]	Annual cost (USD) of scale up to reach High coverage targets (%)[b]
South East Asia	NSP (11.5%) OST (5.9%) ART (3.6%)	$26,844,300 (20% Coverage) $360,975,675 (20% Coverage) $856,463,175 (25% Coverage)	$153,600,300 (60% coverage) $872,526,675 (40% Coverage) $2,859,660,675 (75% Coverage)
Eastern Europe and Central Asia	NSP (11.7%) OST (<1%%) ART (1.1%)	$19,099,100 (20% Coverage) $715,465,800 (20% Coverage) $1,163,126,925 (25% Coverage)	$111,454,300 (60% coverage) $1,466,224,200 (40% Coverage) $3,593,036,925 (75% Coverage)
Latin America and the Caribbean	NSP (2%) OST (<1%) ART (1%)	$8,331,120 (20% Coverage) $427,631,100 (20% Coverage) $690,292,800 (25% Coverage)	$26,844,720 (60% coverage) $857,411,100 (40% Coverage) $2,128,402,800 (75% Coverage)
Middle East and North Africa	NSP (2.0%) OST (1%) ART (<1%)	$1,350,360 (20% Coverage) $23,173,920 (20% Coverage) $34,091,750 (25% Coverage)	$4,351,160 (60% coverage) $47,567,520 (40% Coverage) $102,275,250 (75% Coverage)
Western Europe, North America and Australasia	NSP (17.0%) OST (27.8%) ART (78.5%)	$16,625,550 – –	$238,299,550 $954,741,990 –

[a] *Source*: Mathers et al. (2010).
[b] *Source*: Scale-up calculations by UNSW.

are combined with other evidence-informed, rights-based combination interventions, particularly access to OST and ART (Lacombe & Rockstroh, 2012). Programs which employ a combination of harm reduction strategies have had demonstrable success in improving health outcomes for PWID (Degenhardt et al., 2010). Such a strategy in Amsterdam resulted in a 57% decrease in HIV incidence and 64% decrease in HCV incidence in a distinct cohort (Van Den Berg et al., 2007). Similar positive results have been found in Malaysia, where a combination of harm reduction programs have averted an estimated 12,653 HIV infections since 2006 (Naning et al., 2013). Furthermore, adherence to ART could likely be improved if combined with OST programs (WHO, 2012).

Combination programs that combine harm reduction interventions have also demonstrated good value for money (Degenhardt et al., 2010). This includes a recent study in Ukraine which found that a harm reduction strategy which expands both methadone and ART to PWID is not only more effective than a methadone-only strategy, but is also deemed to be cost-effective at an estimated US$1120/QALY gained (Alistar, Owens, & Brandeau, 2011). Another study in China found the expansion of combination strategies which employ ART, voluntary testing and counselling, and harm reduction to cost an estimated $9310 per QALY gained when compared to a base case of essentially no harm reduction program (Li et al., 2012); this is likely to be around or less than willingness-to-pay thresholds for upper-middle-income countries like China.

Scaling up harm reduction interventions and evidence of returns on investment

Despite increasing prevalence of injecting drug use and established evidence of effectiveness and cost-effectiveness, the coverage of harm reduction programs remains appallingly low (Mathers et al., 2010).

As of 2012, there were 97 countries and territories that supported a harm reduction approach, exemplified either in national policy documents or tolerance or implementation of harm reduction interventions (International, 2012). Yet, high coverage (defined by the 2009 WHO, UNAIDS, UNODC Technical Guide as more than 200 needles or syringes provided per PWID per year) of NSPs has only been achieved in a few countries in Europe, Australia, a small number of countries in Asia, Brazil, and Iran (UNAIDS, 2013; Des Jarlais et al., 2013). A recent review suggested that only 10% of PWID in Eastern Europe and 36% in Central Asia access NSPs, with an average of nine and 92 needle-syringes distributed per PWID per year, respectively (Mathers et al., 2010). As such, an estimated 90% of PWID worldwide are not accessing NSPs. Despite being provided in 77 countries worldwide, there are also significant coverage gaps with OST, which remains unavailable in 81 countries with reported injecting drug use. Furthermore, it is estimated that only 8% of PWID globally have access to OST, with coverage particularly low in parts of sub-Saharan Africa, Latin America and Asia. Encouragingly however, high OST coverage has been reported in Iran, Czech Republic and Western Europe, and several countries in Asia and the Middle East have begun to scale-up their programs; China has recently had the largest OST scale-up program in the world. Uptake of ART by HIV-infected PWID shows the largest disparities with what is required or deemed to be appropriate access. Only 14% of HIV-positive PWID globally have access to ART, with the largest gaps in ART provision in Eastern Europe and Central Asia (where almost no PWID in some countries have access to ART).

It is clear that harm reduction programs have yet to be scaled up or implemented in a way to be commensurate with their expected population benefits and yield the full economic benefits (International, 2012). Even where new initiatives have been implemented, they are generally small-scale (International, 2012). More worryingly, numerous countries with some of the highest HIV burdens among PWID have appeared to significantly scale down harm reduction interventions (International, 2012). This is likely due to previous support from international donors being withdrawn and not replaced by domestic sources.

There are numerous socio-political and legislative reasons for poor coverage of harm reduction. Coverage cannot be improved without first addressing the stigma, discrimination and intolerance that restricts the expansion of harm reduction. Addressing these barriers remains of paramount importance for facilitating effective harm reduction programs. We refer the reader to a complementary commentary in this issue by Strathdee et al. on harm reduction and the law (Strathdee et al., 2015).

The evidence presented here suggests that all harm reduction interventions could be further expanded. The potential reach and costs of scaling up any of the three interventions are dependent not only of the costs of the intervention, but also on the prevalence of injecting drug use and on the current coverage of interventions. In Table 2 we provide our estimates of the total annual costs of scaling up each of the harm reduction strategies from current coverage levels, by region, to meet WHO guideline coverage targets. We note that required costs for ART are greater than for NSPs and OST. However, ART budgets should be separate to harm reduction budgets. In

every region of the world, coverage of NSPs is substantially greater than coverage of OST. OST is more expensive than NSPs and therefore it is not surprising that it will cost a lot more to scale up OST to mid-levels than it would take to scale-up NSPs to high levels. It would be relatively inexpensive to attain mid-coverage levels of NSPs across every region of the world.

Scale up of all three approaches is essential. These interventions can be cost-effective in the short-term according to common locally applied willingness-to-pay thresholds and cost-saving in the long-term. There are economies of scale as programs mature and increase in coverage (Marseille et al., 2007; Menzies et al., 2011). Increasing coverage may require governments to expand national public sector infrastructure, health systems capacity, and outreach services whereas achieving requisite scale efficiency could entail increasing delivery systems with low fixed operation costs, through drop-in centers and other innovative approaches (Lurie et al., 1998). In particular, reductions in unit costs can further improve the cost-effectiveness of these approaches, in particular when these are implemented in an overall comprehensive and evidence-informed manner (Tilson & Bozzette, 2007).

Conclusion

The need to improve health outcomes for PWID, including reducing the high and increasing rates of HIV (and HCV) transmission, remains an urgent task for health providers and governments across the world. The coverage of harm reduction programs among PWID populations is currently too low across almost all global regions and the programs have yet to sufficiently scale up to lead to the population impact commensurate with their known effectiveness and cost-effectiveness. Not only is there an ethical imperative to make harm reduction programs universally available, but in stark contrast to compulsory detention, these approaches are globally effective, represent good value for money and are often cost-saving, indicating their value to improving the health outcomes for PWID and the broader population.

The internationally endorsed priority harm reduction interventions are fully supported by the available evidence. OST, NSPs and ART together are effective in reducing drug dependency, reducing sharing of injecting equipment, improving quality of life and averting HIV infections. Notably, NSPs and OST have been proven to avert HIV cases among PWID, and OST also has greater societal benefits associated with reduction in drug dependency. There is compelling evidence of value for money for each of the three interventions across all regions, with all generally cost-effective in the short-term and very cost-effective to cost-saving when long-term and societal benefits are considered. Importantly, cost-effectiveness ratios in terms of costs per HIV infection averted among PWID are highly favorable, ranging from $100 to $1000. Implementing these strategies in combination would likely improve their effectiveness and cost-effectiveness.

To reverse epidemics of blood-borne viral infections, particularly in a global environment of decreasing HIV/AIDS financial commitments, and to effectively respond to the social and health needs of PWID, it is important to identify the most cost-effective interventions. National governments may wish to re-examine their approaches to responding to PWID and consider how the strong evidence and rationale for harm reduction programs can influence future funding allocations within national public health programs. Although the overall costs of scaling up harm reduction programs will be high, it will be a worthwhile action for governments to adopt; not only do the societal benefits of harm reduction programs exceed treatment costs, but they will also present significant returns on investment due to infections and subsequent health costs which are averted. At the same time, governments need to ensure sufficient health systems and public sector capacity is in place to successfully implement harm reduction strategies. This means investing not only in the strategies themselves but also investing in health systems infrastructure and overcoming or dismantling structural barriers of access for PWID to health care services.

The contents and conclusions of the paper reflect a broad consensus among social and clinical scientists participating in a UNODC Scientific Consultation on HIV/AIDS (UNODC Scientific Consultation, 2014).

Conclusion statements

- There is evidence that opioid-substitution therapy (OST), needle-syringe programs (NSP) and antiretroviral therapy (ART) together have established effectiveness in reducing drug dependency, reducing sharing of injecting equipment, improving quality of life and averting HIV infections.
- The unit costs of harm reduction interventions are relatively low, but can vary by provider type, delivery model and region. Generally, NSPs are least expensive, while the costs of ART are expected to decline by 2020. OST is a structural intervention with other societal benefits: when such benefits are included, the attributable cost for HIV budgets and cost-effectiveness ratios are highly favourable.
- Globally, harm reduction interventions are good value for money, improving health outcomes for PWID. There is compelling evidence of cost-effectiveness for each of the three interventions across all regions. The estimated cost-effectiveness ratios for priority intervention packages for PWID and HIV-positive PWID are highly favorable for all regions, with costs per HIV infection averted ranging from $100 to $1000.
- The coverage of harm reduction programs is currently too low across almost all regions. Although the overall costs of scaling up harm reduction programs will be high, it will a worthwhile action; not only do the societal benefits of harm reduction programs exceed treatment costs, but they also have the potential to provide significant returns on investment for governments.

Acknowledgements

This study was funded by the Australian National Health and Medical Research Council and the World Bank Group. The Kirby Institute is funded by the Australian Government, Department of Health and Ageing. The views expressed in this publication do not necessarily represent the position of the Australian Government. The Kirby Institute is affiliated with the University of New South Wales. The findings, interpretations, and conclusions expressed in this work are those of the author(s) and do not necessarily reflect the views of The World Bank, its Board of Executive Directors, or the governments they represent.

Conflict of interest

All authors have no relevant conflicts of interest to declare.

References

Alistar, S. S., Owens, D. K., & Brandeau, M. L. (2011). Effectiveness and cost effectiveness of expanding harm reduction and antiretroviral therapy in a mixed HIV epidemic: A modeling analysis for Ukraine. *PLoS Medicine*, *8*(3), e1000423.

Anglemyer, A., Rutherford, G. W., Egger, M., & Siegfried, N. (2011). Antiretroviral therapy for prevention of HIV transmission in HIV-discordant couples. *Cochrane Database of Systematic Reviews*, (8), CD009153.

Attia, S., et al. (2009). Sexual transmission of HIV according to viral load and antiretroviral therapy: Systematic review and meta-analysis. *AIDS*, *23*(11), 1397–1404.

Ball, J. C., et al. (1988). Reducing the risk of AIDS through methadone maintenance treatment. *Journal of Health and Social Behavior*, *29*(3), 214–226.

Bastos, F. I., & Strathdee, S. A. (2000). Evaluating effectiveness of syringe exchange programmes: Current issues and future prospects. *Social Science & Medicine*, *51*(12), 1771–1782.

Belani, H. K., & Muennig, P. A. (2008). Cost-effectiveness of needle and syringe exchange for the prevention of HIV in New York City. *Journal of HIV/AIDS & Social Services*, *7*(3), 229–240.

Beyrer, C., et al. (2010). Time to act: A call for comprehensive responses to HIV in people who use drugs. *Lancet*, *376*(9740), 551–563.

Bridge, J., Lazarus, J. V., & Atun, R. (2010). H.I.V. epidemics and prevention responses in Asia and Eastern Europe: Lessons to be learned? *AIDS*, *24*, S86–S94.

Bruggmann, P., & Grebely, J. (2015). Prevention, treatment and care of hepatitis C virus infection among people who inject drugs. *International Journal of Drug Policy*, *26*, S22–S26.

Choopanya, K., et al. (1991). Risk factors and HIV seropositivity among injecting drug users in Bangkok. *AIDS*, *5*(12), 1509–1513.

Choopanya, K., et al. (2013). Antiretroviral prophylaxis for HIV infection in injecting drug users in Bangkok, Thailand (the Bangkok Tenofovir Study): A randomised, double-blind, placebo-controlled phase 3 trial. *Lancet*, *381*(9883), 2083–2090.

Cohen, M. S., et al. (2011). Prevention of HIV-1 infection with early antiretroviral therapy. *The New England Journal of Medicine*, *365*(6), 493–505.

Craig, A. E. A. (2014). *Spending of HIV resources in Asia and Eastern Europe: Systematic review reveals the need to shift funding allocations towards priority populations*.

Craig, A. P., et al. (2013). HIV antiretroviral prophylaxis for injecting drug users. *Lancet*, *382*(9895), 854–855.

Degenhardt, L., et al. (2010). Prevention of HIV infection for people who inject drugs: Why individual, structural, and combination approaches are needed. *Lancet*, *376*(9737), 285–301.

Des Jarlais, D. C., et al. (1996). HIV incidence among injecting drug users in New York City syringe-exchange programmes. *Lancet*, *348*(9033), 987–991.

Des Jarlais, D. C., et al. (2005). HIV incidence among injection drug users in New York City, 1990 to 2002: Use of serologic test algorithm to assess expansion of HIV prevention services. *American Journal of Public Health*, *95*(8), 1439–1444.

Des Jarlais, D. C., et al. (2013). High coverage needle/syringe programs for people who inject drugs in low and middle income countries: A systematic review. *BMC Public Health*, *13*.

El-Bassel, N., et al. (2014). Drug use as a driver of HIV risks: Re-emerging and emerging issues. *Current Opinion in HIV and AIDS*, *9*(2), 150–155.

Emmanuel, F., et al. (2009). Factors associated with an explosive HIV epidemic among injecting drug users in Sargodha, Pakistan. *Journal of Acquired Immune Deficiency Syndromes*, *51*(1), 85–90.

Gibson, D. R., Flynn, N. M., & Perales, D. (2001). Effectiveness of syringe exchange programs in reducing HIV risk behavior and HIV seroconversion among injecting drug users. *AIDS*, *15*(11), 1329–1341.

Gowing, L., et al. (2011). Oral substitution treatment of injecting opioid users for prevention of HIV infection. *Cochrane Database of Systematic Reviews*, (8), CD004145.

Guinness, L., et al. (2010). The cost-effectiveness of consistent and early intervention of harm reduction for injecting drug users in Bangladesh. *Addiction*, *105*(2), 319–328.

Hall, W., et al. (2012). Compulsory detention: Forced detoxification and enforced labour are not ethically acceptable or effective ways to treat addiction. *Addiction*, *107*(11), 1891–1893.

Hammett, T. (2014). Evaluation of HIV prevention interventions for people who inject drugs in low- and middle-income countries – the current and future state of the art. *International Journal of Drug Policy*, *25*(3), 336–339.

Heimer, R. (1998). Syringe exchange programs: Lowering the transmission of syringe-borne diseases and beyond. *Public Health Reports*, *113*(Suppl. 1), 67–74.

Hubbard, R. L., et al. (1988). Role of drug-abuse treatment in limiting the spread of AIDS. *Reviews of Infectious Diseases*, *10*(2), 377–384.

Hurley, S. F., Jolley, D. J., & Kaldor, J. M. (1997). Effectiveness of needle-exchange programmes for prevention of HIV infection. *Lancet*, *349*(9068), 1797–1800.

International, H.R. (2012). *The global state of harm reduction: Towards an integrated response. London, United Kingdom*.

Ivsins, A., Chow, C., Marsh, D., Macdonald, S., Stockwell, T., & Vallance, K. (2010). *Drug use trends in Victoria and Vancouver, and changes in injection drug use after the closure of Victoria's fixed site needle exchange*. Centre for Addictions Research of British Columbia.

Jenkins, C., et al. (2001). Measuring the impact of needle exchange programs among injecting drug users through the National Behavioural Surveillance in Bangladesh. *AIDS Education and Prevention*, *13*(5), 452–461.

Jones, L., Pickering, L., Sumnall, H., McVeigh, J., & Bellis, A. (2008). *A review of the effectiveness and cost-effectiveness of needle and syringe programs for injecting drug users*. Centre for Pulic Health, Liverpool John Moores University.

Kahn, J. G., et al. (2011). Cost-effectiveness of antiretroviral therapy for prevention. *Current HIV Research*, *9*(6), 405–415.

Kelley, C. F., Haaland, R. E., Patel, P., Evans-Strickfaden, T., Farshy, C., Hanson, D., et al. (2011). HIV-1 RNA rectal shedding is reduced in men with low plasma HIV-1 RNA viral loads and is not enhanced by sexually transmitted bacterial infections of the rectum. *Journal of Infectious Diseases*, *204*(5), 761–767.

Kidorf, M., & King, V. L. (2008). Expanding the public health benefits of syringe exchange programs. *Canadian Journal of Psychiatry*, *53*(8), 487–495.

Kwon, J. A., et al. (2009). The impact of needle and syringe programs on HIV and HCV transmissions in injecting drug users in Australia: A model-based analysis. *Journal of Acquired Immune Deficiency Syndromes*, *51*(4), 462–469.

Kwon, J. A., et al. (2012). Estimating the cost-effectiveness of needle-syringe programs in Australia. *AIDS*, *26*(17), 2201–2210.

Lacombe, K., & Rockstroh, J. (2012). HIV and viral hepatitis coinfections: Advances and challenges. *Gut*, *61*(Suppl. 1), pi47–pi58.

Lert, F., & Kazatchkine, M. D. (2007). Antiretroviral HIV treatment and care for injecting drug users: An evidence-based overview. *International Journal of Drug Policy*, *18*(4), 255–261.

Li, J., et al. (2012). The epidemiological impact and cost-effectiveness of HIV testing: Antiretroviral treatment and harm reduction programs. *AIDS*, *26*(16), 2069–2078.

Lohse, N., et al. (2007). Survival of persons with and without HIV infection in Denmark, 1995–2005. *Annals of Internal Medicine*, *146*(2), 87–95.

Long, E. F., et al. (2006). Effectiveness and cost-effectiveness of strategies to expand antiretroviral therapy in St. Petersburg, Russia. *AIDS*, *20*(17), 2207–2215.

Loubiere, S., et al. (2010). Economic evaluation of ART in resource-limited countries. *Current Opinion in HIV and AIDS*, *5*(3), 225–231.

Lurie, P., et al. (1998). An economic analysis of needle exchange and pharmacy-based programs to increase sterile syringe availability for injection drug users. *Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology*, *18*, S126–S132.

MacArthur, G. J., et al. (2012). Opiate substitution treatment and HIV transmission in people who inject drugs: Systematic review and meta-analysis. *British Medical Journal*, *345*, pe5945.

Marseille, E., et al. (2007). HIV prevention costs and program scale: Data from the PANCEA project in five low and middle-income countries. *BMC Health Services Research*, *7*, 108.

Mathers, B. M., et al. (2010). HIV prevention, treatment, and care services for people who inject drugs: A systematic review of global, regional, and national coverage. *Lancet*, *375*(9719), 1014–1028.

Menzies, N. A., et al. (2011). The cost of providing comprehensive HIV treatment in PEPFAR-supported programs. *AIDS*, *25*(14), 1753–1760.

Mumtaz, G. R., et al. (2014). HIV among people who inject drugs in the Middle East and North Africa: Systematic review and data synthesis. *PLoS Medicine*, *11*(6).

Naning, H., Kerr, C., Kamarulzaman, A., Dahlui, M., Ng, Chiu-Wan, Osornprasop, S., & Wilson, D. P. (2013). *Cost-effectiveness and return on investment of HIV harm reduction Programmes for people who inject drugs in Malaysia 2013*.

Ni, M. J., et al. (2012). Net financial benefits of averting HIV infections among people who inject drugs in Urumqi, Xinjiang, Peoples Republic of China (2005–2010). *BMC Public Health*, *12*, 572.

OECD. (2014). *Aid to Developing countries rebounds in 2013 to reach an all-time high*. OECD, Editor.

Open Society Institute. (2004). *Breaking down barriers: Lessons on providing HIV treatment to injection drug users*. New York, USA: Open Society Institute.

Palmateer, N., et al. (2010). Evidence for the effectiveness of sterile injecting equipment provision in preventing hepatitis C and human immunodeficiency virus transmission among injecting drug users: A review of reviews. *Addiction*, *105*(5), 844–859.

Quinn, T. C., et al. (2000). Viral load and heterosexual transmission of human immunodeficiency virus type 1. *New England Journal of Medicine*, *342*(13), 921–929.

Remme, M., et al. (2012). Paying girls to stay in school: A good return on HIV investment? *The Lancet*, *379*(9832), p2150.

Remme, M., et al. (2014). Financing structural interventions: Going beyond HIV-only value for money assessments. *AIDS*, *28*(3), 425–434.

Sarkar, S., et al. (1993). Rapid spread of HIV among injecting drug users in north-eastern states of India. *Bulletin on Narcotics*, *45*(1), 91–105.

Schwartlander, B., et al. (2011). Towards an improved investment approach for an effective response to HIV/AIDS. *Lancet*, *377*(9782), 2031–2041.

Stimson, G. V. (1989). Syringe-exchange programmes for injecting drug users. *AIDS*, *3*(5), 253–260.

Strathdee, S. A., et al. (2012). Towards combination HIV prevention for injection drug users: Addressing addictophobia, apathy and inattention. *Current Opinion in HIV and AIDS*, *7*(4), 320–325.

Strathdee, S. A., Beletsky, L., & Kerr, T. (2015). HIV, drugs and the legal environment. *International Journal of Drug Policy*, *26*, S27–S32.

Tilson, H. A. A., & Bozzette, S. (2007). *Preventing HIV infection among injecting drug users in high-risk countries: An assessment of the evidence*. Washington, DC: Institute of Medicine.

TRan, B. X., & Nguyen, L. T. (2013). Impact of methadone maintenance on health utility: Health care utilization and expenditure in drug users with HIV/AIDS. *International Journal of Drug Policy*, *24*(6), e105–e110.

Tran, B. X., et al. (2012). The cost-effectiveness and budget impact of Vietnam's methadone maintenance treatment programme in HIV prevention and treatment among injection drug users. *Global Public Health*, *7*(10), 1080–1094.

UNAIDS. (2012). *UNAIDS report on the global AIDS epidemic* http://www.unaids.org/en/media/unaids/contentassets/documents/epidemiology/2012/gr2012/20121120_UNAIDS_Global_Report_2012_en.pdf

UNAIDS. (2013). *Global Report UNAIDS report on the global AIDS epidemic 2013*. UNAIDS.

UNODC Scientific Consultation: Vienna, 11 March 2014. (2014). *Science addressing drugs and HIV: State of the Art of Harm Reduction. A Scientific Statement*.

Van Den Berg, C., et al. (2007). Full participation in harm reduction programmes is associated with decreased risk for human immunodeficiency virus and

hepatitis C virus: Evidence from the Amsterdam Cohort Studies among drug users. *Addiction*, *102*(9), 1454–1462.
Vickerman, P., et al. (2006). The cost-effectiveness of expanding harm reduction activities for injecting drug users in Odessa, Ukraine. *Sexually Transmitted Infections*, *33*(10 Suppl.), S89–S102.
Vickerman, P., Miners, A., & Williams, J. (2008). *Assessing the cost-effectiveness of interventions linked to needle and syringe programmes for injecting drug users: An economic modelling report*.
Wammes, J. J., et al. (2012). Cost-effectiveness of methadone maintenance therapy as HIV prevention in an Indonesian high-prevalence setting: A mathematical modeling study. *International Journal of Drug Policy*, *23*(5), 358–364.
WHO. (2009). *Asessessment of compulsory treatment of people who use drugs in Cambodia, China, Malaysia and Vietnam: An application of selected human rights principles*. WHO Western Pacific Region.
WHO, U., UNAIDS. (2009). *WHO, UNODC, UNAIDS Technical Guide for countries to set targets for universal access to HIV prevention, treatment and care for injecting drug users*. World Health Organization.
WHO. (2012). *Social contexts of access to treatment and care for HIV, hepatitis C and tuberculosis among people who inject drugs in European cities*.
Wilson, D. P. (2010). Evidence is still required for treatment as prevention for riskier routes of HIV transmission. *AIDS*, *24*, 2891–2893.
Wilson, D., & Fraser-Hurt, N. (2013). The economics and financing of harm reduction. *IHRA*.
Wilson, D. P., et al. (2008). Relation between HIV viral load and infectiousness: A model-based analysis. *Lancet*, *372*(9635), 314–320.
Wilson, D., et al. (2014). The economics, financing and implementation of HIV treatment as prevention: What will it take to get there? *AJAR – African Journal of AIDS Research*, *13*(2), 109–119.
Wodak, A. (2006). Lessons from the first international review of the evidence for needle syringe programs: The band still plays on. *Substance Use & Misuse*, *41*(6–7), 837–839.
Wodak, A., & Cooney, A. (2005). Effectiveness of sterile needle and syringe programs. *International Journal of Drug Policy*, *16*(Supplement 1), 31–44.
Wodak, A., & Maher, L. (2010). The effectiveness of harm reduction in preventing HIV among injecting drug users. *NSW Public Health Bulletin*, *21*(3–4).
Wood, E., et al. (2002). Factors associated with persistent high-risk syringe sharing in the presence of an established needle exchange programme. *AIDS*, *16*(6), 941–943.
World Health Organization. (2013). *WHO | Injecting drug use*. Available from: http://www.who.int/hiv/topics/idu/en/index.html [accessed 07.17.13]
Wu, W. Z. (2013). Arguments in favour of compulsory treatment of opioid dependence. *Bulletin of the World Health Organization*, *91*(2), 142–145.
Wu, Z. Y., Shi, C. X., & Detels, R. (2013). Addressing injecting drug use in Asia and Eastern Europe. *Current HIV/AIDS Reports*, *10*(2), 187–193.
Yancovitz, S. R., et al. (1991). A randomized trial of an interim methadone maintenance clinic. *American Journal of Public Health*, *81*(9), 1185–1191.