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Elimination of HIV transmission through novel and established prevention strategies among people who inject drugs

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Abstract

Despite the effectiveness of existing HIV prevention strategies for people who inject drugs (PWID), uncontrolled outbreaks of HIV among this group are common and occur around the world. In this Review, we summarise recent evidence for novel and established HIV prevention approaches to eliminate HIV transmission among PWID. Effective HIV prevention strategies include mobile needle and syringe programmes, pre-exposure prophylaxis, supervised injection facilities, and, to a lesser extent, some behavioural interventions. Studies have also shown the cost-effectiveness of long-standing HIV prevention strategies including needle and syringe programmes, opioid agonist therapy, and antiretroviral therapy for prevention. Although each individual intervention can reduce the risk of HIV acquisition among PWID, there is a consensus that a combination of approaches is required to achieve substantial and durable reductions in HIV transmission. Unfortunately, in many settings, the implementation of these interventions is often limited by public and political opposition that manifests as structural barriers to HIV prevention, such as the criminalisation of drug use. Given that there is ample evidence showing the effectiveness of several HIV prevention methods, social and political advocacy will be needed to overcome these barriers and integrate innovative HIV prevention approaches with addiction science to create effective drug policies.

Introduction

Injection drug use causes substantial morbidity and mortality in many settings worldwide.¹ A 2017 report estimated that 15.6 million people inject drugs in 179 countries or territories.¹ Use of contaminated injection equipment is an important route for the transmission of HIV and other blood-borne viruses such as hepatitis C virus (HCV).² The risk of HIV infection

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HR, M-JM, and BDLM designed the concept, search strategy, data collection, and structure of the Review. HR and M-JM led the writing of the manuscript. All authors contributed substantially, reviewed the article for intellectual content, and approved the final version.

Declaration of interests

The authors declare no competing interests.

associated with using an HIV-contaminated syringe (0.63–2.4% per injection) is considerably greater than the risk of HIV transmission associated with penile–vaginal sex among HIV serodiscordant heterosexual couples (0.02–0.05% per act).^{3,4} In 2015, an estimated 17.8% of people who inject drugs (PWID) globally were living with HIV, among whom only a small proportion had access to antiretroviral therapy (ART).^{1,5} As a result of very limited access to ART and other forms of evidence-based HIV prevention, uncontrolled transmission and outbreaks of HIV have persisted in many settings, including regions of Canada, India, Russia, and the USA.^{6,7}

To prevent acquisition of HIV and other blood-borne pathogens among PWID, several effective prevention strategies have been developed, including needle and syringe programmes, voluntary counselling and testing, opioid agonist treatment, supervised injection facilities, and ART.^{8,9} Evidence from several locales, including Australia and the UK, suggest that the early implementation of combination, large-scale HIV prevention programmes for PWID prevented the establishment of generalised HIV outbreaks in these populations.^{10,11} Other settings, such as New York City (USA), Vancouver (Canada), and France provide evidence that implementing a combination of multiple HIV prevention and care strategies can substantially decrease HIV transmission and morbidity and mortality related to AIDS among PWID once an epidemic is established.⁷ Rapid and substantial reductions in HIV incidence were observed in these settings after large-scale implementation of needle and syringe programmes, opioid agonist therapy, and ART. Lasting decreases in HIV incidence were observed several years after initial implementation, with incidence rates as of 2016 below 1 per 100 person-years in all three settings and the virtual elimination of AIDS-related mortality among PWID.⁷

Despite the success of these interventions in multiple settings, global coverage of HIV prevention services is estimated to be far below the level required to achieve control of the global pandemic among PWID.^{10,12} For example, studies predict 200–1000 sterile syringes per year are needed for each PWID and the specific amount varies based on the type of drug use (eg, cocaine users often inject 20–30 times per day¹³); however, an average of only 22 (range 12–42) are distributed.^{12,14} Nearly 83% of PWID primarily inject opioids and only an estimated 8% (range 6–12) are receiving opioid agonist therapy.^{1,12} Finally, 2.8 million PWID are estimated to be living with HIV, just 4% of whom (range 2–18) are receiving ART.^{1,12} Potential explanations for poor coverage of these HIV prevention services have included stigma against illicit drug use, criminalisation as the dominant societal response to drug use, and insufficient provider and public knowledge surrounding the neuropsychiatric causes of addiction, which often manifest as political opposition to harm reduction policies and structural barriers that limit access to addiction services.^{7,15,16} Punitive laws for drug use and possession of injection equipment persist as barriers to the access of crucial HIV prevention services in several countries.^{16,17} Insufficient coverage of programmes has contributed to HIV outbreaks among PWID in Athens (Greece), Dublin (Ireland), Scott County (USA), and Tel Aviv (Israel) in the past 7 years.⁷

In response to these barriers and limited coverage of existing HIV prevention methods, novel strategies and modifications to existing methods have been developed to help to eliminate HIV epidemics among PWID. We review the recent evidence of novel and established HIV

prevention methods among PWID and provide recommendations for the application of these interventions in emerging and existing epidemic settings.

Individual, behavioural, and biomedical interventions

Needle and syringe programmes

The effectiveness of needle and syringe programmes in the reduction of injection-related risk behaviours and HIV incidence among PWID is well established. Evidence from a systematic review and meta-analysis showed that use of needle and syringe programmes was associated with a 44–58% decrease in HIV transmission rates among a pooled sample of 12 023 PWID who contributed 11 984 person-years of follow-up.¹⁸ Needle and syringe programmes are cost-effective for prevention of HIV acquisition in settings such as the USA.⁹ One model-based analysis projected that needle and syringe programme coverage of 50% could avert up to 35 000 HIV infections over 20 years and cost US\$25 000 per quality-adjusted life-year (QALY) gained, an expense well below the \$50 000 cost-effectiveness threshold for health-care interventions in the USA.⁹ Although many early programmes restricted the number of needles provided or operated on a basis of providing one for each returned, increasingly, programmes do not limit the number of needles distributed per client and also provide supplementary equipment to facilitate safer injection.¹⁹ These programmes have now expanded in some settings to distribute needles and syringes through pharmacies, hospitals, vending machines, street outreach, secondary syringe exchange programmes, and mobile needle and syringe programmes in an effort to maximise access to this effective HIV prevention service.²⁰ Mobile needle and syringe programmes are now recommended by the WHO, UNAIDS, and UN Office on Drugs and Crime as an alternative or complementary delivery method of needle and syringe programmes and additional harm reduction services.²¹ Mobile programmes attract high-risk groups of PWID who are difficult to reach and not covered by other models of service, because they reduce barriers such as stigma, transportation or physical mobility challenges, and exposure to local policing.²⁰ Mobile needle and syringe programmes have successfully decreased rates of syringe sharing and have been widely accepted by residents of communities in which they are implemented. Furthermore, findings from a randomised controlled trial showed that delivery of case management through a mobile needle and syringe programme facilitated entry into drug treatment.²⁰

Despite being a cost-effective method of HIV prevention, opposition to the implementation of standalone and mobile needle and syringe programmes continues. Both micro-level (eg, local communities objecting to the presence of harm reduction organisations) and macro-level (eg, national bans on needle and syringe programmes or their funding) barriers have hindered the expansion of these programmes in some countries with the highest burdens of HIV among PWID, such as Russia and the USA.^{6,17}

Behavioural interventions

Evaluations of the efficacy of behavioural interventions to decrease risk of HIV transmission among PWID have produced contradictory results.²² A study from 2006 showed some benefit of behavioural interventions for frequency of injection drug use, although the effect

of these interventions on the frequency of needle and syringe sharing was not significant.²³ However, a randomised controlled trial published in 2015 that incorporated motivational interviewing in an HIV prevention intervention found that participants in the motivational interviewing group were 50% less likely to report any type of injection risk behaviour than were participants in a brief educational intervention group. Both groups displayed significant decreases in several HIV risk behaviours, including used syringe sharing.²⁴ Other recent trials evaluating behavioural interventions have shown promising results, particularly among couples and sex workers who inject drugs.²⁵ Observational evidence from a multicentre study of an innovative community-based educational intervention to reduce injection-related risk showed significant reductions in HIV and HCV risk practices, and these benefits persisted 6 months after conclusion of the intervention.²⁶

Pre-exposure prophylaxis (PrEP)

The Bangkok Tenofovir Study²⁷ was the first to show efficacy of antiretroviral prophylaxis for HIV infection among PWID. Although the reduction in incidence associated with use of PrEP was substantial, effectiveness was moderated by adherence to therapy. The estimated reduction in risk of HIV infection was 48.9% in the overall sample, 58.0% among those with at least 75% adherence, and 83.5% among those with at least 97.5% adherence.²⁸ In 2017, the US Centers for Disease Control and Prevention (CDC) released updated clinical practice guidelines, which recommend that PrEP be considered for any adult who has injected drugs in the past 6 months and has reported sharing injection or drug preparation equipment or has an elevated risk of sexual HIV acquisition.²⁹

Economic analyses of PrEP effectiveness in the USA have estimated that 50% coverage among PWID could avert up to 37 000 HIV infections and cost \$300 000 per QALY gained over 20 years, with even the lower 95% confidence interval for this estimate (\$162 000) well above typical thresholds of cost-effectiveness (\$50 000).^{9,30} However, cost-effectiveness improves significantly with increased adherence, and the health benefits associated with PrEP are greatest among people with the highest risk of HIV infection (eg, male PWID who have sex with men).³¹ Because HIV prevalence is a useful correlate of risk, focusing PrEP in communities with high prevalence where other prevention services are scarce might yield the most value and potentially cost less than \$100 000 per QALY.³¹

Opioid agonist therapy

The two most commonly prescribed pharmacotherapies for opioid use disorder are methadone and buprenorphine, with the latter often formulated as buprenorphine-naloxone.³² Systematic reviews examining the effect of methadone maintenance therapy on HIV risk behaviours among high-risk PWID found that this approach significantly decreased frequency of injection drug use and sharing of injection equipment, and resulted in a 54% reduction in the risk of HIV acquisition.^{33,34} Adherence was identified as the most important factor in HIV risk reduction, and further efforts are required to enhance access and adherence to methadone maintenance therapy to maximise its benefits.³³ A randomised controlled trial evaluating the effect of buprenorphine-naloxone on HIV prevention among HIV-negative, opioid-dependent PWID was terminated early owing to a lower than expected number of outcome events (ie, incident HIV infections).³⁵ However, there were significant

reductions in the frequency of injection drug use and sharing of used injection equipment among those receiving buprenorphine-naloxone, compared with baseline.³⁵ Another trial comparing methadone maintenance therapy with buprenorphine-naloxone showed significant reductions in injection-related HIV risk behaviours in both study groups, with no differences for frequency of opioid use, number of injections, used-needle sharing, and sharing other injection equipment.³⁶ Although more participants were retained in the methadone group, HIV risk behaviour was equally and significantly decreased in both groups.³⁶ A study quantifying the effect of opioid agonist therapy on injection frequency estimated that methadone maintenance therapy and buprenorphine-naloxone decreased the number of injections by about 55%, and a systematic review found that opioid agonist therapy increased ART coverage, adherence, and viral suppression among PWID.^{34,37}

A guideline published in 2018 recommends that the model of opioid agonist therapy should incorporate provider-led counselling, long-term substance use monitoring, comprehensive preventive and primary care, psychosocial services, and specialist care.^{38,39} Although traditionally offered in specialist care facilities, provision of opioid agonist therapy in primary care settings maintains equivalent efficacy for some populations, with the added benefit of addressing common comorbidities.^{40,41} The most effective model of opioid agonist therapy care for PWID depends on the population and local setting; a common feature of successful programmes is coordinated health-care teams with clinical care managers who previously worked as advanced practice clinicians.³⁸

A cost-effectiveness analysis of opioid agonist therapy in the USA projected that 50% coverage could avert up to 22 000 HIV infections over 20 years and cost \$18 000 per QALY gained,⁹ well below the conventional cost-effectiveness threshold of \$50 000 per QALY.³⁰ This study also found that compared with needle and syringe programmes, HIV testing and treatment with ART, and PrEP, opioid agonist therapy has the potential to be the highest value investment even if it averts fewer HIV infections than other interventions. The authors attributed this result to the direct impact of opioid agonist therapy on the length and quality of life among treated individuals.⁹

ART

Seek, test, treat, and retain initiatives aim to suppress HIV transmission by engaging all people living with HIV in effective ART. Prompt initiation of ART upon diagnosis not only produces therapeutic benefits for the individual, but also lowers HIV viral load at the community level, and confers a potential preventive effect (ie, herd immunity) for the populations at risk.⁴² Suppression of viral load among those living with HIV reduces the risk of transmission, even if HIV-positive people engage in injection or sexual risk behaviours.^{42,43} The benefits of seek, test, treat, and retain strategies have been reflected in reforms to health-care policies, including the elimination of a CD4 cell count threshold for ART initiation, and endorsing of immediate ART initiation after diagnosis in some settings.⁴⁴ Seek, test, treat, and retain initiatives have achieved substantial increases in the prevalence of individual-level viral load non-detectability and decreased incidence of HIV.^{45,46} A projection of the cost-effectiveness of HIV testing and treatment with ART in the USA estimated that 50% coverage could avert 6700 HIV infections over 20 years and cost \$27

000 per QALY gained.⁹ Despite the success and cost-effectiveness of these initiatives, only 4% of HIV-positive PWID globally are estimated to be receiving ART.¹² The challenges of clinically managing HIV in people with co-occurring substance use are compounded by punitive criminal justice-based approaches that criminalise drug use, lower levels of ART access, negatively affect adherence, and decrease the likelihood of viral load non-detectability among PWID.⁴⁷ Additionally, given the prevalence of comorbid mental health disorders and addiction among HIV-positive PWID, multifaceted seek, test, treat, and retain interventions tailored to the unique needs of PWID will be needed to maximise the effectiveness of these initiatives.⁴⁸

Physical environment interventions

Supervised injection facilities provide a legally sanctioned setting in which PWID can inject illicit substances with sterile equipment under medical supervision. These facilities have existed in European countries since the 1980s; the first state-sanctioned facility in North America opened in Vancouver, Canada in 2003 (figure).⁴⁹ About 90 supervised injection facilities have been established in Australia, Canada, and Europe, and they have substantial benefits without any apparent negative effects on public health and safety.^{50–52} Modelling studies estimate that an existing supervised injection facility located in Vancouver, Canada, averted an average of 35 HIV infections per year (range 19–57).⁵¹ The projected benefits of establishing additional facilities in other North American cities estimate that one facility could prevent over 350 HIV infections over 20 years and cost CAN\$6127 per QALY gained.⁵³ Political opposition remains the primary barrier to the expansion of supervised injection facilities in many countries, and this resistance is often based on concerns about increased levels of crime and illicit drug use in communities where they are established.⁵⁴ However, evidence from North America's first facility indicates that drug-related crime or community drug use has not increased and instead the facility has had benefits at the community level, including reductions in measures of public disorder and increased enrolment in detoxification and addiction treatment programmes.^{49,55–57}

Although legally sanctioned supervised injection facilities have been present since 1986, as of 2017, there have been recommendations to modify the operation and policies within existing and future facilities to reduce HIV transmission among PWID.⁵⁴ A major limitation of many facilities is that staff are not legally permitted to provide injection assistance for clients. As many as a third of PWID require assistance with injecting, and being unable to inject autonomously is an independent risk factor for HIV infection, overdose, and experiencing violence.⁵⁴ In some settings the prevalence of HIV among those requiring assistance with injecting is more than double the prevalence of those not requiring assistance.⁵⁸ As a response to this high prevalence, unsanctioned, peer-run supervised injection facilities that provide injection assistance have been established, which have reduced the risks associated with traditional restrictions, while also increasing coverage by removing sociostructural barriers to use of the facilities.^{54,59} Because a disproportionate number of women require assistance with injecting, and women are particularly vulnerable to violence in illicit drug markets, the world's first women-only supervised injection facility was established in Vancouver, Canada, in 2017. Additional novel recommendations for the application of supervised injection facilities include efforts to increase access by

implementing services in hospitals and prisons where injecting safely can be challenging, and creating mobile facilities to reach individuals who have difficulty accessing fixed sites, such as people with disabilities.⁵⁴

Social network interventions

Peer-based HIV prevention strategies typically involve recruiting PWID through street outreach programmes who are then trained to promote the adoption of safer injection behaviours throughout their drug use networks. A systematic review and meta-analysis of 30 peer-based intervention studies found a 63% reduction in equipment sharing among PWID.⁶⁰ A randomised controlled trial among young PWID from five US cities identified a substantial decrease in equipment sharing in the peer-education intervention group; however, this effect was restricted to PWID who showed high-risk injection behaviour at baseline.⁶¹ A cluster randomised controlled trial identified a significant reduction in HIV incidence associated with a social network intervention among PWID.⁶² The intervention included five small group training sessions delivered over 2 weeks to provide peer leaders with skills to educate their injection networks about injection risk reduction behaviours. The intervention group included the social network intervention in addition to testing and counselling, whereas the control group included only testing and counselling. Over a 28 month follow-up period, the authors reported a hazard ratio for HIV incidence of 0.53 ($p < 0.001$) among the social network intervention group.⁶² In an 8 year longitudinal study of a cross-border intervention in China and Vietnam, peer education coupled with peer-assisted needle or syringe distribution was associated with significant reductions in injection risk behaviours and HIV prevalence that were not observed in neighbouring regions without these interventions.⁶³

HIV interventions for couples might also reduce HIV risk among PWID.⁶⁴ A randomised controlled trial among 300 heterosexual couples, in which one or both partners reported injection drug use, found that a risk-reduction intervention over five sessions reduced the incidence of HIV infection by 69% over a 12 month follow-up period. However, these differences were not significant, and the effect was driven mainly by changes in sexual behaviour.⁶⁴ Given the increased risk of HIV acquisition among the sexual and drug injecting partners of people diagnosed with HIV, the WHO and CDC recommend HIV partner testing services to increase rate of diagnosis and initiation of HIV care.^{65,66} The documented benefits of partner and couples HIV testing services include improved access, adherence, and retention in treatment and care services, and serodiscordant couples are able to consider additional HIV prevention methods such as condom use, ART, and PrEP to prevent HIV acquisition among HIV-negative partners.^{32,66,67} The table summarises selected evidence evaluating novel and established HIV prevention strategies.

Policy environment interventions

Despite the well established benefits of existing HIV prevention methods for PWID, the overall effect of these interventions is largely contingent upon governmental support. Policy-related interventions for PWID typically include efforts to decrease the health risks associated with the criminalisation of drug use, promote novel harm reduction approaches to

prevent HIV, and ensure that law enforcement activities do not interfere with service access among PWID.⁸ The removal of legal restrictions to facilitate harm reduction services for PWID has effectively decreased HIV incidence in several countries, including those with the highest burden of injection drug use.⁶ In Asia and Ukraine, reforms to punitive drug policies and improved access to HIV prevention and treatment services have successfully increased the coverage of ART and opioid agonist therapy among PWID.⁶ However, an unwillingness to fund these programmes (and in some cases active resistance to these interventions) has persisted in some countries, including Russia and the USA. In the USA, federal funds can now be used to support syringe service programmes, following demonstration of a so-called determination of need that indicates a jurisdiction is already experiencing or is at high risk of a blood-borne disease outbreak resulting from injection drug use; however, funds cannot be used to purchase sterile needles or syringes for drug injection.⁶⁸ Moreover, the coverage of opioid agonist therapy remains modest in many US settings.^{6,9} The Russian Government's refusal to fund needle and syringe programmes led to a 60% decrease in coverage among PWID from 2010 to 2011; even the dissemination of information about opioid agonist therapy is now prohibited.⁶

Federal and state laws banning the possession of sterile injecting equipment for non-medical purposes remain a key barrier to the effective provision of HIV prevention services for PWID in many settings. However, a state US law prohibiting non-medical use of needles (a felony punishable by up to 3 years in prison) was suspended during the 2015 HIV outbreak in Scott County, Indiana, which contributed to significantly decreased injection risk behaviours.^{17,69} The restrictive needle and syringe programme policy in Scott County delayed the implementation of an effective HIV prevention strategy until after an outbreak had already occurred. Temporary suspension of the ban is an admission that policy makers recognised the effectiveness of needle and syringe programmes, but the unwillingness to fund these programmes as a prevention strategy reaffirms misconceptions and stigma.¹⁷ Removal of the ban on using municipal revenue to fund needle and syringe programmes in Washington, DC, is another example of a policy intervention that showed the benefits of a harm reduction policy. A forecasting analysis of these programmes in this setting suggested that the intervention averted 120 cases of HIV over 2 years.⁷⁰

Policies governing street-level policing practices also influence HIV risk behaviours among PWID. Specifically, police surveillance or increased interactions with law enforcement have been associated with reduced access to needle and syringe programmes, decreased willingness to carry sterile injection equipment, disruption of safe injecting, syringe sharing, displacement from health and social services, and providing assistance to others to initiate injection drug use, all of which increase the risk of HIV transmission.^{71–76} Some police departments that have had policy shifts from punitive strategies to a harm reduction approach have substantially decreased police practices that hinder harm reduction initiatives among PWID, including the confiscation of drug use paraphernalia.⁷⁷ Because policing is a common structural barrier to the access of HIV prevention methods, educating police about the harm reduction strategies and promoting progressive law enforcement policies will be crucial to create an environment that can maximise the effectiveness of individual HIV prevention interventions.⁸

Combination interventions

The general scientific consensus is that a combination of HIV prevention strategies is needed to effectively combat HIV outbreaks; no recommended single strategy addresses all risk factors for HIV transmission, and greater improvements are often observed when multiple interventions are delivered together.⁸ For example, methadone maintenance therapy delivered in conjunction with counselling psychology or contingency management produces a more substantial decrease in the frequency of injection drug use and HIV incidence than has the therapy alone.⁷⁸ Supplementation of voluntary counselling and testing for HIV with methadone maintenance therapy has also been associated with greater reductions in used needle sharing compared with voluntary counselling and testing alone.⁷⁹ An ecological study of PWID in Estonia found that the combined application of needle and syringe programmes and ART resulted in significant decreases in HIV incidence from 2005 (20.7 HIV cases per 100 person-years) to 2011 (7.5 HIV cases per 100 person-years).⁸⁰ A combination HIV prevention intervention in India incorporated needle and syringe programmes and safer injection education in conjunction with sexual risk interventions and found significant improvements in injection practices and consistent condom use, although rates of needle and syringe sharing and HIV prevalence remained unchanged.⁸¹ In response to an HIV outbreak in Athens, Greece, a combined intervention of needle and syringe programmes, HIV testing, linkage to opioid agonist therapy and HIV care, or ART resulted in reductions in injection frequency and syringe sharing over 1 year (2012–13). The incidence of HIV infection per 100 person-years decreased from 7.8 to 1.7.⁸² A model-based economic analysis of the expansion of a combination of HIV prevention strategies projected that scale-up of opioid agonist therapy, needle and syringe programmes, and coverage of seek, test, treat, and retain initiatives to 50%, in that order, would be cost-effective and each additional intervention expansion would cost less than \$50 000 per QALY gained. The expansion of these interventions is estimated to prevent up to 43 400 HIV infections over 20 years, which could translate to a 27% decrease in HIV prevalence among PWID.⁹

An additional benefit of providing HIV prevention services in combination is that it increases the likelihood that PWID will regularly access HIV testing services. The diagnosis of HIV among PWID and their sexual or injection partners is necessary to increase access to HIV care and prevention (eg, ART and PrEP), and is essential to curb viral transmission among PWID.^{32,67}

In low-income and middle-income countries where resources to address HIV prevention can be limited, selection of the combination of interventions to implement will depend on the cost-effectiveness of each intervention. Opioid agonist therapy seems to be the most cost-effective intervention, even when it prevents fewer infections, because it has a direct effect on the length and quality of life.⁹ Additionally, the evidence also indicates that increasing coverage of opioid agonist therapy (\$18 000 per QALY gained), followed by increasing needle and syringe programme coverage (\$25 000 per QALY gained) and then increasing ART coverage (\$27 000 per QALY gained) all to 50% can be a cost-effective approach to maximise the benefit of these interventions and could be applicable in settings with limited resources.⁹

Importantly, many of these interventions are also effective HCV prevention strategies. The sharing of injection equipment is the main risk factor for HCV transmission among PWID, and HCV has higher transmissibility through syringe sharing than does HIV.⁸³ Two of the primary prevention interventions for HIV and HCV among PWID are opiate agonist therapy and needle and syringe programmes, and scaling up these interventions to 80% coverage has been estimated to achieve a 29–90% decrease in HCV incidence in three UK settings over 15 years.^{22,84} Similar to HIV prevention, delivery of these interventions in combination displayed a greater effect on HCV prevention than did either intervention individually.⁸⁵

Conclusion

The use of illicit drugs by injection substantially contributes to morbidity and mortality on a global scale and is a fundamental component of the HIV pandemic. Needle and syringe programmes, opioid agonist therapy, and ART can curb HIV transmission and can successfully prevent generalised HIV outbreaks if implemented on a large scale, as well as decrease HIV transmission in response to HIV outbreaks. Many novel interventions, such as mobile needle and syringe programmes, PrEP, peer-based education and network interventions, and peer-run supervised injection facilities also have promise for HIV prevention, as have modifications to existing strategies. Improving the coverage of established interventions will be vital to prevent potential HIV outbreaks among PWID, and specific interventions such as facilitating assisted injection could be particularly beneficial for PWID who are unable to inject independently and experience a disproportionate burden of HIV.⁵⁸ Any single intervention, even with high coverage, is likely to have a minor effect on HIV transmission unless implemented concurrently with other strategies. The benefit and cost-effectiveness of combined approaches to HIV prevention have been repeatedly shown through empirical evidence and model-based projection studies. However, the success of any HIV intervention approach will be moderated by institutional support. Improving public and political support for evidence-based HIV prevention, addiction science, and drug policy will be crucial to remove existing barriers to HIV prevention services and eliminate HIV outbreaks among PWID.

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Search strategy and selection criteria

We searched published literature in PubMed, MEDLINE, and Embase up to April, 2018. The specific search terms for each database are included in the appendix. We used keywords relating to the three principal topics that included “HIV”, “prevention” and “injection drug use”. The results were restricted to English language articles and human studies. To focus on novel evidence on HIV prevention methods, we restricted our search to articles published after 2008. Eligibility criteria for the articles retrieved included: a sample that included or was restricted to PWID; evaluation of an intervention designed to decrease HIV transmission; and analysis of outcomes of HIV incidence, HIV prevalence, or injection risk behaviour (eg, needle or syringe sharing). The reference lists of relevant articles were also reviewed to identify additional studies. The data extracted from the eligible articles were based on the PICOT format and included study design, study location, sample size, sample characteristics (age, gender, ethnicity), type of drug use, prevention method, length of intervention, co-interventions, outcome variable, outcome measurement, major findings or effect size, and study duration. Studies were excluded if they did not focus on PWID or focused on sexual risk reduction rather than injection risk reduction.

Figure:
Photograph of the supervised injection facility established in 2003 in Vancouver, BC, Canada

Table:

Summary of selected evidence evaluating novel and established HIV prevention strategies

	Outcomes analysed	Modifications in service or implementation	Cost-effectiveness (\$ per QALY)
NSP	Injection risk behaviours, ¹⁸ HIV incidence ⁹	Unlimited distribution; ²⁰ distribution through hospitals, pharmacies, secondary syringe exchange, mobile NSPs ²⁰	US\$25 000 ⁹
Behavioural interventions	Injection frequency; ²³ injection risk behaviours ²⁴	Motivational interviewing; ²⁴ educational interventions based on self-determination theory ²⁶	..
PrEP	HIV incidence ²⁷	Tenofovir supplemented with HIV testing and counselling ²⁷	US\$300 000 ⁹
OAT	Injection frequency; ^{33–35} injection risk behaviours; ^{33–35} HIV incidence ^{33,34}	Models of care including provider-led counselling, substance use monitoring, preventive and primary care, psychosocial services and specialist care; ³⁹ providing OAT in primary care settings; ^{40,41} providing coordinated health-care teams managed by advanced practice clinicians ³⁸	US\$18 000 ⁹
ART	HIV incidence ^{45,46}	Elimination of a CD4 cell count threshold for ART initiation and immediately initiating ART following diagnosis in some settings ⁴⁴	US\$27 000 ⁹
SIF	Injection risk behaviour, syringe sharing; ⁵² HIV incidence; ⁵⁴ overdose mortality ⁵⁰	Peer-run SIFs providing assisted injections; ^{54,59} women-only SIFs; ⁵⁴ mobile, hospital-based and prison-based SIFs proposed ⁵⁴	CAN\$6127 ⁵³
Peer-based interventions	Injection risk behaviour, equipment sharing; ^{60,61} HIV incidence ⁶²	Outreach among peers and social networks to contact and train PWID about risk reduction and HIV services ^{60,62,63}	..
Couples-based interventions	HIV incidence ⁶⁴	Risk reduction interventions and HIV testing to promote initiation of care and prevention services ^{32,64,66,67}	..

NSP=needle and syringe programme. QALY=quality-adjusted life-year. PrEP=pre-exposure prophylaxis. OAT=opioid agonist therapy. ART=antiretroviral therapy. SIF=supervised injection facility. PWID=people who inject drugs.