HIV in people who use drugs 2

Prevention of HIV infection for people who inject drugs: why individual, structural, and combination approaches are needed

Louisa Degenhardt, Bradley Mathers, Peter Vickerman, Tim Rhodes, Carl Latkin, Matt Hickman

HIV can spread rapidly between people who inject drugs (through injections and sexual transmission), and potentially the virus can pass to the wider community (by sexual transmission). Here, we summarise evidence on the effectiveness of individual-level approaches to prevention of HIV infection; review global and regional coverage of opioid substitution treatment, needle and syringe programmes, and antiretroviral treatment; model the effect of increased coverage and a combination of these three approaches on HIV transmission and prevalence in injecting drug users; and discuss evidence for structural-level interventions. Each intervention alone will achieve modest reductions in HIV transmission, and prevention of HIV transmission necessitates high-coverage and combined approaches. Social and structural changes are potentially beneficial components in a combined-intervention strategy, especially when scale-up is difficult or reductions in HIV transmission and injection risk are difficult to achieve. Although further evidence is needed on how to optimise combinations of interventions in different settings and epidemics, we know enough now about which actions are effective: the challenge is to deliver these well and to scale.

Introduction
In most world regions, HIV infection is concentrated in subsets of the population exposed to particular HIV transmission risks, such as people who inject drugs.\(^1\) Injecting drug use takes place in 151 countries,\(^3\) with an estimated 11–21 million such users in 2007, of whom 0·8–6·6 million were estimated to be living with HIV.\(^4\)

HIV transmission is a risk for all populations of injecting drug users (IDUs), with potential for the virus to spread rapidly between those who inject drugs (via injections and sexual risk) and, possibly, to the wider community through sexual transmission.\(^5\) The risk of infection after injection with an HIV-contaminated syringe is estimated to be 0·63–2·4% (median 0·8%; around 1 in 125 injections),\(^6\) with a potentially lower, community-wide transmission rate of 0·04·6–0·13·4% for risk behaviour.\(^6\)

Search strategy and selection criteria
We used several search strategies and focused wherever possible on identification of systematic reviews and meta-analyses. First, with respect to interventions to prevent HIV infection, we searched in: the Cochrane Library; the Centre for Reviews and Dissemination (University of York); Evidence-Based Medicine Reviews; the Campbell Collaboration Library of Systematic Reviews; DRUG; Global health; and Project Cork (tailored search terms for each database are described in detail in the webappendix pp 1–3). Second, relating to structural interventions for prevention of HIV infection in injecting drug users, we did a systematic search for published work in: PubMed; Medline; the Cochrane review library; and Embase (search terms listed in the webappendix pp 3–4); and we reviewed reference lists of relevant articles. Finally, we summarised a published systematic review\(^7\) of needle and syringe programmes, opioid substitution treatment, and antiretroviral treatment for HIV-positive people who inject drugs.

Key messages
- Opioid substitution therapy (OST), needle and syringe programmes (NSPs), and antiretroviral therapy (ART) reduce risks of HIV infection in injecting drug users (IDUs)
- Individual-based and network-based psychosocial interventions can reduce injecting and sexual risk; people who inject drugs can play an important part in development and delivery of such responses
- Augmented research and programme attention needs to be directed towards psychostimulant injectors, since proven pharmacotherapies for substitution do not exist as they do for opioids
- Model projections suggest high coverage of ART, OST, and NSPs in combination are important for reduction of incidence of HIV infection in IDUs by more than 50%; very high intensity and coverage of single interventions is necessary to achieve similar effects; short-term, small-scale, single interventions are unlikely to be effective
- Current coverage of interventions for injecting drug use is inadequate; annually worldwide, perhaps 5% of drug injection users are covered by a sterile needle and syringe provided by an NSP; eight clients receive OST for every 100 IDUs (range 6–12); and four IDUs receive ART for every 100 HIV-positive IDUs (range 2–18)
- Structural interventions might be needed when scale-up is difficult or when intervention efforts do not reduce injecting risk and transmission of HIV infection; an innovative evaluative evidence base is needed to understand the effect of structural interventions
- Surveillance of the epidemic and response is crucial, but typically poor; studies of transmission of HIV infection and effects of interventions should have funding priority and be nested in ongoing surveillance programmes; evaluation of interventions should include cost-effectiveness studies
- Limitations in evidence need not limit response; sufficient justification exists on human rights and public-health grounds for scaling up now; evidence-based prevention of HIV infection should be a policy priority in all countries where injecting drug use takes place
Reduction of injections and injecting risk behaviours

**Needle and syringe provision**

By increasing the amount of clean equipment in circulation and keeping to a minimum the time that infected needles are in use, the number of unsafe injections can be reduced. A range of distribution models have been developed, including: free NSPs, through fixed and outreach models; vending machines selling injecting equipment; sales of injecting equipment, typically through pharmacies; and distribution of equipment by IDUs or their peers. NSPs are the most studied models. Strong evidence shows that these programmes reduce risk from injections, thereby increasing safe injection. A less direct link exists between NSPs and reduction of HIV incidence (see Reduction of HIV incidence). Their effect is likely to be proportional to the volume of needles and syringes distributed and entering circulation and the number of IDUs receiving sufficient sterile syringes to cover all injections.

**Agonist and antagonist pharmacotherapy**

By reduction of drug use and, therefore, injection frequency, effective interventions for drug dependence can reduce unsafe injection. OST is the mainstream of treatment for opioid dependence. This strategy reduces injecting and increases safe injections; it is associated with many improvements, including health and social functioning. High doses and extended treatment are associated with further reductions in drug use and HIV risk, moreover, outcomes are better if OST is delivered alongside psychosocial interventions. Methadone and buprenorphine are listed by WHO as essential for treatment of opioid dependence, in view of strong evidence of their effectiveness. Methadone and buprenorphine are listed by WHO as essential for treatment of opioid dependence, in view of strong evidence of their effectiveness. Heroin-assisted treatment (medical prescription of diacetylmorphine with supervised self-administration) with psychosocial support can be effective at reduction of illicit heroin use for individuals who have failed repeatedly with other OST approaches.

Despite substantial research investment, current pharmacotherapies for cocaine or (meth)amphetamine (rINN [met]amfetamine) dependence are not effective. Oral naltrexone (an opioid antagonist) is efficacious during treatment for heroin dependence, but low client interest, daily dosing, and high rate of dropouts limit its effectiveness. Findings of a Cochrane review concluded it did not retain patients or reduce relapse compared with placebo. A controlled trial of implantable naltrexone has been undertaken, but controlled evidence to show its effectiveness is insufficient.

**Psychosocial treatments for drug dependence**

Non-pharmacological treatments are used for all forms of drug dependence. Therapeutic communities, cognitive behavioural treatment, and other psychologically based interventions are typical modalities. Psychosocial interventions can be delivered one-on-one by a counsellor to an IDU, in a group, or if a user of injecting drugs has a

Interventions targeting people who inject drugs

Table 1 details evidence of the effect of different interventions on various outcomes of interest (a glossary describing these strategies is in the webappendix p 5). The grades (A–D) describe the highest level of evidence available for the domains. Several points are salient. First, the strength of evidence varies across interventions. Second, at present, approaches with the greatest potential effect seem to be needle and syringe programmes (NSPs), opioid substitution treatment (OST), and ART. Third, data for the effect of interventions on some outcomes are lacking. Finally, no one strategy encompasses all HIV risk factors in IDUs, which suggests that a combination of approaches is needed.
<table>
<thead>
<tr>
<th>Intervention</th>
<th>Effect</th>
<th>Level</th>
<th>Refs</th>
<th>Testing for HIV and informing individuals of their serostatus</th>
<th>Number of injecting episodes</th>
<th>Injecting risk behaviour</th>
<th>Number of sexual partners</th>
<th>Sexual risk behaviour</th>
<th>HIV infectivity</th>
<th>HIV incidence</th>
<th>Cost-effectiveness</th>
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<tbody>
<tr>
<td>Testing for HIV and informing individuals of their serostatus</td>
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<td>↓ A* 12</td>
<td>↓ A* 12</td>
<td>↓ A* 12</td>
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<td>Individual behavioural interventions addressing HIV risk</td>
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<td>↓ A 13</td>
<td>↓ C 13,14</td>
<td>↓ A 13-16</td>
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<tr>
<td>Couple interventions addressing HIV risk</td>
<td>↓ A† 17</td>
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<td>-</td>
<td>-</td>
<td>↓ B* 18</td>
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<tr>
<td>Network or peer-based interventions addressing HIV risk</td>
<td>↓ A 13</td>
<td>↓ A 19</td>
<td>..</td>
<td>↓ A 13,19</td>
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<td>Provision of sterile injecting equipment (typically needles and syringes)</td>
<td>X A 20</td>
<td>↓ A 20,21</td>
<td>-</td>
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<td>↓ C 21</td>
<td>Y A 20,22</td>
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<td>Condom provision</td>
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<tr>
<td>Opioid substitution therapy</td>
<td>↓ A 20,25-27</td>
<td>↓ A 20,25</td>
<td>↓ A 20,25</td>
<td>X A 20,25</td>
<td>-</td>
<td>-</td>
<td>↓ C 20,28</td>
<td>Y A 20</td>
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<td>Opioid antagonists (oral)</td>
<td>X C 29,30</td>
<td>X C 29,30</td>
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<tr>
<td>Opioid antagonists (implant)</td>
<td>↓ B 29,30</td>
<td>↓ B 29,30</td>
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<tr>
<td>Pharmacological treatments for psychostimulant dependence</td>
<td>X A 31-33</td>
<td>X A 31-33</td>
<td>X A 31-33</td>
<td>X A 31-33</td>
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<tr>
<td>Cognitive behavioural therapy for psychostimulant dependence</td>
<td>↓ A 34</td>
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<tr>
<td>Treatment of sexually transmitted infections</td>
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<td>Antiretroviral treatment</td>
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<td>A* 38</td>
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<td>A* 38</td>
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<td>D 39</td>
<td>↓ A*D 38,39</td>
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<tr>
<td>Supervised injecting centres</td>
<td>X C 40,41</td>
<td>↓ C 40,41</td>
<td>-</td>
<td>-</td>
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<td>-</td>
<td>-</td>
<td>Y D 42,43</td>
<td>-</td>
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</tr>
<tr>
<td>Compulsory detention of drug users</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>↑ D* 44-46</td>
<td>↑ D* 44-46</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>N D 47</td>
<td>-</td>
</tr>
</tbody>
</table>

Y=yes. N=no. X=intervention does not seem to have a significant effect on outcome. ↑=outcome could be increased by the intervention. ↓=outcome is decreased by the intervention. —=no evidence located of an effect of this intervention on outcome. A=consistent conclusions across meta-analyses, high-quality systematic reviews, or several randomised controlled trials. B=evidence from one or two randomised controlled trials only. C=high-quality systematic reviews with some inconsistent conclusions from authors; or several consistent ecological studies or cohort studies. D=cross-sectional association, case series suggesting outcome, or single cohort study. * Review did not refer to drug users or IDUs alone. † Most studies examined couples or family interventions among clients receiving opioid substitution therapy. IDUs not specifically examined in this review.

Table 1: Current evidence for effects of interventions on HIV risk behaviours and HIV incidence in people who inject drugs.
sexual partner, as a couple. Evidence of effectiveness against psychostimulant dependence is strongest for cognitive behavioural therapy and contingency management, although the specific interventions trialled vary widely across studies, so the capacity to make bold statements about which elements are accountable for reductions in injecting drug use is limited.

**Detoxification**

Medically supervised detoxification, undertaken in an inpatient setting and entailing drugs to reduce discomfort of the individual (either symptomatic relief, or, for opioid detoxification, tapered doses of a substituted opioid), is effective to ensure the process is completed. This approach is not recommended as a stand-alone intervention to achieve sustained abstinence, in view of very high relapse rates.

**Behavioural interventions to reduce risk behaviours**

The conclusion of a Cochrane review of behavioural strategies to reduce injecting and sexual risk suggested that support is limited for widespread use of formal multisession psychosocial interventions; brief, standard, educational approaches seem to be the most cost-effective option. In a meta-analysis, family and couple therapy, delivered as an adjunct to methadone treatment, was superior to individual treatment (which was also effective) for reduction of drug use.

Behavioural interventions to deter initiation of injection or to encourage IDUs to shift to non-injecting routes of administration have been the subject of some research, but as yet they do not seem to be effective for reduction of injecting. In trials of strategies targeted at present IDUs to decrease their initiation of non-users of injecting drugs to injecting, participants reported lower levels of injecting in front of non-IDUs, increased disapproval of initiation of injecting, and fewer requests or agreements to initiate non-users to injection.

**Compulsory detention**

In some nations, most notably in Asia, extrajudicial systems exist, with detention of drug users in closed settings—typically operated by the military, government security, or police—for what is claimed to be treatment of drug misuse. This situation is different from imprisonment for the criminal offence of drug use or supply offences (see discussion of HIV risk in prisons in Physical environment interventions). Drug dependence is seldom an entry criterion (and is rarely confirmed medically), so entrants might not need drug treatment. Typically, no appeals process is in place; release happens after set durations, commonly longer than clinically indicated, or is on the basis of unrelated outcomes (eg, being able to recite drug laws).

Detainees are sometimes forced to comply with non-evidence-based interventions. Typically, detoxification is not assisted medically nor is treatment supervised by health personnel. Evidence-based and effective drug therapy and prevention of HIV transmission are delivered rarely. Conditions in some facilities have been reported as overcrowded and unsanitary.

Accumulating evidence suggests that HIV risk behaviours arise within such closed settings, and risk could be raised in detention compared with in the community. High rates of relapse to drug use and re-entry to these closed settings (70–100%) suggest that a sustained effect does not result from this approach; no data show diminished HIV incidence. The conclusion of

### Table 2: Compulsory detention as an intervention for drug use

<table>
<thead>
<tr>
<th>Nature of compulsory detention</th>
<th>Number detained (12 months)</th>
<th>Number detained at one point in time</th>
<th>Number in OST at one point in time</th>
<th>Number in other drug treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vietnam 109 centres, with entry via committal by family, the community, or arrest for a positive urine test, drug possession, or report of drug use</td>
<td>NK (2008)</td>
<td>&gt;60 000 (2008)</td>
<td>1484 (2009)</td>
<td>NK (2009)</td>
</tr>
</tbody>
</table>

Data taken from ref 2. Year of data shown in parentheses. Countries listed were those in which compulsory detention as an intervention for drug use was identified. This detention is distinct from imprisonment after arrest and sentencing for a criminal offence, which is not featured here. Numbers of clients in forms of drug treatment other than OST are known underestimates: although many interventions were sometimes reported, the number of clients in every form of treatment was rarely known. OST=opiod substitution therapy. NK=the form of intervention exists in this country, but the number of clients is not known. *Number of clients in 12-month period. †Mamedova A, UNODC Office in Ashgabat, Feb 5, 2010, personal communication.
external assessments is that adverse effects on drug use and HIV risk can arise with compulsory detention, in addition to human rights violations. Table 2 describes these forms of compulsory detention and compares their extent with that of other forms of treatment for drug use. In some countries, compulsory detention is the most usual intervention, and resources are directed to it rather than at effective prevention of HIV transmission.

Reduction of sexual risk behaviours
We do not know the proportions of incident HIV cases in IDUs that are attributable to sexual transmission or caused by injection; some evidence suggests that sexual transmission is an important cause of HIV infection in people who inject drugs and it is certainly an important risk for the non-injecting partners of IDUs. Reduction of sexual risk behaviours in this group is, therefore, a priority.

Sexual risk-reduction strategies are well studied in other populations. Condom provision combined with education (sometimes peer interventions) decreases unprotected sex. Outcomes of treatment of STIs in a range of groups, including men attending STI clinics and sex workers, suggest incidence of both STIs and HIV might fall after treatment. Although not examined directly in populations of IDUs, we can expect a similar effect in this group.

Evidence from the USA suggests behavioural strategies can reduce unprotected sex by drug users, including those who are HIV positive. Conclusions of a Cochrane review were that multisession interventions were no more effective than a solitary session for reduction of sexual risk, and single-session approaches were, therefore, more cost effective than one entailing several sessions. Evidence is scarce to support interventions with couples to lower sexual risk. Network and peer-led approaches targeting sexual risk are effective and cost effective for reduction of risk. OST diminishes some sexual risk behaviours (eg, many sexual partners) but not others (eg, extent of condom use). HIV testing and counselling
Testing and notification of IDUs of their HIV serostatus is an important step in enabling them to make informed decisions about their behaviours and to consider treatment. HIV testing and counselling has been associated with a decline in injecting and some sexual risk behaviours. However, context is important: testing without access to risk-reduction materials or information, or without access to ART for those who are HIV positive and need treatment, is not likely to be effective at lowering HIV incidence.

Reduction of HIV incidence
At first glance, interventions that diminish self-reported risk behaviours might be expected to cut HIV incidence. The relation is complex, however: findings of many studies show only modest associations between reported needle-sharing and HIV infection; high rates of HIV infection are recorded in IDUs who say they have never shared a needle and the relation between changes in sharing frequency and HIV transmission could be non-linear. The level of background risk (ie, HIV prevalence and distribution in a community, determining the likelihood of shared equipment being contaminated) can also lead to so-called risk redundancy: if infection risk

Panel 1: Modelling of combined and high-coverage interventions to prevent HIV infection
We adapted an HIV transmission model with data of risk behaviour of IDUs (webappendix pp 6–17) to generate a range of frequencies for HIV infection around the world. HIV prevalence of simulated epidemics was 1–73% (webappendix p 8). We projected the 5-year effect of strategies to prevent HIV infection (NSPs, OST, ART, or a combination of these) on HIV incidence across a range of modelled epidemics. Coverage of OST and NSPs was defined as partial (IDUs receiving OST or high NSP coverage, full (OST and not injecting, or OST and high NSP coverage), or none or less than partial (no OST, low NSP coverage). Work to quantify the effectiveness of full or partial coverage is poor, so conservative estimates of variables were derived from many studies (webappendix pp 6–17). Effectiveness of ART on HIV incidence was estimated by meta-analysis of the effect of ART on heterosexual HIV transmission within discordant couples. We assumed point efficacy estimates (60% for OST, 40% for NSPs, and 90% for ART) applied to an individual’s infection risk per unit time; we also undertook an uncertainty analysis of these variables. The model analysis included different coverage of OST and NSPs, all levels of which have been seen in some setting, and ART in IDUs with CD4 counts less than 200 or 350 cells per μL. We assumed that: recruitment of eligible IDUs to ART, or an increase to partial or from partial to full NSP and OST, is constant (10%, 25%, or 50% per year, depending on scenario); that IDUs leave from full to partial or from partial to none or less than partial at a constant rate (average duration 12 months); and so after 5 years, a higher proportion than at initiation will currently be exposed to the intervention (x axis of figure 1).

In the model, we also assessed the combined effect of OST, NSPs, and ART (figure 1, scenario D), and we undertook a subanalysis to project the effect of ART for other recruitment criteria (figure 2). Detailed methods and limitations are in the webappendix pp 6–21, and see discussion of areas of uncertainty in panel 2. Note, this modelling of OST and NSPs applies only to populations in which most IDUs inject opioids, and sexual risk reduction and transmission has not been modelled.

IDU=injecting drug user. NSP=needle and syringe programme. OST=opioid substitution treatment. ART=antiretroviral treatment.
is sufficiently high, reduction—but not elimination—of risk behaviours might not be sufficient to decrease infection (panel 2). HIV incidence is not typically measured, so data are also scarce, and most studies would, in any case, be underpowered to detect any effect.

In heterosexual populations, consistent condom use is estimated to lower HIV incidence by 80%. Ecological data suggest that OST and NSP expansion are associated with reductions in HIV incidence in IDUs, though separate effects and level of dose or coverage of intervention are rarely examined. In our model (panel 1) we focus on the effect of provision of high-intensity NSPs to increasing proportions of the IDU population (accumulating evidence indicates an intervention effect at this level).

In expert consensus statements endorsed by WHO, researchers agree that we have an imperative to investigate highly active ART as a preventive strategy, in view of its effects on HIV viral load. Lowering viral load prevents HIV transmission between serodiscordant sexual partners; data suggest HIV incidence could fall by 90%. Provision of ART could, therefore, also diminish HIV incidence in IDUs. In one prospective cohort of IDUs, the concentration in plasma of HIV-1 RNA predicted community-level HIV incidence in this population after adjustment for injection and sexual risk; the decline happened as ART coverage grew from 43% to 70% and as proportions treated with highly active ART increased from 8% to 99%.

After known exposure to HIV, post-exposure prophylaxis prevents HIV infection if administered correctly and in time (within 72 h of exposure). Wider access to this treatment for IDUs has been advocated, but it has not been studied empirically. In a Cochrane review, use of pre-exposure prophylaxis could not yet be recommended in any at-risk group, including IDUs, because of a paucity of evidence on effectiveness, although trials are nearing completion.

**Cost-effectiveness**

No data for cost-effectiveness are available for most IDU-focused strategies to prevent HIV infection (table I). The strongest evidence is with NSPs and OST. Although not based necessarily on controlled trial evidence, economic modelling across a range of epidemic settings in several countries indicates that when NSPs decrease HIV transmission they are cost effective. OST is highly likely to be cost effective for reduction of HIV incidence and disability-adjusted life-years, a large proportion of which are attributable to HIV infection, particularly for individuals undergoing continuous treatment of long duration. Cost-effectiveness studies of ART for prevention of HIV infection in IDUs have been called for; this therapeutic approach is cost effective for prevention of mother-to-child transmission.

In studies of supervised injecting centres, researchers have concluded that they are cost effective for reduction of HIV infection in high-prevalence settings.
Conversely, data from compulsory detention centres in southeast Asia suggest that expenditure would continue to increase without necessarily reducing costs for prevention of HIV infection and care of detainees.66

**Combined interventions in prevention**

In reviews of prevention, researchers have noted that combinations of interventions are more likely to have an effect than single interventions;20,103,104 this finding is not surprising since no one approach addresses all outcomes of importance (injections, injection risk, sexual risk, and HIV infectivity; table 1). Accordingly, data from cohort and modelling studies have shown that the effects of NSPs and OST on HIV incidence in IDUs are negligible if delivered as stand-alone strategies.35,87 With combinations of OST and ART, OST assists IDUs who are HIV positive to stabilise across many domains,29,35–38 and increases adherence to ART.105–112 The third article in this Series covers this aspect in more detail.111

Empirical assessments of the effect of combined approaches on HIV transmission are scarce.20,21,35,104 Existing evidence from studies of OST or NSPs are too heterogeneous to permit valid synthesis of effects on HIV incidence.20,21,35,58,90 Tilson and colleagues noted that “evaluations of multi-component HIV prevention have primarily examined their impact on HIV risk behaviour...and while such studies consistently show that these programs reduce drug-related HIV risk behaviour, questions remain about their impact on HIV incidence”.20 One exception was the Amsterdam cohort112 in this study, methadone and 100% supply of clean injecting equipment from NSPs (enough clean syringes for all injections) diminished HIV incidence by more than two-thirds. However, the study had insufficient power to measure separate effects of the two interventions.47

A key question remains: what proportion of the IDU population needs to be exposed to several interventions to achieve substantial reductions in HIV incidence and prevalence? In panels 1 and 2 and figures 1 and 2, we present model projections that use data for OST, NSPs, and ART to assess the effect of escalation of coverage of these strategies on HIV incidence in IDUs. The strength of this particular model is that the intervention effect is consistent with available evidence of results on HIV incidence—no theoretical parameters are included about how an approach could lead to changes in injection risk behaviour and effect on HIV transmission. Other variables about intervention coverage and risk behaviour have all been noted directly (see webappendix pp 6–21, for methodological details).

Projections suggest the following outcomes. First, solitary interventions alone can have limited effect on HIV incidence unless implemented at high coverage and intensity (figure 1, scenarios A, B, and C). Second, provision of ART to all HIV-positive IDUs with CD4 counts lower than 350 cells per μL has a much greater

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**Panel 2: Modelling results and uncertainty analyses**

**Results of mathematical modelling**

The projections in figure 1A suggest that high coverage of opioid substitution therapy (OST) and needle and syringe programmes (NSPs; 50% annual recruitment to just OST and NSPs, leading to 51% of injecting drug users [IDUs] on partial or full OST or NSPs after 5 years) alone could lead to a 20% (10–90% interval 11–39%) decrease in HIV incidence depending on setting. Antiretroviral treatment (ART) to HIV-positive IDUs with CD4 count lower than 200 cells per μL, without OST and NSPs, generates a diminished effect (figure 1B), whereas increasing eligibility criteria to CD4 count less than 350 cells per μL (figure 1C) doubles the number of IDUs on ART (40% of HIV-positive IDUs and 75% of eligible IDUs on ART after 5 years for 50% annual recruitment) and achieves a comparable effect to OST and NSPs. When NSPs and OST are combined with ART for IDUs with CD4 count less than 200 cells per μL (figure 1D), with high coverage of both interventions (50% annual recruitment), the median reduction in HIV incidence would be 29% (17–50%) after 5 years. This effect increases to 37% (22–65%) if ART eligibility was CD4 count lower than 350 cells per μL (figure 1D), which gives intervention coverage levels that have been recorded in Germany, the Netherlands, and Spain.1 In these scenarios, 25% of modelled epidemics project a greater than 50% fall in HIV transmission. The effect of these intervention scenarios on HIV prevalence after 20 years is shown in the webappendix pp 12.

**Uncertainty analyses**

For a range of ART eligibility criteria, the projections in figure 2 show the effect of just ART (not including OST and NSPs) on HIV incidence, and suggest that treatment of all HIV-positive IDUs, if feasible (% of infected IDUs on ART after 5 years is shown as transparent bars in figures 1 and 2), could further increase its effect on HIV incidence compared with ART eligibility criteria of CD4 count less than 200 or 350 cells per μL. However, even at high coverage, this strategy will still not ensure 50% reduction in HIV incidence after 5 years. By contrast, treatment of only IDUs with AIDS would have little effect on prevention of HIV infection. Two important areas of uncertainty remain. First, heterogeneity in epidemics of injecting drug use generated uncertainty in the potential effect of interventions (error bars in figures 1 and 2). Effects are reduced in populations with raised HIV prevalence, especially in populations with the greatest injecting risk (webappendix p 11) because of high transmission possibility. This uncertainty could have been reduced by fitting to specific settings.12 Second, we were unable to synthesise uncertainty around intervention effects adequately. Although much evidence suggests OST and NSPs are effective,20 few studies have quantified consistently the separate and combined effects of OST and NSPs. Data of many ecological studies indicate clearly that NSPs are associated with reduced HIV transmission, and findings of several studies show that extended OST exposure diminishes HIV transmission,10 but few controlled assessments have taken place. Moreover, results of studies comparing HIV incidence in IDUs exposed and not exposed to NSPs are inconsistent,20,12 and do not permit reliable synthesis. Published work in which records are taken of the level of NSPs (IDUs exposed to high syringe coverage) and OST, and their effect on HIV incidence, are rare (eg, the Amsterdam cohort study).47 However, although these data suggest that combined interventions are highly effective and provide support for our variables, they were of insufficient power to generate independent OST and NSP effect estimates. When uncertainty in efficacy estimates for OST and NSPs were included in the model projections, they suggested the effect of OST or NSPs could be up to 50% greater than the point estimate for any specific epidemic scenario (webappendix p 13), which indicates that, in some populations, 50% decreases in incidence could be achieved with intensive OST or NSPs. Precision was much greater for ART effect projections (5% difference either way from point estimates), but these estimates are also limited because of a paucity of empirical data for reductions in HIV infectivity in IDUs on ART and for treatment adherence by active IDUs if ART were offered early in the infection.
effect on HIV incidence than provision of ART only to those with CD4 counts less than 200 cells per μL, or with diagnoses of AIDS (figure 1, scenarios B and C, and figure 2). Third, medium-to-high coverage is needed for a substantial effect on HIV incidence to be detected. Finally, combination interventions with medium-to-high coverage must be sustained over many years to exert a substantial effect on HIV incidence (figure 1, scenario D) and prevalence (webappendix p 12). Findings of uncertainty analyses also suggested that an augmented effect is achieved when HIV prevalence and risk behaviours are lower (panel 2, webappendix p 13).

Current intervention coverage
Measurement of the scale of interventions is a challenge and is inconsistent across countries and international agencies, and quality of data describing the epidemic and the response varies substantially (panel 3). We know, however, that NSPs, OST, and ART are being implemented in an increasing number of countries, though with very large differences in coverage.

In a systematic review, researchers noted that NSPs had been introduced in 82 of 151 countries where injecting drug use takes place, accounting for 80% of the estimated global IDU population (table 3). Data for the number of clients and volume of injecting equipment distributed were gathered and, globally, suggested 8% (range 5–11%) of IDUs had accessed an NSP at least once in a 12-month period and, overall, 22 (12–42) needles or syringes were provided per IDU per year. Injection frequency is highly variable, but if we estimate that, on average, an IDU might inject 400 times per year, these data suggest only 5% of injections are covered by sterile equipment provided by an NSP.

OST was available in 71 countries (65% of the estimated global IDU population) and was confirmed as unavailable in 54 (34%). Globally, estimations suggested that eight clients were receiving OST for every 100 IDUs. In many countries, not all OST clients are IDUs; further, not all IDUs inject opioids (particularly in Latin America). Nonetheless, at a global level, OST clearly covers only a small proportion of IDUs. Data for provision of ART to IDUs was sparser: in 47 countries reporting the number of IDUs receiving ART, four for every 100 HIV-positive individuals were receiving ART.

Exceptions to these globally low levels include Australia and several western European countries, which had high coverage for all three strategies. Many nations, however, had very low coverage; in view of the results of the modelling shown in figure 1, clearly, few countries could reasonably expect to substantially reduce national HIV incidence in IDUs, at their current levels of intervention combination and coverage.

Potential of social and structural interventions
Interventions operating at the population or community level are known as structural interventions. As discussed in the first paper in this Series, social and structural factors can inhibit the capacity of IDUs to reduce their risk of HIV infection or diminish the extent to which prevention strategies are delivered and used. In circumstances when interventions have not been introduced or scale-up is inadequate, or when the effect of strategies on HIV transmission is limited (as shown by the outcomes of the modelling presented earlier), we might need to identify and counter the effect of structural factors to prevent HIV transmission.

Structural interventions aim to bring a contextual change in physical and social environments, mediating injecting drug use and HIV risk by removal of barriers to risk reduction or by enabling protective conditions. Table 4 shows a heuristic of the HIV risk environment: different types of environment (physical, social, economic, policy) interact with diverse levels of effect (micro or macro). We outline the likely end results of these environments and outcomes for HIV risk or intervention effectiveness and suggest social-structural

Panel 3: Gaps in knowledge about coverage of core services to prevent HIV infection for IDUs
- Data for the HIV epidemic in injecting drug users (IDUs), and programme responses, are often of poor quality and can, in many cases, be absent. Unless information is gathered routinely on prevention activities, we will have difficulties understanding why some epidemics might not be weakening and what is needed in those countries. These findings are crucial to inform policy, aid advocacy, and move from unverified data to those that increase clarity while acknowledging uncertainty. Some important examples are below.
- Communication of HIV-prevention information is an important part of the response, yet information about how many IDUs are exposed to these messages is not obtained nationally or globally.
- Estimation of the number of HIV-positive IDUs receiving or in need of antiretroviral treatment (ART) is difficult. Many IDU population estimates are for current IDUs only, and many studies of HIV sero-prevalence are undertaken in sentinel IDU populations that might not be broadly representative. ART registries sometimes do not record history of injecting drug use, or note injecting drug use only if it is identified as the most likely exposure category.
- Data for the extent of drug treatment for IDUs other than opioid substitution treatment are scarce.
- A paucity of data for IDU population size, HIV prevalence, and service provision over time prevents measurement of intervention effect.
- Programme information describing the volume of services is sometimes incomplete, and service quality is very difficult to measure. Few data are gathered to allow estimates of service accessibility or equity.
strategies that might address them. Evidence of structural prevention of HIV infection in IDUs is emerging, but conclusions are largely theoretical, and although we can expect structural approaches to be highly effective for reduction of risk or to enable protective behaviours or initiatives to take place, much more must be done to assess these interventions in a controlled way. Here, we note selected examples.

### Physical environment interventions

Injecting drug use in prison is more likely to involve risky injecting than that in the community, though a direct effect on HIV incidence has not been studied. Provision of needles and syringes in prisons has not been linked to increased injection.

One strategy targeting changes in the micro-physical environment is the supervised injecting centre (table 1). These centres have potential community effect, but are present in only a few locations (61 cities in eight countries). They are typically located in large, open-drug-market areas, where risky drug use is concentrated and IDUs congregate. Although models differ across countries, all centres provide sterile injecting equipment and a hygienic environment in which preobtained drugs can be injected under professional supervision. Observational assessments in Vancouver, Canada, and Sydney, Australia, have suggested that these centres attract IDUs who are at greatest risk of HIV infection, facilitate education about safe injection, reduce syringe sharing, and increase referral or entry into withdrawal management and drug treatment.

### Evidence of prevention interventions

Evidence-based prevention interventions are effective for reduction of HIV risk behaviours within prison, and evidence of effectiveness of physical environment interventions is emerging, but conclusions are largely theoretical, and although a direct effect on HIV incidence has not been linked to increased injection.

Evidence of evidence-based prevention interventions is effective for reduction of HIV risk behaviours within prison, 121,122 though a direct effect on HIV incidence has not been linked to increased injection.

Evidence of physical environment interventions is emerging, but conclusions are largely theoretical, and although a direct effect on HIV incidence has not been linked to increased injection.

### Table 1: Estimated regional and global coverage levels of three interventions to prevent HIV infection

<table>
<thead>
<tr>
<th>Regions</th>
<th>Countries implementing NSP (% ERIP)</th>
<th>Countries implementing OST (% ERIP)</th>
<th>Countries implementing both NSP and OST (% ERIP)</th>
<th>Needles and syringes distributed per IDU per year [n countries contributing data; % ERIP]</th>
<th>Number of OST recipients per 100 IDUs [n countries contributing data; % ERIP]</th>
<th>Ratio of IDUs receiving ART for every 100 IDUs living with HIV [n countries contributing data; % HIV+ERIP]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eastern Europe (injecting drug use identified in 18/18 countries)</td>
<td>18 (100%)</td>
<td>16 (48%)</td>
<td>16 (48%)</td>
<td>9 (7 to 14) [12; 91%]</td>
<td>1 (&lt;1 to 1) [18; 100%]</td>
<td>1 (&lt;1 to 44) [15; 95%]</td>
</tr>
<tr>
<td>Western Europe (injecting drug use identified in 27/28 countries)</td>
<td>23 (100%)</td>
<td>25 (100%)</td>
<td>23 (100%)</td>
<td>59 (39 to 89) [21; 50%]</td>
<td>61 (48 to 79) [22; 97%]</td>
<td>89 (52 to NR) [13; 46%]</td>
</tr>
<tr>
<td>East and southeast Asia (injecting drug use identified in 16/17 countries)</td>
<td>10 (87%)</td>
<td>7 (86%)</td>
<td>7 (86%)</td>
<td>30 (7 to 68) [16; 100%]</td>
<td>4 (3 to 5) [16; 100%]</td>
<td>4 (2 to 8) [5; 78%]</td>
</tr>
<tr>
<td>South Asia (injecting drug use identified in 9/9 countries)</td>
<td>6 (99%)</td>
<td>6 (71%)</td>
<td>4 (70%)</td>
<td>37 (27 to 50) [9; 100%]</td>
<td>19 (15 to 25) [8; 99%]</td>
<td>1 (1 to 2) [3; 65%]</td>
</tr>
<tr>
<td>Central Asia (injecting drug use identified in 5/5 countries)</td>
<td>5 (100%)</td>
<td>2 (51%)</td>
<td>2 (51%)</td>
<td>92 (71 to 125) [4; 90%]</td>
<td>&lt;1 (&lt;1 to &lt;1) [5; 100%]</td>
<td>2 (1 to 3) [4; 92%]</td>
</tr>
<tr>
<td>Caribbean (injecting drug use identified in 6/15 countries)</td>
<td>1 (16%)</td>
<td>1 (16%)</td>
<td>1 (16%)</td>
<td>.. [1; 37%]</td>
<td>5 (4 to 7) [2; 53%]</td>
<td>..</td>
</tr>
<tr>
<td>Latin America (injecting drug use identified in 18/20 countries)</td>
<td>5 (67%)</td>
<td>2 (29%)</td>
<td>1 (20%)</td>
<td>&lt;1 (&lt;1 to 1) [11; 85%]</td>
<td>&lt;1 (&lt;1 to &lt;1) [12; 81%]</td>
<td>1 (1 to 4) [2; 69%]</td>
</tr>
<tr>
<td>Canada and USA (injecting drug use identified in both countries)</td>
<td>2 (100%)</td>
<td>2 (100%)</td>
<td>2 (100%)</td>
<td>23 (17 to 33) [2; 100%]</td>
<td>19 (9 to 19) [USA only; 87%]</td>
<td>..</td>
</tr>
<tr>
<td>Pacific Island States and Territories (injecting drug use identified in 11/16 countries)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 [9; 96%]</td>
<td>0 [7; 91%]</td>
<td>0 [2; 4%]</td>
</tr>
<tr>
<td>Australia and New Zealand (injecting drug use identified in both countries)</td>
<td>2 (100%)</td>
<td>2 (100%)</td>
<td>2 (100%)</td>
<td>202 (148 to 334) [2; 100%]</td>
<td>23 (17 to 39) [Australia only; 69%]</td>
<td>22 (10 to 89) [Australia only; 88%]</td>
</tr>
<tr>
<td>Middle East &amp; north Africa (injecting drug use identified in 21/22 countries)</td>
<td>8 (35%)</td>
<td>4 (13%)</td>
<td>3 (3%)</td>
<td>&lt;1 (&lt;1 to 1) [18; 78%]</td>
<td>1 (&lt;1 to 1) [20; 69%]</td>
<td>..</td>
</tr>
<tr>
<td>Sub-Saharan Africa (injecting drug use identified in 16/47 countries)</td>
<td>2 (2%)</td>
<td>4 (27%)</td>
<td>1 (1%)</td>
<td>&lt;1 (&lt;1 to &lt;1) [12; 93%]</td>
<td>1 (&lt;1 to &lt;1) [12; 74%]</td>
<td>&lt;1 (&lt;1 to 2) [2; 29%]</td>
</tr>
<tr>
<td>Global (injecting drug use identified in 151/200 countries and territories)</td>
<td>82 (80% EGIP)</td>
<td>71 (65% EGIP)</td>
<td>63 (61% EGIP)</td>
<td>22 (12 to 42) [124; 91% EGIP]</td>
<td>8 (6 to 12) [126; 92% EGIP]</td>
<td>4 (2 to 18) [47; 66% HIV+EGIP]</td>
</tr>
</tbody>
</table>

Data are mid points; ranges in parentheses are upper and lower limits. OST—opioid substitution therapy; ART—antiretroviral therapy; NSP—needle and syringe programme. EGIP—estimated regional IDU population. NR=estimate greater than parity and not reported. Regional estimates were only approximated when data were available for at least two countries (apart from the USA and Australia, which each formed more than 50% of the population in their two-country regions). Estimates are intended to serve as a guide for comparable measures of coverage across regions and are not intended to be taken as accurate counts. The number of countries for which regional and global estimates were made is presented in each cell; this number indicates level of confidence in the estimates produced. Coverage estimates include countries where no interventions are delivered, so the total number of countries for which data are available might exceed the number of countries in which interventions are implemented. See reference 2 for details of countries in the regions and for each indicator: “Total differs from that reported in reference 2 because of the addition of Afghanistan, which began treating its first OST clients in February, 2010 (Magueo O, Médecins du Monde, Kabul, Afghanistan, Feb 24, 2010; personal communication). Table adapted from reference 2 with permission of Elsevier.

Table 3: Estimated regional and global coverage levels of three interventions to prevent HIV infection.
Social environment interventions

Peer initiatives—entailing outreach to peer IDUs, training of peer IDUs, or a combination—reach users of drugs through their social networks, promoting safer injections and sexual behaviour. In a systematic review of 30 peer-intervention studies, researchers reported a 63% reduction in equipment sharing (odds ratio 0·37 [95% CI 0·20–0·67]) and an almost doubling in condom use (1·92 [1·59–2·33]). Evidence of an effect on HIV transmission, however, is absent. Since the intervention is delivered within social networks, trials would need to be cluster randomised, which would add to sample size, expense, and complexity. Effective peer-education projects have been implemented in China and northern Vietnam, requiring little support. In addition to peer and network-level approaches, community consultation can allow for local groups to be educated about prevention of HIV infection and reduce opposition to interventions that might be controversial, including advocacy for less restrictive policies about needle and syringe provision.

Economic environment and multisectoral interventions

Interventions targeting health and economic welfare could have effects on prevention of HIV infection. Evidence suggests that micro-finance strategies, in combination with community mobilisation and access to education or employment, can bring about reductions in HIV risk behaviours, including in women affected by poverty or sex work. Findings also indicate that access to stable housing diminishes vulnerability to HIV infection in IDUs. Economic and other multisectoral initiatives could create a so-called enabling environment for HIV prevention, by raising the likelihood of IDUs entering and remaining in contact with prevention interventions, including OST, NSPs, and ART.

Policy environment interventions

Policy environment interventions can operate at many levels. One focus is on strategies to change the legal environment. This approach could include efforts to lessen the health risks that IDUs face because of the criminalisation of drug use; remove prohibition of interventions to prevent HIV infection; and alter legislation or law enforcement activities that reduce access to services. The legal status of OST and NSP provision will have an important effect on attempts to implement these interventions. Relaxation of legal restrictions on provision of sterile needles and syringes increases their availability and accessibility and reduces levels of risk behaviour in IDUs, without adverse effects.

In many countries, policy makers have a poor understanding about the science of addiction, which directly affects the formulation of evidence-based policies to prevent HIV infections in IDUs. At a micro-local level, police surveillance on the street is linked to reluctance of IDUs to carry sterile needles and syringes, reduced use of NSPs, and interruption of safe injecting. Such policing practices can displace drug users geographically, disrupting social networks of support. Interventions that address these factors could facilitate prevention of HIV infection. Training of police and policy makers in the science of drug use and prevention of HIV infection could be one approach. Strategies could also target programme or intervention policy, because policy-driven barriers to scale-up of effective interventions—related to limitations on access and quality—represent a major structural obstacle to an intervention’s scope, coverage, and quality.

Improvement of HIV prevention for people who inject drugs

Prevention of HIV infection in IDUs is achievable. We know how HIV is transmitted, and we recognise a core set of strategies that can limit its spread. Model projections described here suggest not only that combination and increased coverage of interventions will prevent HIV transmission but also that high levels of coverage need to be sustained for long periods. The effect of these core strategies is greatest when background HIV prevalence is low. Therefore, delays to introduction and scale-up of interventions will serve only to make prevention of HIV infection more difficult (and more expensive) than if they are introduced promptly. Intervention effect is also greatest when levels of HIV risk are lowest—in other words, when the fewest IDUs are engaging in unsafe injection or unprotected sex.

All these findings have important implications, but most vitally, that approaches must be combined. IDUs should know the risks they face and be aware of their serostatus. Some interventions are effective for lessening risk of HIV transmission by reducing unsafe injecting and sexual behaviour and injections overall; moreover, initiatives are available to decrease HIV infectivity if exposure happens. Without combination of these approaches, however, the effect on the HIV epidemic can only be modest, particularly in high-prevalence high-risk settings.

Coverage of effective prevention

In some countries, we do not know if interventions to prevent HIV infections are being implemented. However, in many nations, we are aware that preventative strategies (eg, NSPs and OST) are not undertaken, and when interventions do exist, coverage is generally limited. The level of combined approaches needed to prevent and maintain low HIV prevalence in IDUs is achieved at present by only a few high-income countries. Some nations have managed to avert an HIV epidemic or have decreased HIV transmission to low endemic levels, including Australia and the UK; both countries have high coverage of several combined interventions, including—but not restricted to—NSPs, OST, and ART.
Here, we have briefly reviewed evidence for an effect of several interventions on HIV risk and incidence. Evidence of benefit from randomised controlled trials (regarded as the gold standard) is available for strategies such as OST, some drug-dependence treatments, and behavioural techniques, some of which have been shown to be efficacious, typically with measurement of injecting and sexual risk (rather than HIV incidence). For most initiatives, however, the only evidence is from ecological, cross-sectional, case-control, and cohort studies. Further,
much evidence in support of these interventions is assessed via self-reported behaviours rather than objective measures of HIV incidence.

Limitations of evidence for some interventions, or paucity of knowledge about evidence for others, might present an obstacle to implementation of programmes. For example, some cite the concern that NSPs could actually increase or encourage injecting; although this fear has not been substantiated empirically, such concerns no doubt underlie resistance to NSPs in some settings. Limited treatment of HIV-positive IDUs by medical professionals, because of fears of poor adherence, could be another example, as noted in the third paper in this Series.

These limitations are only one part of the problem of narrow coverage of interventions. Many countries now have some level of implementation of even the most controversial initiatives, such as OST and NSPs: the difficulty in many nations is that the level of implementation is low. Treatments that are efficacious in difficult clinical trials will only be effective in the community if they are provided in sufficient doses to and enough people—some of the biggest issues are scope and quality, and many obstacles stand in their way. In many instances, programmes are run as pilots, with little scale-up once pilot funding ceases. OST is usually provided in restrictive and sometimes punitive ways, including a need to register on government registers (sometimes implying removal of certain citizenship rights or difficulty in accessing employment); in some countries, prerequisites for treatment further diminish ease of access (such as recorded previous treatment failure or age restrictions). OST is typically provided in doses well below those outlined as optimum in international guidelines, and despite evidence that extended treatment is beneficial, many programmes have limitations on OST duration. These boundaries can affect a treatment’s outcome, from the perspective of both human rights and health effects.

Examination of the impediments and barriers to scale-up of high-coverage, high-quality HIV prevention for IDUs worldwide is imperative. Once identified, it is necessary to develop (and evaluate) interventions that create enabling environments for prevention of HIV infection, including changing national and local policies or laws. We also, therefore, draw attention to emerging evidence in support of structural-level initiatives. These seek to bring about contextual and community-level changes as one element in a combination-intervention approach to prevention, enhancing the quality and coverage of strategies that we know work.

**Better understanding of IDU populations and contexts**

Populations of IDUs are diverse, and this difference matters for risk of HIV infection. Some characteristics will confer additional risk, shape intervention effectiveness, or impinge on access. Such groups include those who are imprisoned, women, young people, men who have sex with men, homeless people, displaced populations, and individuals in an ethnic minority. Evidence for preventive strategies in people who inject psychostimulants is sparse and needs to be a priority in regions where this form of drug use predominates. Nonetheless, one fact remains true across settings and populations: HIV infection cannot be prevented without targeted scale-up of interventions that work.

As shown in the modelling exercise above (see Combined interventions in prevention, and panel 2), the effect of the three core interventions to prevent HIV infection is affected greatly by the level of injecting risk within a population, so care must be taken to ensure that effective behavioural interventions to reduce risk are targeted appropriately and broadly and at people engaging in the highest levels of injecting risk. Moreover, drug use is a social behaviour and risk is shaped by social setting. We need to capitalise on naturally occurring social influence processes to address prevention of HIV infection. Involvement of peers, both in informing about risks and in dissemination of interventions to reduce them, is effective. They could have a crucial role in bringing about a high-coverage combination intervention response.

**Improvement of the evidence base**

The evidence base for the effectiveness of strategies to prevent HIV infection is weaker than desirable, and weaker than many have claimed. To some extent, this weakness is attributable to complications of surveying a mobile, vulnerable, and marginalised population. Additionally, large-scale trials or cohort or other studies that have good measures of HIV incidence and intervention exposure are scarce, and careful assessment of the effect of combined approaches is even rarer. Nonetheless, we have summarised here some good evidence that a range of interventions reduce injecting risk behaviour; furthermore, economic and other modelling data suggest that several strategies (NSPs, OST, and ART) can prevent HIV infection and be cost effective. Clearly, controlled trials of these three approaches with a no-intervention control group are now unethical.

We agree with the Committee on the Prevention of HIV Infection among Injecting Drug Users in High-Risk Countries that further research is needed to “identify the most effective and cost-effective combination of programs”; the key priority now is for countries to implement and scale up multicomponent prevention programmes, and proper evaluation of combined interventions must take place. Longitudinal studies, although resource-intensive, can provide valuable insights into the effect of strategies over time. Randomisation of the introduction or scale up of interventions at staged intervals, in a stepped-wedge design, can generate substantial power and good evidence on the influence of preventive initiatives. Serial cross-sectional studies that include serological methods
to identify recent seroconversion and measure intervention exposure, which can be incorporated into continuous monitoring and surveillance, could also be used to assess a strategy’s effect.145,146

Current limitations of evidence need not lessen the response to HIV prevention. Core interventions have not been shown to do harm; for many initiatives, several lines of evidence suggest both some direct or indirect benefit, and a mechanism of action to prevent HIV infection that is biologically plausible. Further assessment of the effectiveness of interventions, to strengthen the evidence base, should go together with delivery and scale-up.

By contrast, we know enough about how HIV is transmitted and the heterogeneity of injecting risk; studies in which injecting risk is described need not be undertaken at the expense of intervention. Modelling data—such as those reported above (see Combined interventions in prevention) and in the first article in this Series147—can be used to predict expected values or targets for increases in intervention coverage. Our priorities should be public-health action to promote and implement scale-up of core prevention strategies, assessment of an intervention’s effect and of factors that facilitate interventions, and adaptations that might be necessary to boost a positive effect. Such adaptations could be examined by mixed methods, including qualitative approaches and process assessment, and might lead to new structural interventions. Investigation of individual and structural factors governing risk of injecting drug use might be needed if intervention effectiveness is found to be lower than expected. Innovations in preventive approaches, including development of structural programmes for prevention of HIV infection, also need to be subject to rigorous assessment to elucidate the causal pathways of their intervention effects.

Resourcing and targeting of response

Scientific evidence of intervention effectiveness is not the only factor that persuades policy makers and governments to take action. Some strategies have undergone much scientific investigation, seem to be effective methods to prevent HIV infection, are endorsed by the UN as essential to the response to the HIV epidemic,148,149 yet clearly have not been introduced widely in many countries. Additional arguments for their expansion must be persuasive and communicated widely. One such argument is based on human rights, since most countries have signed the Universal Declaration of Human Rights.150 Some interventions have been proposed as contrary to the human rights of IDUs; failure to implement known effective strategies has been debated similarly in other instances. These contraventions are discussed in the sixth paper in this Series.7

Evidence of cost-effectiveness is another reason for scale-up,152 yet careful studies showing cost-effectiveness of many interventions are scarce—an unfortunate gap that should be filled by future research. In view of the high disease burden of HIV attributable to injecting drug use, evidence that interventions are cost effective will present an additional argument for governments and policy makers to increase coverage. Current resources provided for research and implementation of the response to HIV infection in IDUs are deemed insufficient: globally, an estimated US$0·03 are spent per IDU per day, far short of the amount needed.148 UNAIDS estimated that in 2009, 19% of global resources needed for prevention of HIV infection should be targeted towards IDUs,149 yet perhaps 1% was allocated in this way.146,150 A boost to funding by a factor of 20, however, requires strong arguments that shifting of investments will save money and augment population-level health.

In part, then, more persuasive evidence is needed, communicated more successfully in ways that are understood by people making decisions at all levels. Clear information about the amount and combination of interventions needed at different epidemic and risk levels is needed, to target policy advice appropriately. Decisions on how to allocate resources should be informed by findings of the effectiveness of interventions, the scale and geography of need, and assessments of how well current strategies are meeting this need.

Conclusions

Prevention of HIV infection needs high coverage and combined approaches. Single interventions, even at high coverage, are likely to achieve only modest reductions in HIV transmission, particularly in settings with very high levels of HIV risk behaviours. Governments, policy makers, and public-health officials must be engaged and convinced of the importance of scaling up. Further lines of evidence could assist in justification of rapid scale-up when resistance occurs, including evaluation of combined interventions and scale-up, and data showing cost-effectiveness. Social and structural changes are a potentially important element in a combination-intervention approach to HIV prevention, especially in situations for which scale-up is difficult or when HIV transmission and injecting risk behaviour are not diminished as expected. We know enough about what can be effective in prevention of HIV infection. The challenge is to deliver these programmes well, and to scale.

Contributors

LD contributed to the overall structure and concept for the paper, and led reviews and writing of the report. BM contributed to structure, writing, and argument of the paper. PV undertook modelling analyses and jointly devised the modelling analysis plan with MH, LD, and BM; he also commented on the report. MH contributed to writing, editing, and analysis. TR contributed to the overall concept and structure of the paper and writing of the report, particularly in relation to social and structural interventions. CL commented on the argument and structure of the paper, reviewed the report, and was especially involved in the section on social and structural interventions.
Steering committee
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Conflicts of interest
We declare that we have no conflicts of interest.

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