

## HIV in people who use drugs 3



# Treatment and care for injecting drug users with HIV infection: a review of barriers and ways forward

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We review evidence for effectiveness, cost-effectiveness, and coverage of antiretroviral therapy (ART) for injecting drug users (IDUs) infected with HIV, with particular attention to low-income and middle-income countries. In these countries, nearly half (47%) of all IDUs infected with HIV are in five nations—China, Vietnam, Russia, Ukraine, and Malaysia. In all five countries, IDU access to ART is disproportionately low, and systemic and structural obstacles restrict treatment access. IDUs are 67% of cumulative HIV cases in these countries, but only 25% of those receiving ART. Integration of ART with opioid substitution and tuberculosis treatment, increased peer engagement in treatment delivery, and reform of harmful policies—including police use of drug-user registries, detention of drug users in centres offering no evidence-based treatment, and imprisonment for possession of drugs for personal use—are needed to improve ART coverage of IDUs.

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### Introduction

Although antiretroviral therapy (ART) has changed the natural history of HIV disease, it has also drawn attention to important gaps in HIV testing and treatment access. In industrialised countries, physicians have routinely delayed or withheld ART for injecting drug users (IDUs), fearing non-adherence, complications related to comorbidities, or development of antiretroviral resistance.<sup>1–3</sup> Denial of ART or systemic delays in treatment to IDUs have been reported in low-income and middle-income countries in eastern Europe and Asia, where IDUs represent the largest share of the HIV-infected population, as well as in countries with substantial subepidemics in IDUs.<sup>4–6</sup> Although studies frequently do not control for causes of mortality unrelated to HIV, IDUs infected with HIV continue to have an increased risk of death even in countries with well established ART delivery systems.<sup>7,8</sup>

An estimated one in three new HIV infections outside sub-Saharan Africa are in IDUs.<sup>9</sup> Data for access and adherence to ART in IDUs in countries with low and middle incomes are sparse. No global analysis of the number of IDUs on ART compared with

### Key messages

- Although most analyses of adherence and access to antiretroviral therapy (ART) have focused on individuals, systemic and structural elements of treatment failure such as stigma in health-care settings, police practices, and patterns of detention and incarceration need further investigation
- Injecting drug users (IDUs) have successfully started ART in at least 50 countries, with evidence showing clearly that these patients can achieve excellent virological outcomes
- Early adherence to ART is associated with long-term virological response, with behavioural support and provision of opioid substitution treatment (OST) increasing treatment success in IDUs
- IDUs are disproportionately less likely than are other patients with HIV infection to receive ART, even in countries where this group represents most of the HIV-positive population; in the five countries with the largest HIV epidemics concentrated in IDUs, IDUs were 67% of HIV cases and only 25% of those receiving ART in 2008
- Cost-effectiveness data show clear benefits of targeting of ART to IDUs in areas with concentrated HIV epidemics, and savings ratios as high as 7:1 for provision of drug treatment compared with social and medical costs of drug use
- Systemic barriers to ART and OST provision include stigmatisation of IDUs in health settings, medical treatment separated by specialties, bans on treatment of active IDUs, hidden or collateral fees, and multiple requirements for treatment initiation or modification
- Structural barriers to treatment provision include use of police registries and harassment of patients, detention of IDUs, and harassment of physicians who prescribe opioids
- In countries with large HIV epidemics in IDUs, many IDUs are detained or incarcerated in settings in which ART and OST are unavailable
- Necessary measures to improve ART coverage of IDUs are improved data collection, inclusion of OST in combination treatment, integration of treatment for co-infections, and use of community-based treatment models and peer support
- In view of persistent human-rights violations and negative health effects of policing, detention, and incarceration, law and policy reform is needed to improve ART coverage of IDUs

### Search strategy and selection criteria

We searched the Cochrane Central Register of Controlled Trials, Medline, AIDSline, PsychInfo, and Web of Science, without restriction on language, for studies published between 1991 and 2010. Keywords were “adherence”, “antiretroviral”, “AIDS”, “buprenorphine”, “cost-effectiveness”, “hepatitis C”, “HIV”, “intravenous”, “injection”, “illicit”, “methadone”, “prison”, “substance abuse”, “tuberculosis”, and “treatment”. Abstracts presented at international and regional HIV and infectious disease meetings between 2004 and 2010, grey literature from assessments done in eastern Europe and Asia, and country reports to the UN on progress towards treatment scale-up were also reviewed. Results of findings on cost and cost-effectiveness were first converted to 2008 US\$ at the official exchange rate at the year of publication and then adjusted to 2009 US\$ on the basis of the Gross Domestic Product deflator from the US Bureau of economic analysis.

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their proportion of cumulative HIV infections has been attempted since 2006.<sup>10</sup> A 2008 review of barriers and facilitators to ART for IDUs cited only two research studies outside Europe, Australia, or North America.<sup>11</sup> In a systematic review of IDU access to ART undertaken in 2010, data were unavailable for two-thirds (66%) of 138 countries.<sup>12</sup> A few low-income and middle-income countries with small injection-driven HIV epidemics, such as Georgia, have reported universal ART access for all patients for whom treatment is medically indicated.<sup>13</sup> Many others, including China, have a national policy of free universal access to ART, but in practice have disproportionately low access among IDUs.<sup>14</sup>

We review information about efficacy, cost-effectiveness, and coverage of ART and substitution treatment for patients who inject opioids, with particular attention to the five low-income and middle-income countries with largest HIV epidemics in IDUs. We also identify systemic and structural barriers to treatment access for IDUs and steps to remove these barriers.

### ART for IDUs

Investigators have extensively documented late testing for HIV in IDUs, low uptake of ART, treatment interruptions or failure related to active injecting drug use, and the need to manage treatment of HIV and common comorbidities such as hepatitis C and tuberculosis.<sup>15–19</sup> Nonetheless, IDUs have successfully started ART in at least 50 countries.<sup>12</sup> Citing evidence that IDUs enjoy significant clinical benefit from ART and that virological resistance does not differ between IDUs and other patients, WHO has issued clinical protocols detailing first-line and second-line ART regimens for IDUs, management of side-effects, and key considerations for treatment of comorbidities.<sup>3</sup> The protocols state clearly that active injecting drug use should not be a criterion for ART exclusion and that drug-dependence treatment is not necessary before ART initiation. All UN member states have endorsed universal access to ART for patients infected with HIV<sup>9</sup>—a commitment that is reiterated in many regional declarations and national plans.

In view of increased likelihood of treatment interruption or discontinuation among IDUs, especially in patients who actively inject drugs or who are imprisoned,<sup>20,21</sup> many investigators have examined mechanisms at individual and system levels to increase ART adherence in this group. Methadone and buprenorphine—which were added to WHO's essential medicines list in 2005, and are generally referred to as opioid substitution treatment (OST)—are among the best-researched of the support strategies, with data showing increased likelihood of ART uptake,<sup>22,23</sup> treatment adherence,<sup>24,25</sup> and improved virological response for IDUs receiving OST.<sup>26</sup> Panel 1 shows examples of interventions at individual and health-system levels that have increased retention and treatment adherence in patient populations that include IDUs.

Although concern about development of antiretroviral resistance is frequently cited by physicians as a reason to withhold ART from IDUs,<sup>3,45</sup> health providers are inaccurate in their estimation of which patients will adhere to ART.<sup>46</sup> Furthermore, few studies have directly compared rates of resistance between IDUs and other patients. In the largest of the available studies (n=1191), investigators compared HIV resistance to all major classes of antiretroviral drugs in IDUs and other patients during the first 30 months of ART, and noted no difference in rates of resistance.<sup>47</sup> A 2010 meta-analysis concluded that IDUs had no greater odds of developing antiretroviral resistance than did other patient populations.<sup>48</sup>

High rates of injecting and sexual risk behaviour are often reported in IDUs in low-income and middle-income countries,<sup>49–51</sup> confirming the need for interventions that effectively address several HIV risks. Results of several studies confirm effectiveness of RNA suppression in reducing sexual transmission of HIV,<sup>52,53</sup> with results of mathematical modelling suggesting that universal voluntary HIV testing followed by immediate ART uptake could prevent 95% of sexually transmitted HIV infections within 5 years.<sup>54</sup> Universal treatment as preventive intervention has not been clinically tested, even in people at risk of sexually transmitted HIV infection; possible differences in biological mechanisms of parenteral HIV infection and social and structural obstacles to HIV testing and treatment for criminalised groups make further investigation essential before the model is extended to IDUs. Preliminary evidence suggests that reductions in community-level RNA are predictive of reduced HIV incidence in IDUs, irrespective of risk behaviours such as syringe sharing.<sup>55</sup> Reductions in injecting drug use,<sup>25</sup> sexual risk behaviour,<sup>56,57</sup> and use of alcohol and illicit drugs<sup>57</sup> have also been documented after initiation of ART.

Investigators have modelled the effects on HIV incidence of targeting ART in cities or countries with epidemics concentrated among IDUs. A 2006 study examined the effects of targeting of ART to IDUs in St Petersburg, Russia. With no ART, investigators estimated that HIV prevalence would reach 64% in IDUs and 1.7% in non-IDUs after 20 years. If treatment were targeted to IDUs, more than 40 000 infections would be prevented, of which 75% would be in non-IDUs.<sup>58</sup> In the first report in this Series, Strathdee and colleagues<sup>59</sup> estimated that scale-up of ART, OST, and provision of sterile injection equipment to reach 60% of IDUs in need in Odessa, Ukraine would avert an estimated 41% of new HIV infections during the next 5 years.

### Access to ART and OST

Over-reliance on police and drug treatment statistics, inconsistencies in classification and definitions of injecting drug use, and inconsistent data hamper estimates of the number of IDUs and extent of ART coverage in this population.<sup>60,61</sup> Despite these limitations,

data show clearly that IDUs are disproportionately less likely than are others with HIV infection to receive ART, even in countries where IDUs are the largest share of those infected with HIV. Five countries—Russia, China, Malaysia, Ukraine, and Vietnam—have what might be termed megaepidemics in IDUs (ie, more than 75 000 registered HIV cases, with the largest share of these in IDUs). Together, these countries account for an estimated 2.72 million HIV cases, and roughly half (47%) of IDUs living with HIV in low-income and middle-income countries.<sup>60</sup> Examination of ART coverage of IDUs in these countries helps us to understand the limitations of present treatment efforts.

Of the five countries, all but Malaysia have received support from international donors to increase ART access.<sup>62-64</sup> In Malaysia, people with HIV infection were initially required to pay for one of three ART drugs—a restriction that resulted in de-facto exclusion of IDUs from treatment—but the country has since moved to importation and manufacture of generic drugs and universal provision of ART without charge.<sup>65</sup> Vietnam and China also offer universal access to ART using Global Fund support and some domestically produced drugs.<sup>14,66</sup> All five countries have explicitly recognised

IDUs as a key target for ART in their national plans, and have committed government funds to scale up ART.<sup>67</sup> In all five countries, the largest share of cumulative HIV infections of known origin are in IDUs, although in China IDUs are not the absolute

### Panel 1: Interventions to improve adherence to antiretroviral therapy (ART)

#### Devices to aid adherence

- Improved adherence associated with use of mobile-phone alarms and wall-chart reminders (China).<sup>27</sup>
- 76% adherence achieved with electronic paging devices and Medication Event Monitoring System caps (alongside directly observed ART, mobile health services, and outreach; USA).<sup>28</sup>
- Use of preloaded pillboxes associated with an undetectable viral load in 86% of patients who had previously not adhered to ART (alongside peer counselling, case management, and social workers; USA).<sup>29</sup>

#### Peer counselling at point of ART delivery

- Associated with 95% retention of predominantly injecting drug user (IDU) patients on ART (ten regions of Russia).<sup>30</sup>
- Help with HIV disclosure and adherence yielded an undetectable viral load in 86% of patients who had previously not adhered to ART (alongside case management, preloaded pill boxes, and social work; USA).<sup>29</sup>

#### Case management (help to resolve issues with medical care and family relationships) and nurse counselling

- Improved adherence achieved through group discussions, individual counselling, and consultations with medical clinics (Brazil).<sup>31</sup>
- Increased adherence and decreased viral load reported in patients receiving three nurse counselling sessions in a 6-month period (France).<sup>32</sup>

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- Case management, mental health or chemical dependency counselling, and transport subsidies resulted in increased regularity of clinic visits and 15–18% increased patient retention (USA).<sup>33</sup>

#### Integrated treatment

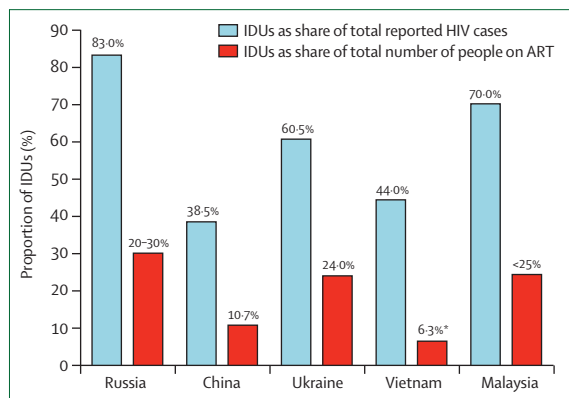
- 54% of patients achieved an undetectable viral load when ART was delivered at needle exchange; 69% chose to enter drug treatment (USA).<sup>34</sup>
- Combined tuberculosis treatment, ART, and buprenorphine was associated with undetectable HIV viral load, increased CD4 cell count, and sputum negative tuberculosis test after 6 months (Ukraine).<sup>35</sup>

#### Directly observed treatment

- Direct administration of ART (alongside drug treatment counselling and pager) resulted in 76% adherence in patients who injected cocaine, heroin, or both; 35% of patients were homeless, and 57% were severely depressed.<sup>28</sup> Randomised trial results showed increased reduction in viral load in patients receiving directly observed therapy (USA).<sup>36</sup>
- 56% of patients receiving directly observed ART at their methadone maintenance site achieved an undetectable viral load, compared with 32% of IDUs on methadone who self-administered ART (USA).<sup>37</sup>
- IDUs receiving directly observed community-based tuberculosis treatment achieved similar cure rates to patients who were not IDUs; non-adherence was reduced to a median of 5% (Russia).<sup>38</sup>
- Four of five patients achieved an undetectable viral load when offered direct ART administration at a methadone clinic and take-home evening doses of ART and a Sunday dose of methadone (USA).<sup>39</sup> An undetectable viral load was reported in 59% of methadone patients offered once-daily directly administered ART and 72% of those treated twice a day, with 89% of patients using concomitant heroin or cocaine (Canada).<sup>40</sup>

#### Incentives or contributions for food or transport costs

- Monetary incentives associated with greater adherence to hepatitis B vaccination than outreach alone (USA).<sup>41</sup>
- IDUs offered a US\$5 incentive adhered to treatment at a higher rate with (71%) or without (68%) active outreach compared with those who received outreach alone (13%; USA).<sup>42</sup>
- Distribution of free antituberculosis drugs and nutritional supplements improved adherence and outcomes in IDUs (India).<sup>43</sup>
- Patients offered vouchers for adherence to ART or methadone had 78% adherence compared with 56% in those who were not offered vouchers (USA).<sup>44</sup>



**Figure 1: IDUs as share of total HIV cases and of patients receiving ART, 2008**  
Data sources: number of IDUs infected with HIV,<sup>60</sup> total HIV cases,<sup>68</sup> IDUs on ART in Russia,<sup>69</sup> China,<sup>74</sup> Ukraine,<sup>70</sup> Vietnam,<sup>12,68</sup> and Malaysia.<sup>65</sup> IDU=injecting drug user. ART=antiretroviral therapy. \*Data are for 2009.

majority. Patients who contracted HIV through injecting drug use are disproportionately less likely to receive ART than are those infected heterosexually (figure 1). IDUs were 67% of HIV cases in these five countries in 2008, but only 25% of the patients receiving ART.

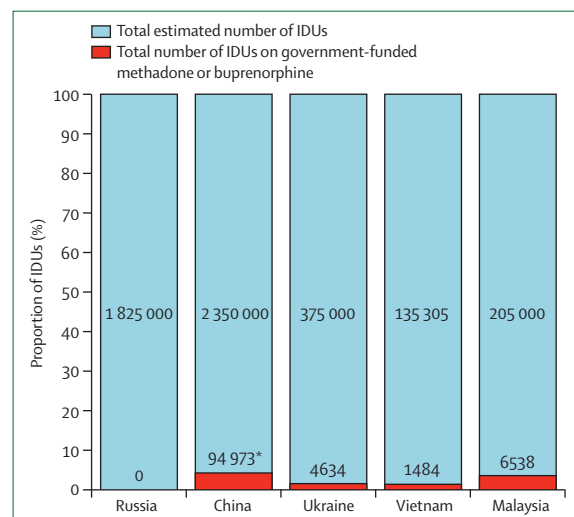
All countries with megaepidemics in IDUs apart from Russia have started OST; in Russia, methadone and buprenorphine remain illegal for use in addiction treatment. Ukraine began buprenorphine provision in 2004, and increased the number of patients receiving OST substantially by adding methadone treatment in 2008. In Malaysia in 2009, in addition to patients treated in government clinics, as many as 10000 people received substitution treatment from private physicians.<sup>65</sup> China has scaled up OST more rapidly than any other low-income or middle-income country, with more than 94000 patients on methadone treatment by the end of 2008. Nonetheless, no country with a megaepidemic among IDUs offers OST to even 5% of these patients. Considered together, the five governments with the largest established injection-driven HIV epidemics provide OST to less than 2% of IDUs in their countries. Although some IDUs inject stimulants rather than opioids, and so are ineligible for OST, coverage is strikingly low (figure 2).

### Cost-effectiveness of ART and OST

Data for cost-effectiveness of ART show additional benefits of targeted treatment in countries where HIV epidemics are concentrated in IDUs. In the 2006 study that modelled benefits of targeting of ART to IDUs in St Petersburg, researchers showed that the intervention added 650000 quality-adjusted life-years (QALYs) at a favourable ratio of US\$1501 per QALY gained. Universal (untargeted) treatment prevented more infections than did targeted provision, but was less cost effective, adding 950000 QALYs at a cost of \$1827 per QALY gained. Treatment targeted to patients who were not IDUs was least effective and least cost effective, adding only 400000 QALYs at a cost of \$2572 per QALY gained.<sup>58</sup>

Although cost-effectiveness data for methadone and buprenorphine treatment are largely drawn from trials in industrialised countries, a 2006 study calibrated costs of these medicines to epidemiological and economic conditions in each of the 14 regions in the world. With representative assumptions (eg, a 35% reduction in mortality with methadone compared with no treatment), the cost-effectiveness of methadone averaged \$2236 (2003) worldwide, with estimated costs ranging from \$408 in high-mortality African countries to \$3726 in low-mortality North American countries.<sup>72</sup> In a WHO model designed to compare cost-effectiveness of alternative interventions in every region, the cost per disability-adjusted life-year (DALY) averted for methadone maintenance ranged from \$458 in Brazil, Mexico, and other low-mortality countries in the Americas to \$2749 in Nepal, India, and other high-mortality countries in southeast Asia.<sup>73</sup> Preliminary findings from Kazakhstan's methadone pilot programme suggest that the yearly cost is \$220 per patient, and that scale-up could reduce government expenditure on drug-dependence treatment by \$2.2 million per year.<sup>74</sup>

Research in industrialised countries has shown that methadone and buprenorphine treatment are less costly than is no drug treatment when considering social costs of drug use, and that the economic value of drug treatment increases substantially when including the amount that citizens are willing to pay per crime averted (eg, armed robberies, estimated at 0.4 per drug treatment client).<sup>75</sup> Using a benefit-cost framework, the California Treatment Outcome Project assigned monetary values to changes in non-health outcomes such as crime, imprisonment, and law enforcement. The average weighted cost of 9 months' treatment was \$1583 and the corresponding benefits were \$11487, for a benefit-to-cost ratio of 7:1.<sup>76</sup>



**Figure 2: IDUs receiving government-funded methadone or buprenorphine treatment, 2009**

Data sources: total estimated number of IDUs,<sup>60</sup> methadone and buprenorphine coverage in China, Ukraine, and Vietnam<sup>12</sup> and Malaysia.<sup>77</sup> IDU=injecting drug user. \*Data are for 2008.

No studies of cost-effectiveness of methadone or buprenorphine have been reported from penitentiary systems in low-income countries. Results of an Australian study showed that prison-based methadone treatment was no more costly than were similar interventions in community settings, and estimated the economic cost per inmate per year (including the value of correctional officers' time) at \$4201. Inclusion of reductions in risk to inmates and others yielded incremental cost-effectiveness ratios of \$11000 per additional heroin-free year, \$359000 per death averted, and \$32000 per hepatitis C infection averted.<sup>77</sup> Investigators comparing costs of methadone treatment to long-term detention, which is common for IDUs in Vietnam, reported that outpatient methadone treatment, HIV testing, counselling, and education could be accomplished for less than the costs of involuntary detention, with much greater effectiveness.<sup>78</sup>

### Identifying systemic and structural barriers to treatment

With few exceptions,<sup>4,140</sup> researchers studying the association between illicit drug injection and ART failure have focused on the drug user as the unit of analysis, identifying active drug use, attitudes toward treatment, and individual conditions such as social support, housing, or belief in treatment effectiveness as factors in treatment success.<sup>15,22,79,80</sup> Advocates for HIV prevention have urged a move beyond assessment of individual risk to consideration of factors that contribute to social or structural risk or the risk environment.<sup>38,81-83</sup> A similar reframing of HIV treatment is needed in view of the fact that many health-care providers regard drug dependence as an issue of morality rather than a medical disorder, that health systems impose conditions on IDUs seeking treatment that are difficult to meet, and that greater numbers of IDUs in all countries with megaepidemics in IDUs are engaged by police, detention centres, and penitentiary institutions than by programmes providing ART. Treatment failures can be understood in these instances to be systemically or structurally induced rather than emerging from the individual.

Treatment providers are often poorly educated about addiction, and regard IDUs as troublesome or non-compliant patients. In China, for example, 50% of physicians working in substance misuse surveyed in 2005 had no previous training related to drug use or dependence.<sup>84</sup> Regulations barring or discouraging provision of ART or hepatitis C treatment to active drug users cause patients to lie about illicit drug use, reinforcing physician prejudices that label IDUs as untrustworthy.<sup>4</sup> In Russia, an 18-city survey revealed that all cities required patient review by external medical commissions before ART initiation; in ten cities, active drug use was regarded as grounds for denial of treatment.<sup>85</sup>

IDUs are reluctant to share details about their practices or even to seek treatment for acute issues such as opioid overdose, abscesses, or AIDS-related infections, especially in countries where public campaigns cast drug use as a

social evil and where health providers are seen as closely linked to systems of social control.<sup>4,86,87</sup> Fear of stigma is often cited by IDUs as a reason for delay of treatment in China, as well as in Russia and Ukraine.<sup>27,88-90</sup> A 2009 survey of 949 IDUs recruited by snowball sample in Vietnam and four other Asian countries showed that nearly one in six had been denied treatment outright.<sup>91</sup> In Malaysia, 67% of people infected with HIV surveyed reported having experienced discrimination in health-care settings, including refusal of services, breaches of confidentiality, and verbal abuse, with 25% noting that these reactions occurred very often.<sup>92</sup>

Systems that require IDUs to make visits to many different clinics, and those that demand collateral fees for ART or immune-system monitoring, also induce non-adherence. In Russia and Ukraine, as elsewhere in the former Soviet Union, medical treatment has historically been separated by discipline, with tuberculosis hospitals, AIDS centres, and narcological (drug treatment) dispensaries all claiming exclusive authority for treatment of their specialty.<sup>4</sup> In Ukraine, for example, IDUs co-infected with HIV and tuberculosis have reported that ART clinics will not treat them until they have completed inpatient tuberculosis treatment, and that tuberculosis hospitals will not offer methadone or buprenorphine. Although integrated sites are now being piloted, treatment interruption—particularly discharge from tuberculosis treatment as a result of active drug use or HIV infection—has been common.<sup>93-95</sup> Female IDUs report that AIDS centres and narcological dispensaries will not treat sexually transmitted infections or refer them to obstetricians and gynaecologists, and that doctors frequently disparage them or tell them they should return to the narcological dispensary.<sup>96</sup>

Informal fees or collateral costs for laboratory tests, treatment drugs, or physician care are a substantial barrier for drug-dependent IDUs in all five of the countries that we have considered.<sup>97,98</sup> In two regions in China, charges to patients were estimated to vary between 116% and 350% of average yearly income, despite the free ART programme.<sup>99</sup> Demands for collateral fees are only one of many barriers to methadone and buprenorphine treatment in low-income and middle-income countries with IDU-driven HIV epidemics. Other barriers include reviews by panels of physicians before admission, restrictions on dose adjustments, requirements that providers cease or reduce doses after urine tests showing illicit drug use, and demands that prospective patients show several documented periods of drug-free treatment, even in countries where that treatment is unaffordable or unavailable.<sup>100</sup>

IDUs seeking publicly funded drug-dependence treatment in each of the five countries have their names added to government registries that, by practice or by law, are shared with the police. Registered IDUs report being subject to stop-and-frisk procedures or repeated urine testing by police, denial of basic privileges such as driving

licences and employment, and in Russia and Ukraine, removal of child custody rights.<sup>101–103</sup> These sanctions apply to people who have completed drug treatment as well as those receiving OST. In China, methadone patients presenting national identity cards to check into a hotel or register children for school have reported that police arrive shortly thereafter to demand a urine test.<sup>103</sup> Unsurprisingly, IDUs report that fear of registration is a deterrent to seeking of treatment.<sup>88,89,95</sup>

Other forms of police harassment, including arrest of methadone patients outside clinics, searches of patient homes, removal of ART from IDUs by police convinced that the drugs are illicit, and detention in police facilities, also deter ART or drug-dependence treatment.<sup>4,93</sup> In Ukraine, IDUs can be detained for up to 72 h without charge, with police using painful withdrawal from opioid dependence, or threat of it, to coerce confessions to unsolved crimes or to extract bribes.<sup>93,95</sup> In Malaysia, detention on suspicion of drug use can extend to 2 weeks, with positive urine tests followed by flogging and remand to compulsory treatment.<sup>104</sup> International human rights experts have noted that use of a painful medical disorder to extract confessions, which is reported by IDUs in many countries, meets the definition of torture.<sup>105</sup>

In Malaysia, China, and Vietnam, suspicion of drug use or a positive urine test can result in detention in compulsory rehabilitation centres. Detainees in these centres, which are often run by the police or military, are not medically assessed for addiction severity or need of treatment, and in China and Vietnam have no access to lawyers, trial, or right of appeal. Roundups of alleged drug users are frequent, especially before national holidays or in conjunction with national war-on-drugs campaigns designating drugs, drug users, and drug dealing as social

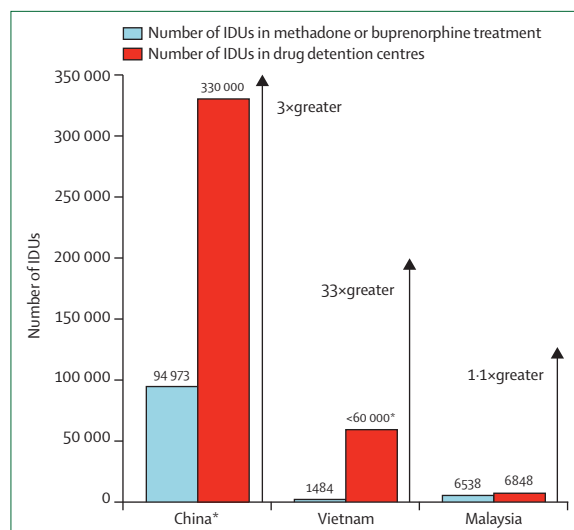
evils.<sup>4,106</sup> Despite reported HIV prevalence ranging from 10% to 65%, ART is largely unavailable to detainees in the centres, as is evidence-based treatment for drug dependence.<sup>107–110</sup> Detainees are instead required to do military-style drills and chant slogans, and are punished for infractions of centre rules with beatings, food deprivation, sexual assault, and physical and verbal abuse by guards or inmates acting at the behest of guards. In violation of international labour law, China and Vietnam force detainees to work, often in the service of private companies.<sup>103,108</sup>

Estimated rates of return to drug use after release from rehabilitation centres range from 75% to 95%.<sup>111</sup> With the notable exception of Malaysia, where the government has shifted funding to methadone treatment and reduced the numbers of people in compulsory drug-free rehabilitation by 29% since 2003,<sup>65</sup> the number of centres and length of detention has increased, with detention reaching 4 years in Vietnam and 2 years in China in 2009.<sup>110,112</sup> The numbers of drug users in these centres exceed the numbers in government-funded outpatient treatment in all countries where drug detention is practised (figure 3).

For IDUs charged with a crime, pretrial detention is another barrier to treatment. Pretrial detainees in Russia and Ukraine often await trial for a year or more; both countries have been found guilty by the European Court of Human Rights of ill-treatment of detainees and violations of due process.<sup>4</sup> Conditions reported by detainees in Russian pretrial detention facilities include denial of medical treatment for life-threatening disorders, below freezing temperatures, food deprivation, isolation without cause, and beatings by guards.<sup>114</sup>

Imprisonment after conviction is also associated with interruption of ART and OST. In Malaysia, for example, possession of any amount of illicit substance is punishable by flogging and imprisonment for up to 2 years. In Ukraine, IDUs can be sentenced for up to 3 years for possession of less than one daily dose of a homemade opioid that is most often injected.<sup>95</sup> Between 1998 and 2003, Russian authorities imprisoned IDUs for up to 4 years for residue found in a used syringe. Although the country has since eased drug penalties, people possessing 0.5 g of heroin can still be imprisoned for up to 3 years.<sup>115</sup>

Access to ART in prisons is restricted or unavailable in all five countries. In Malaysia in 2009, fewer than one in 15 detainees estimated to be infected with HIV received ART.<sup>65</sup> In Ukraine, where an estimated one in three participants in HIV services has been in prison,<sup>116</sup> officials report that ART was available to fewer than one in ten of the estimated 6062 incarcerated people infected with HIV in 2009.<sup>117</sup> In Russia, where more than 49 000 people with HIV were incarcerated in 2009,<sup>118</sup> patient accounts suggest that bureaucratic delays, scarcity of trained personnel, and unsanitary conditions impede or prevent access to treatment (panel 2). Incarceration interrupts ART in Vietnam, with prisoners held without treatment and then released if they become



**Figure 3: Number of IDUs receiving government-funded methadone or buprenorphine treatment versus those in drug detention, 2009**

Data sources: methadone or buprenorphine treatment in China and Vietnam,<sup>12</sup> Malaysia;<sup>71</sup> drug detention in China,<sup>71,113</sup> and Vietnam and Malaysia.<sup>12</sup> IDU=injecting drug user. \*Data are for 2008.

seriously ill.<sup>119</sup> None of the countries with megaepidemics in IDUs offers OST in prison, though Malaysia has begun starting prisoners on a 6-month course of methadone treatment before release.<sup>65</sup>

Risk of fatal opioid overdoses is higher in IDUs recently released from prison or from drug-free treatment settings.<sup>120</sup> Risk is compounded by restricted access to medications to reverse opioid overdose. Naloxone, which is administered by intramuscular injection or intranasally to reverse such overdoses, is often unavailable or limited to clinical settings.<sup>121</sup> Although data for overdose fatalities are scarce, the proportion of IDUs reporting non-fatal overdoses ranges from 30% to 80% in China, Vietnam, Thailand, and various countries of the former Soviet Union.<sup>122–125</sup> In Russia, more than five times as many deaths were caused by drug overdoses than by AIDS in 2006; in 2008 in St Petersburg, where 75% of IDUs reported having overdosed, only two of 190 ambulances stocked naloxone, and police refuse to provide rescue breathing to IDUs in respiratory arrest.<sup>121,122</sup>

Extreme drug penalties also affect physicians and patients who are not IDUs. In Ukraine, police have searched the homes of OST providers and threatened them with arrest if they did not provide patient lists.<sup>126</sup> In Russia, the ban on OST extends to discussion of the treatment; one physician's website providing evidence about methadone was closed after inquiries from the prosecutor general.<sup>127</sup> Availability of drugs for pain relief is sharply constrained by over-regulation. In a 1995 study, almost half of 50 countries surveyed cited health providers' fear of legal prosecution as a deterrent to opioid prescription for palliative care.<sup>128</sup> Russia and Ukraine both impose severe regulations on prescription of opioids for pain relief, limiting prescription privileges to particular specialties, requiring that physicians obtain a special permit to prescribe, setting arbitrary dose limits, and imposing restrictions on the sites where opioids can be dispensed or the number of days for which pain relief can be prescribed before renewal of the prescription.<sup>129</sup> Although China eased regulations for prescription of opioids for pain relief in 2005, prescribing physicians and patients both still have to secure special permits, with patients required to renew permits every 2 months.<sup>130</sup> The deterrent effects of such measures on availability of pain treatment are well documented.<sup>129</sup> Vietnam, by contrast, sharply eased regulations in 2008, obliging hospitals to stock opioids if no pharmacies in the district do, abolishing the maximum daily dose, and allowing prescriptions to be issued for 30 days rather than 7 days.<sup>131</sup> The effects of these changes on availability of opioids for pain relief in the country remain undocumented.

## Ways forward

Barriers to ART for IDUs in the countries that we have considered are emblematic, not exceptional. Treatment separated by specialty,<sup>4</sup> discrimination by health-care providers,<sup>132</sup> police harassment,<sup>116,133</sup> and interruption of

### Panel 2: Trying to survive

"When they brought me to the prison, I said that I had HIV and AIDS and that I had started taking ART [antiretroviral therapy] because my clinical condition called for it. When I got to prison, I explained my situation to all the doctors who saw me, I explained, that having the medicines was a matter of life and death for me, that I can't interrupt the treatment. They told me to calm down...And they didn't give me anything. They told me they didn't have those medicines, they didn't have connections with the AIDS Center...Basically, they were out of the loop and they didn't have anything. This is how it [treatment] looked: they opened the feeding bunk and threw in all the pills—here you are, take it...And that's it! The nurse gave the same pills to everyone—and each inmate had a different diagnosis. She would give us all the same pill and said, 'swallow it'. They didn't check at all if people were treated or not. If you come to the doctor's office, they give you pills and look in your mouth to make sure you swallow them. If you don't swallow and you take a pill with you from there, you get 15 days in a punishment cell. So [one] guy kept eating the pills...In the end he got ascite [fluid in the abdomen], drum belly. And he died.

When I got there [medical correctional facility], I told all the doctors that I had advanced AIDS, told them everything, showed my last medical records...But nothing, no effect. When I came there in 2007, many inmates with HIV had been transferred there and they didn't know what to do with them. They hadn't even registered us as HIV patients—we were listed as TB [tuberculosis] patients. So they put all the inmates with HIV in one barrack and didn't let us out at all. I got very sick in spring of 2007 or 2008. I had a fever of 40 [°C] for a whole week. The doctors couldn't do anything, they couldn't understand what was going on. At that time, all people with HIV had to be isolated. Even in the prison hospital, they put us in the isolation chamber in the basement. Can you imagine?! A punishment isolation chamber. The chamber I was put in was very small, about 2 meters long. There were two of us there. They didn't do anything. For two or three weeks I sat in the isolation chamber and then was just sent back. They didn't even list us people with HIV anywhere. Because an HIV patient in the prison means a certain diet, state subsidies, some additional money is supposed to be allocated for an inmate with HIV. And they didn't have it. We spent one year, even more, listed as TB patients, not HIV patients; there was no HIV."

*An excerpt from Anya Sarang's interview with KP, who had recently been released from a Russian prison, 2009.*

HIV treatment in drug detention centres or prison<sup>134</sup> have been documented in many other low-income and middle-income countries with HIV epidemics or subepidemics concentrated in IDUs. OST programmes in most countries with low and middle incomes remain in perpetual pilot status. In Kyrgyzstan, Moldova, and Azerbaijan, failure to ensure adequate supply of OST

has resulted in sudden cessation of treatment or clinically inappropriate reduction of doses.<sup>100</sup> Across southeast Asia, fewer than 12 000 of an estimated 800 000 IDUs had access to methadone or buprenorphine in 2009.<sup>6</sup>

Systematic collection of data for IDU access to HIV treatment and care is a first step toward appraisal and transcendence of barriers to ART for IDUs. Although the US President's Emergency Plan for AIDS Relief has been required since 2009 to obtain information about number of IDUs reached by US-funded services, these data remain unavailable.<sup>135</sup> The Global Fund to Fight AIDS, Tuberculosis and Malaria, which between 2001 and 2008 has awarded about \$180 million for HIV prevention in IDUs,<sup>136</sup> does not ask grantees to detail IDU-related spending, even in countries where most of the HIV-infected population are IDUs. As the American historian Patricia Cohen has noted, "that which is not counted does not count".<sup>137</sup> Data collection should also include an equity ratio comparing share of HIV infections in IDUs to share of IDUs on ART.

Resource requirements associated with scale-up of treatment to IDUs are substantial. Assessment of costs and benefits of such investment, however, have been infrequent, and need to measure not only life-years gained and reductions in HIV transmission, but also broad benefits of OST such as reduction in crime, imprisonment and law enforcement, improved family relationships, return to gainful employment, and reduction in demand for illicit drugs. In China, for example, a review by the national methadone working group estimated that treatment of 200 000 heroin users with methadone would remove as much as \$483 million from the illegal drug market.<sup>138</sup> Cost reductions can also be obtained through changes in treatment delivery systems. Most low-income and middle-income countries, for example, do not allow take-home doses of OST, sharply constraining treatment scale-up and increasing costs of service delivery. Use of generic rather than brand-name drugs, or increased application of cost-reduction mechanisms such as compulsory licensing, could also reduce costs.<sup>139</sup>

Although analysts have increasingly discussed the importance of risk-environment analysis to assess effects on treatment,<sup>4,59,140</sup> metrics to undertake such analysis are needed. Rather than focusing on active drug use, comorbidities, or assessments of individual patient stability to establish treatment readiness, a systemic approach might measure physician attitudes towards IDUs, regulatory restrictions on provision of ART or OST, and reported levels of police harassment as determinants of adherence.

In view of the effectiveness of OST for improvement of adherence to and outcomes of ART, reconceptualisation of combination treatment to include methadone or buprenorphine is essential. Surveys of ART in countries with injection-driven HIV epidemics should include data for OST accessibility, availability, and price, and initiatives to increase treatment access should emphasise OST as

well as ART availability. High prevalence of co-infection with tuberculosis in HIV-positive IDUs draws attention to the need for similar integration of ART, OST, and tuberculosis treatment; half the 26 countries that WHO designates as high burden for multidrug-resistant tuberculosis have injection-driven HIV epidemics.<sup>141</sup> Treatment of hepatitis C, which is endemic in IDU networks in low-income and middle-income countries, also demands attention and integration with ART. The price of hepatitis C drugs is another structural obstacle impeding an effective response.

One approach to extending treatment coverage and reducing the deterrent effect of stigma experienced by IDUs in health clinics might be the use of peer support. In resource-poor settings with HIV epidemics that are not driven by IDUs, task-shifting through use of treatment companions (*accompagnateurs*) and weekly home delivery of ART by lay field officers has improved ART adherence and allowed for scale-up of treatment.<sup>142</sup> Although IDUs are often described as having antisocial personalities, most drug users function in social networks to obtain and to administer drugs; conversely, treatment systems that often isolate IDUs from all external social supports display antisocial behaviour.<sup>4</sup> A new framework would establish directly observed therapy as an intervention that could effectively take place not only in settings overseen by clinicians, but also in the social settings of IDUs themselves.

Community-based programmes are likely to be especially important for the growing numbers of stimulant injectors in countries with injection-driven HIV epidemics<sup>59,143</sup> and for opioid injectors who also use amphetamine-type stimulants, for which no pharmacological substitution treatment exists. Programmes in Brazil delivering ART to cocaine injectors have increased patient retention and satisfaction through outpatient counselling services and clinics offering food, adherence support, laundry services, and waiting-room debates.<sup>31</sup> Methods such as peer-driven interventions and contingency management have increased engagement of stimulant users with HIV prevention or drug-dependence services.<sup>144,145</sup>

These systemic improvements, however, are unlikely to succeed without action to resolve the fundamental structural tension between public health approaches that treat IDUs as patients and law enforcement approaches that seek to arrest them. Police registries, arbitrary detention, and imprisonment of people who have committed no crime apart from the possession of drugs for personal use are barriers to treatment and care that cannot be overcome by counselling, electronic reminders, or peer support. The Secretary General of the UN and the head of the Joint UN Programme on HIV/AIDS have both publicly acknowledged the importance of decriminalisation of IDUs to increase HIV prevention and treatment access,<sup>146,147</sup> and the Executive Director of the Global Fund has urged decriminalisation of petty drug possession on public health grounds.<sup>148</sup> Human

rights experts, including the special rapporteurs on torture and health and the UN High Commissioner on Human Rights, have emphasised that drug users do not forfeit their rights as a result of illegal behaviours and that existing drug control approaches subject IDUs to serious abuses.<sup>105,149</sup> The health effects of human-rights protections for IDUs need to be better assessed, since legal empowerment strategies, access to an attorney, legal reform, or change in pretrial detention practices might be as crucial to containment of HIV as are sterile syringes or ART.

Laws mirror political processes. Although health professionals need to increase their focus on structural obstacles to ART provision, a basic challenge remains in the reversal of social forces, including popular opinion, that portray IDUs as already dead or less than human, and so deserving of less-than-human rights. Resurrection of IDUs from this status is beyond the healing power of ART alone, although reformation of HIV treatment systems can help to emphasise that IDUs, including those actively injecting, are capable of making positive choices to protect their health and that of their communities. Treatment advocates and policy makers would be aided by returning to the original universal access document, the 1948 Universal Declaration of Human Rights, to guide the formation of an approach that will help IDUs and others vulnerable to HIV to receive equitable treatment and care.

#### Contributors

DW guided overall research and parameters of the paper, wrote the introduction and sections on coverage, barriers, and ways forward, and coordinated revisions by and communications between other authors. MPC contributed to review, analysis, and summary of studies on ART adherence and virological outcomes and OST effects on ART, and to review and reorganisation of the overall report structure. DS contributed to literature review, data analysis, and data interpretation related to costs and cost-effectiveness of ART, OST, and other interventions for people who inject drugs.

#### Steering committee

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#### Conflicts of interest

We declare that we have no conflicts of interest.

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