

# 3.1: The silent epidemic: Responding to viral hepatitis among people who inject drugs

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## Introduction

Hepatitis B (HBV) and hepatitis C (HCV) are the two most common forms of viral hepatitis. They are also the most common blood-borne viral infections to affect people who inject drugs. While the urgency of preventing and treating HIV infection among people who inject drugs has overshadowed the more 'silent' epidemic of viral hepatitis,<sup>a</sup> the latter is increasingly recognised as a major public health problem, particularly in cases in which people living with HIV are co-infected with HBV and/or HCV.

Both HBV and HCV can be effectively treated and cured. However, treatment uptake remains extremely low among people who inject drugs in those settings in which it is available. In most low- and middle-income countries treatment is generally unavailable or prohibitively expensive. Access to prevention and treatment for viral hepatitis among people who inject drugs is often hampered by a lack of expertise among health care providers. Evidence shows that providing integrated and patient-oriented prevention and treatment services are effective in engaging and retaining people who inject drugs in services and successfully treating viral hepatitis.

There is a need to build prevention and treatment service capacity. The coordination between HBV and HCV treatment services and HIV, TB and mental health services is critical. Meaningful consultation with drug user organisations and the inclusion of drug users or 'peer workers' in service delivery models is not only best practice,<sup>1</sup> but also provides an important mechanism to improve prevention and treatment literacy among

drug using populations. This chapter provides a global overview of viral hepatitis among people who inject drugs and summarises the international response in policy and programmes.

## An introduction to viral hepatitis

Viral hepatitis infection is widespread. It is estimated that 170 million people are living with HCV and two billion people are infected with HBV, of whom 360 million have chronic HBV infection. The majority of these people live in low- and middle-income countries. Viral hepatitis can cause liver fibrosis, dysfunction and ultimately cirrhosis and cancer of the liver, all resulting in increased morbidity and mortality. The global burden of disease due to acute hepatitis B and C and to cancer and cirrhosis of the liver is high (about 2.7% of all deaths) and is forecast to become a higher ranked cause of death over the next two decades.<sup>2</sup>

### **Hepatitis B: Prevalence and transmission**

HBV is transmitted primarily through blood and infected bodily fluids. The most common routes of transmission are from mother to child (vertical or perinatal transmission), person to person in early childhood (horizontal transmission), unsafe medical injection (iatrogenic transmission), sexual transmission and via the sharing of injecting equipment. Approximately 60% of the global population lives in areas where HBV infection is highly endemic. HBsAg is the marker in the blood that indicates active HBV infection. The prevalence of this marker in the general population of a defined geographical area provides a measure of how endemic the virus is. Endemicity varies considerably around the world (see Table 3.1.1).

a In this chapter viral hepatitis refers to hepatitis B and C and not other types of viral hepatitis such as hepatitis A, D, and E.

A comprehensive approach to eliminating HBV transmission is necessary to address infections acquired perinatally and during early childhood, as well as those acquired by adolescents and adults.

**Table 3.1.1: Characteristics of hepatitis B epidemics<sup>3 4</sup>**

Hepatitis B endemicity	HBsAg prevalence among general population <sup>5</sup>	Main modes of transmission
<b>Low</b>	<2%	<ul style="list-style-type: none"> <li>Most new infections occur among young adults via sexual transmission and sharing injecting equipment<sup>6</sup></li> </ul>
<b>Intermediate</b>	2–7%	<ul style="list-style-type: none"> <li>Vertical, perinatal, horizontal, health-care-related and sexual transmission all occur</li> </ul>
<b>High</b>	≥8%	<ul style="list-style-type: none"> <li>Vertical, perinatal and horizontal transmission in early childhood are most common</li> <li>70% to 90% of adult population has serologic evidence of prior HBV infection</li> </ul>

People who inject drugs are at increased vulnerability to infection through the sharing of injecting equipment. The prevalence of HBV among people living with HIV (HBV/HIV co-infection) varies widely, for example, ranging from between 5% and 10% in the United States to between 20% and 30% in Asia and parts of Sub-Saharan Africa.<sup>7</sup> It is higher in areas where vertical and perinatal HBV transmission is high and lower in areas where exposure to HBV is limited to adulthood. This is because although the rate of chronic HBV infection among HIV-positive adults exposed to HBV is increased compared with HIV-negative individuals, it is much lower than the risk of developing chronic HBV in early childhood.

### **Hepatitis C: Prevalence and transmission**

HCV is transmitted primarily through contaminated blood, blood products and injecting equipment. The sharing of other equipment such as tourniquets, filters and spoons has also been associated with HCV transmission although this is less common.<sup>6</sup> Sharing injecting equipment among people who inject drugs is the most common route of HCV transmission. In high-income countries, a greater proportion of HCV infections in the population is attributable to injecting drug use, while in low- and middle-income countries iatrogenic transmission (through medical and other unsterile injections) continues to occur.<sup>8,9</sup> Among people who inject drugs, the incidence of infection appears higher in low- and middle-income countries compared with high-income countries, illustrating that the epidemic of HCV among people who inject drugs is more recent in the developing world.<sup>10</sup>

Both HBV and HCV are more easily transmissible than HIV. Therefore, viral hepatitis prevalence in any given population of people who inject drugs is often much higher than HIV prevalence. Furthermore, studies of HCV infection in drug users who do not inject indicate an increased risk of HCV infection. A 2007 synthesis of available high-quality data regarding HCV infection among non-injecting drug users found a range of prevalence from 2% to 35% across thirty-five studies globally.<sup>11</sup> In addition, non-injecting drug users may transition to injecting drug use, increasing their risk of infection with blood-borne viruses.

Sexual transmission of HCV is rare.<sup>12</sup> Recent studies suggest that traumatic sexual practices and HIV co-infection may be conducive to HCV transmission.<sup>13,14,15</sup> Research from the Netherlands highlights that sexual transmission of HCV is occurring among HIV-positive, non-injecting but substance-using men who have sex with men, engaging in traumatic sexual practices.<sup>16</sup> Also, the presence of ulcerative sexually transmitted infections (STIs) may facilitate HCV sexual transmission.<sup>17</sup>

HCV prevalence in prisons and other detention settings is high as a result of the large numbers of injecting drug users who spend time in detention, combined with risk behaviours such as injecting and non-sterile tattooing that often occur in these settings.<sup>18</sup> As shown in Table 3.1.2, across the limited number of countries for which data are available, prison populations consistently contain a high proportion living with HCV (see Chapter 3.5 on prisons).<sup>19</sup>

Overall, data on viral hepatitis among people who inject drugs are scarce and comparison is often difficult as data have been collected over different time periods and/or using different collection methods between and within countries. While such data must be interpreted with great caution, a crude analysis indicates that HCV, in particular, is highly prevalent among people who inject drugs. Table 3.1.3 provides an overview of the currently available data for the ten countries making up 70% of the estimated global HIV burden among people who inject drugs.

Brazil, China, Indonesia, Italy, Kenya, the Russian Federation, Thailand, the US, Ukraine and Viet Nam account for half of the total estimated population of injection drug users (8.1 million people) and two-thirds of the estimated global population of people who inject drugs and are living with HIV (2.1 million people).<sup>20</sup> The average HIV prevalence among people who inject drugs in these ten countries is approximately 25%, whereas the HCV prevalence is much higher, up to 60%. In addition, in eight of these countries (the exceptions are Ukraine and Kenya) for which data are available, three-quarters of the people who inject drugs and are living with HIV are co-infected with HCV. Some of these countries, including China, the Russian Federation and Viet Nam, have rates of HIV/HCV co-infection in populations of injectors of over 90%.

Table 3.1.4 provides an illustrative overview of the prevalence of chronic HCV (HCVAb) and HBV infection (HBsAg) in these ten countries. Although only viral hepatitis status is presented here, a majority of people who inject drugs and are living with HIV in most countries are co-infected with either HCV or HBV or both viruses together. There is wide variation in the quality of the data between and within countries, and data for HBV status among people who inject drugs is less extensive than that of HCV. It should be noted that the prevalence of chronic HBV in injectors reflects population prevalence despite generally being higher, while the burden of HCV among people who inject drugs is universally high regardless.

**Table 3.1.2: Prevalence of HCV among people who inject drugs and prisoners in selected countries<sup>21 b</sup>**

Country or territory	Adult HCV prevalence among people who inject drugs	HCV prevalence among prisoners
Bahrain	81%	-
Brazil	39.5–69.6%	-
Czech Republic	21–59%	18–78%
Estonia	90%	82–97.4%
Germany	75%	80% (prisoners with a of history of injecting, Berlin)
India	92%	-
Indonesia	60–98%	-
Iran	35%	18.7%
Japan	55.1–60%	-
Kazakhstan	65.7%	-
Mauritius	95%	-
New Zealand	70%	80% (prisoners with a history of injecting)
Pakistan	89%	-
Saudi Arabia	69%	-
Sweden	83.8%	-
Thailand	90%	-
Ukraine	70–90%	-
UK	41%	30–44% (prisoners with a history of injecting)
US	50–80%	30–40%

**Table 3.1.3: Crude analysis of estimated prevalence of HIV among people who inject drugs (IDUs) in top ten priority countries (using mid-point estimates)<sup>20 c</sup>**

Country	Number of people who inject drugs	HIV prevalence among people who inject drugs	Number of IDU living with HIV	Percentage of global total number of IDU living with HIV <sup>d</sup>
Russia	1,825,000	37.15%	677,988	22.6%
Brazil	800,000	48%	384,000	12.8%
US	1,857,354	15.57%	289,190	9.6%
China	2,350,000	12.3%	289,050	9.6%
Ukraine	375,000	41.8%	156,750	5.2%
Indonesia	219,130	42.5%	93,130	3.1%
Thailand	160,528	42.5%	68,224	2.3%
Kenya	130,748	42.9%	56,091	1.9%
Viet Nam	135,305	33.8%	45,733	1.5%
Italy	326,000	12.1%	39,446	1.3%
<b>Total</b>	<b>8,179,065</b>		<b>2,099,602</b>	<b>70%</b>

b No new data were collected systematically since 2008.

c Since this table was prepared, updated information has become available for Brazil and Ukraine – see regional chapters for details.

d Mathers et al (2008) estimate that 3 million people who inject drugs are living with HIV.

**Table 3.1.4: Crude analysis of estimated prevalence of HCV and HBV in ten highest priority countries<sup>22e</sup>**

Country	Percentage of people who inject drugs living with HCV	Number of people who inject drugs living with HCV	Number of people who inject drugs living with HCV (mid-range estimate)	Percentage of IDUs with chronic HBV (HBsAg)	Number of IDUs with chronic HBV (HBsAg)	Number of IDUs with chronic HBV (HBsAg) (mid range estimate)	Population prevalence of HBV (HBsAg)
Russia	54–97% <sup>23 24 25</sup>	985,500 to 1,770,250	1,377,875	4–9% <sup>26 27</sup>	73,000 to 164,250	118,625	Intermediate
Brazil	10–83% <sup>28 29 30 31</sup>	80,000 to 664,000	372,000	2–7% <sup>30 32 33</sup>	16,000 to 56,000	36,000	Intermediate
USA	35% <sup>34</sup>	650,074	650,074	2–11% <sup>35</sup>	37,147 to 204,309	120,728	Low
China	61.4% <sup>36</sup>	1,442,900	1,442,900	2.9–16.9% <sup>37 38 39</sup>	68,150 to 397,150	232,650	High
Ukraine	61–79% <sup>40 41 42 43</sup>	228,750 to 296,250	262,500	6.7–10.9% <sup>41 44</sup>	25,125 to 40,875	33,000	Intermediate
Indonesia	60–98% <sup>45</sup>	131,478 to 214,747	173,113	n/a	n/a	n/a	High
Thailand	4–97% <sup>46 47 48 49</sup>	6,421 to 155,712	81,067	9.5–14% <sup>46 50</sup>	15,250 to 22,474	18,862	High
Kenya	42–61% <sup>51 52</sup>	54,914 to 79,756	67,335	6.30% <sup>52</sup>	8,237	8,237	High
Viet Nam	46–74% <sup>53 54</sup>	62,240 to 100,126	81,183	14.2% <sup>53</sup>	19,213	19,213	High
Italy	60% <sup>55</sup>	196,252	196,252	n/a	n/a	n/a	Low

n/a = data not available

## Epidemiology by region

### Western Europe

HCV infection in Western Europe was most commonly spread by unsafe medical procedures, blood and blood products during the early twentieth century. With the introduction of universal precautions and screening of blood and blood products during the early 1980s, transmission shifted to sharing of injecting equipment among drug users. In northern Europe, the population prevalence is between 0.1% and 1%. The population prevalence of HCV in Western Europe is between 0.2% and 1.2% and in southern Europe is between 2.5% and 3.5%.<sup>56</sup>

Western European countries generally have low HBV endemicity, although there are significant variations. The prevalence of HBsAg in Italy has decreased from 3% in the 1980s to less than 1%.<sup>57</sup> There is less information available about HBV/HIV co-infection.

### Eurasia

There is limited information about HCV prevalence in Central and Eastern Europe and Central Asia. Nevertheless, the available data indicate higher prevalence than in Western Europe, with very high prevalence among some risk groups, including people who inject drugs.<sup>58</sup> Most studies of people who inject drugs and are living with HIV in the region have found HCV/HIV co-infection prevalence to be greater than 80%.<sup>21</sup>

The epidemiology of HBV and HBV/HIV co-infection in Eastern Europe is less well understood. In general, HBV prevalence among the general population and among people who inject drugs in Central Europe and Central Asia is higher than in Western Europe.

### Asia and Oceania

HCV prevalence in Asia and the Pacific varies between countries. HCV infection is due to unsterile medical injections,<sup>8 9</sup> contaminated blood transfusions,<sup>59</sup> traditional cultural practices<sup>60</sup> and, more recently, injecting drug use.<sup>61</sup> While iatrogenic transmission still occurs in some countries, transmission as the result of injecting drug use is increasing.<sup>62</sup>

Population HCV prevalence ranges from 1.4% in Australia to 5.6% in north-western Thailand. HCV is very common among people who inject drugs in Asia and almost universal among those who are living with HIV.<sup>63 64</sup> HCV/HIV co-infection is a major issue in Asia as it is estimated there are between 735,000 and 1.4 million people who inject drugs and are living with HIV<sup>20</sup> in the region.

Hepatitis B is endemic in most of Asia, with some notable exceptions, including Singapore and Taiwan. Few studies have examined the prevalence of HBV/HIV co-infection among people who inject.

<sup>e</sup> Further detail about cited studies can be found in Table 3.1.5. The data cited are not of uniform quality and should be interpreted as illustrative of the burden of viral hepatitis among people who inject drugs rather than as an accurate measure of the burden of disease. These data result from the inclusion of data from published sources rather than confirmed cases collected in national surveillance systems. HCV status refers to HCVAb prevalence in cited studies. Note that the presence of HCV seropositivity may not indicate HCV RNA viraemia. HBV status refers to HBsAg in order to indicate the current burden of disease as HBV DNA status indicating viraemia was not available in the epidemiological literature. Since this table was prepared, updated information has become available for Brazil and Ukraine – see regional chapters for details.

## **Middle East and North Africa**

HBV and HCV prevalence in the Middle East and North Africa vary significantly. In the eastern Mediterranean region, it is estimated that unsterile medical injections are responsible for 2.5 million HBV infections, 600,000 HCV infections and 2,200 HIV infections annually,<sup>65</sup> which account for 58% of all HBV infections, 82% of HCV infections and 7% of HIV infections.

The country with the highest population HCV prevalence globally is Egypt (15% to 20%), a result of the use of unsterile injections during schistosomiasis eradication programmes from the 1960s through to 1987.<sup>66,67</sup> Other countries report much lower HCV prevalence. The Middle East and North Africa region has an intermediate level of HBV endemicity. Apart from in Iran, there is little available data on viral hepatitis among people who inject drugs in the region.

## **Sub-Saharan Africa**

Population HCV prevalence in Africa varies by country but is generally high.<sup>68,69</sup> Iatrogenic transmission was important in the development of the African HCV epidemic.<sup>70,71</sup> Much of Africa has a high level of HBV endemicity, with an estimated fifty million people living with chronic HBV in Sub-Saharan Africa and the population HBsAg prevalence is between 9% and 20%.<sup>72</sup> Transmission is mainly perinatal and during early childhood rather than vertical alone.<sup>73</sup> Little is known about HCV and HBV prevalence among people who inject drugs in Africa.

## **North America**

The prevalence of chronic HCV is approximately 1.3% in the United States<sup>74</sup> and 0.7% in Canada. Over 60% of new infections in Canada are attributable to injecting drug use,<sup>75</sup> with a similar proportion in the US.<sup>76</sup>

HBV prevalence in the US is low and decreasing, although it remains elevated in some immigrant groups and indigenous communities.<sup>77,78,79</sup> While sexual transmission is most common, around 12% of all acute HBV cases in the US occur in individuals with a history of injecting drug use. In Canada, 34% of acute HBV cases occur among people who inject.<sup>80</sup>

## **Latin America and the Caribbean**

The population prevalence of HCV in Latin America varies by country, but is generally less than 1%. Most HCV infections in Latin America are the result of contaminated blood products, although there are places in which injecting drug use is an important risk factor such as the northern states of Mexico and major urban areas in Central and South America. Overall, HCV prevalence among people who inject drugs is high in Latin America. It is also elevated among non-injecting cocaine users in Brazil and Argentina. Studies of HCV infection in people who inject drugs and are living with HIV have shown very high proportions of co-infection.

Central and South America is mostly considered a region of low HBV endemicity, although there are some exceptions, including the Amazon region. It is estimated that there are some 400,000 new HBV infections in Latin America annually.<sup>81,82</sup> HBV prevalence among people who inject drugs is less understood although there are some studies from major Latin American cities.<sup>33,83</sup>

There is little data available on the prevalence of viral hepatitis in the Caribbean. One exception is the Dominican Republic, which has high HBV endemicity.

## **Prevention of viral hepatitis**

Universal infant immunisation, catch-up immunisation of at-risk populations, improved screening of blood products, prevention of transmission in health care settings and safer injecting and sexual practices are common prevention strategies recommended for HBV and HCV. Due to screening of blood donors and products, HBV and HCV transmission via blood products has been virtually eliminated in developed and many developing countries. Transmission of HBV and HCV via medical procedures, including injections, is rare in developed countries but continues to occur in developing countries.

The availability of HCV testing since 1989 resulted in the introduction of blood product screening in the early 1990s in Australia, Europe and the US. As of 2005 HCV screening is available and used in at least 129 countries, 110 of which screen 100% of their blood supply.<sup>84</sup> In those high-income countries that have initiated screening, the number of new HCV infections has dropped dramatically, but what remains are alarming HCV epidemics almost exclusively among people who inject drugs.

The global expansion of HBV vaccination, including of health care workers, has resulted in a decline in acute HBV cases, a reduction in the proportion of deaths attributable to cirrhosis of the liver or liver cancers and falling prevalence of HBsAg in vaccinated populations.<sup>85</sup> As discussed below, in the absence of an effective HCV vaccine, harm reduction interventions are the principle programmatic measures that can be applied at the community level to prevent HCV infection, as well as HBV infection among non-vaccinated individuals.

## **Hepatitis B vaccination**

The HBV vaccine, which has been available since 1981 and is safe, effective and inexpensive, forms the mainstay of HBV prevention. Following the actions and resolutions outlined in Box 3.1.1, as of 2008, 177 countries had incorporated HBV vaccination as an integral part of their national infant immunisation programmes, and an estimated 69% of the 2008 birth cohort received three doses of HBV vaccine.<sup>86</sup> However, there are still many countries, particularly in Africa, South East Asia and Latin America in which HBV vaccine coverage levels are significantly lower. Furthermore, vaccination rates among most-at-risk populations, such as people who inject drugs, are low worldwide, with some exceptions.

There are few clinical issues related to HBV vaccine and there is no reason why it should not be given as a matter of course to people who use drugs. For people living with HIV, the vaccine response may be affected by some factors such as viral load, CD4 cell count, sex, age, type and duration of antiretroviral therapy (ART) and type of AIDS-defining illness. In order to obtain adequate protection, it is essential that people living with HIV are vaccinated as early as possible in the course of their disease.<sup>86</sup>

## Harm reduction measures

WHO, UNODC and UNAIDS recommend a comprehensive set of evidence-based measures for HIV prevention, treatment and care for people who use drugs both in communities and closed settings. These measures include:<sup>87</sup>

- Needle and syringe programmes (NSPs)
- Opioid substitution therapy (OST) and other drug dependence treatment
- Voluntary HIV counselling and testing
- Antiretroviral therapy
- Prevention and treatment of STIs
- Condom programming
- Targeted information, education and communication
- Hepatitis diagnosis, treatment and vaccination
- Tuberculosis prevention, diagnosis and treatment.

Measures such as NSPs, OST and other drug dependence treatment, condom programming and the prevention and treatment of STIs are also relevant for the prevention and treatment of viral hepatitis. Given that HBV and HCV are more infectious than HIV, coverage levels of these interventions would need to be higher than those recommended for HIV in order to have an impact on the epidemic.<sup>88</sup> Simple measures should also be included such as advising those people living with viral hepatitis to reduce consumption or abstain from alcohol, as well as providing other injecting paraphernalia such as tourniquets, filters and spoons.

People who inject drugs, men who have sex with men, and individuals with multiple sex partners, who have not been vaccinated against HBV, are at an increased risk of HBV infection through sex. Hepatitis C can also be transmitted sexually, particularly in the context of HIV co-infection. As with HIV prevention, safer sex practices (e.g. the consistent and correct use of condoms) are critical to reduce the incidence of HBV and HCV infection among at-risk groups and measures to promote safe sex need to be scaled up.

## Treatment and clinical management of viral hepatitis

### Hepatitis B

Not everyone who tests positive for hepatitis B requires treatment. Only in cases of chronic (or active) infection is treatment necessary. As previously noted, people who inject drugs may be more likely to develop chronic disease, particularly if they are also living with HIV. They may also experience a reactivation of HBV if they have recently acquired HIV.

### HBV/HIV co-infection

Not all people living with HIV/HBV co-infection require treatment for HBV. However, for those who do require treatment, it is generally lifelong for both infections. The antiretroviral (ARV) regimens for HIV/HBV co-infected individuals with active HBV disease should contain more than one ARV with both anti-HIV and anti-HBV activity (e.g. lamivudine [3TC] or emtricitabine [FTC] plus tenofovir [TDF]). Several studies have demonstrated that HIV/HBV co-infected individuals have a three- to six-fold increased risk of developing chronic HBV disease, an increased risk of cirrhosis and a seventeenfold increased risk of death when compared with HBV-positive individuals without HIV infection.<sup>89,90</sup>

However, recognising when HBV needs to be treated and the provision of adequate clinical management of HBV disease are still a challenge in the majority of resource-limited settings.

The lack of adequate HBV and HCV treatment policy guidance for resource-limited settings is reflected in the 2006 version of WHO recommendations for ART for HIV infection in adults and adolescents,<sup>91</sup> which provided limited guidance on managing HIV in people co-infected with HBV and/or HCV. However, the importance of viral hepatitis as a public health issue in the context of HIV has been progressively recognised. In 2007 the WHO European Region developed standardised clinical protocols for the management of HBV/HIV co-infection, HCV/HIV co-infection and prevention of hepatitis A, B and C virus infection in people living with HIV, particularly for those who inject drugs, an important population affected by HIV and viral hepatitis in this region.<sup>92</sup>

In 2009 WHO's recommendations for ART for HIV infection in adults and adolescents were reviewed and the revised guidelines make specific recommendations about ART management of HBV/HIV co-infection,<sup>93</sup> including that all people living with HIV should be screened for HBV infection and that ART should be initiated in all co-infected individuals who require treatment for HBV infection irrespective of CD4 cell count or clinical stage of HIV disease.

### Hepatitis C

Current treatment for HCV consists of pegylated interferon and ribavirin combination therapy for twenty-four weeks in genotypes 2 and 3 and forty-eight weeks in genotype 1 and most other genotypes.<sup>94</sup> Pegylated interferon needs to be administered subcutaneously, is complex to deliver (i.e. requires a cold supply chain and weekly injections), costly and not generally available through the public sector in resource-limited settings. Treatment efficacy is influenced by the HCV genotype, and side effects, including mental health complications, are common.

The current high cost of pegylated interferon, due to patents held by two pharmaceutical companies,<sup>f</sup> means that treatment is unavailable for most people who need it in low- and middle-income countries. Furthermore, there are no generic drugs currently available in the global market. The lack of technical capacity of professionals to deliver treatment is also a major barrier to access. Treatment is further complicated by issues of logistics (diagnosis, cold chain), the toxicity of the agents, the unpredictable nature of response to treatment and the need for long-term follow-up.

### HCV/HIV co-infection

As observed with HBV/HIV co-infection, HCV/HIV co-infection is also significantly associated with progression to advanced liver disease and is a leading cause of death among people living with HIV. Data suggest that HIV infection accelerates HCV-related disease progression and mortality,<sup>95,96</sup> but the effect of HCV on the rate of HIV disease progression remains difficult to distinguish. A recent meta-analysis showed an increase in the overall risk of mortality, but did not demonstrate an increased risk of AIDS-defining illnesses among people living with HCV/HIV co-infection.<sup>97</sup>

<sup>f</sup> Schering Plough's (recently merged with Merck & Co.) patent on pegylated interferon α2b expires in 2015 and Roche's patent on pegylated interferon α2a expires in 2017.

While many studies suggest that the sustained viral response rates of HCV therapy in HIV co-infected individuals are significantly lower than in people without HIV,<sup>98 99 100</sup> other studies have found higher response rates in this population.<sup>101</sup>

With regards to HCV treatment interactions with ART, a large multicentre observational cohort study conducted in Europe examined the level of toxicities of different ART regimens used for HIV/HCV co-infection and did not find significant differences.<sup>102</sup> However, important pharmacological interactions between ribavirin with abacavir (ABC), atazanavir (ATV), didanosine (ddI), stavudine (d4T) and zidovudine (AZT) have been described and can be associated with severe toxicity.<sup>102</sup> Viral hepatitis can adversely affect HIV treatment through the liver toxicity of some antiretroviral agents, which is becoming a major cause of morbidity and mortality among HBC/HIV and HBV/HIV co-infected people.<sup>89 97</sup>

As reported in the 2008 Global State of Harm Reduction report, there is very little available information on the extent to which people who inject drugs are receiving HCV treatment around the world. Responses to HCV among people who inject drugs are nascent or non-existent in most middle- and low-income countries.<sup>21</sup> In Asia, countries are just beginning to address HCV. In the Middle East, North Africa and Sub-Saharan Africa, information on the availability of HCV treatment is very limited. In Iran, where harm reduction services have been dramatically scaled up in recent years, HCV testing and treatment is available to some people. These services are available in South Africa, however, the

degree to which people living with HIV have access to them is unknown. In Latin America and the Caribbean, access to HCV-related services appears limited, although Brazil has a universal access policy to HCV treatment, including for people who inject drugs.<sup>21</sup>

Increased access to HCV management is most urgently needed in Asia and Eastern Europe as these regions have the highest HIV/HCV co-infection prevalence. Low-threshold accurate HCV diagnosis is not always available and the prohibitive costs of drugs to treat HCV prevent the majority of people who require HCV treatment from accessing it. In several countries, people who use drugs are explicitly excluded from HCV treatment. In some a period of abstinence from drug use is required before treatment can be initiated, while in others treatment is left to the discretion of the medical doctor.<sup>21</sup> Scaling up HIV, HBV and HCV testing, diagnosis and treatment and removing barriers to accessing services are critical steps required to address these dual epidemics among people who inject drugs.

### **International response to viral hepatitis**

The international response to viral hepatitis (among drug using populations and in general) is gradually gaining pace. As illustrated in Box 3.1.1, the World Health Assembly (the governing body of the WHO) has long been vocal on the threat posed by viral hepatitis and the necessity of taking prevention interventions to scale.

**Table 3.1.5: Further information on data sources from table 3.1.4**

Country	Sites and number of participants in study on HCV	Sites and number of participants in study on HBV
Russia	Togliatti City (n = 411 IDUs) <sup>23</sup> Moscow, Volgograd and Barnaul (n = 1,473 IDUs) <sup>24</sup> St Petersburg (n = 446 IDUs) <sup>25</sup>	Tver' region Russia (n = 352 IDUs) <sup>26</sup> St Petersburg (n = 910 IDUs) <sup>27</sup>
Brazil	Sao Paulo (n = 205 IDUs) <sup>28</sup> Rio de Janeiro (n = 606 IDUs) <sup>29</sup> Salvador, São José do Rio Preto, Florianópolis, Itajaí, Porto Alegre, Gravataí (n = 847 IDUs) <sup>30</sup> Rio de Janeiro (n = 606 IDUs) <sup>31</sup>	Rio de Janeiro (n = 609 IDUs) <sup>32</sup> Rio de Janeiro (n = 102 IDUs) <sup>33</sup> Salvador, São José do Rio Preto, Florianópolis, Itajaí, Porto Alegre, Gravataí (n = 847 IDUs) <sup>30</sup>
US	Los Angeles, Chicago, New York, Baltimore (n = 5,088 IDUs) <sup>34</sup>	Unspecified US location <sup>35</sup>
China	16 provinces mainly in southern and eastern China (n = 15,236 IDUs) <sup>36</sup>	South-west China (n = 406 IDUs) <sup>37</sup> Guangxi (n = 117 IDUs) <sup>39</sup> South-west China (n = 333 IDUs) <sup>38</sup>
Ukraine	Vinnitsa (n = 315 IDUs) <sup>40</sup> Various regions Ukraine (n = 470 IDUs) <sup>41</sup> Vinnitsa (n = 112 drug users) <sup>42</sup> Various regions Ukraine <sup>43</sup>	Location (n = 450 IDUs) <sup>44</sup> Various regions Ukraine (n = 470 IDUs) <sup>41</sup>
Indonesia	Jakarta (n = 560 IDUs), other locations not specified <sup>45</sup>	n/a
Thailand	Chiang Mai (n = 98 IDUs) <sup>46</sup> Northern Thailand (n = 1,859 drug users) <sup>47</sup> Songkla and Pattani provinces (n = 453) <sup>48</sup> Northern Thailand (n = 60) <sup>49</sup>	Northern Thailand <sup>50</sup> Chiang Mai (n = 98 IDUs) <sup>46</sup>
Kenya	Nairobi (n = 146 IDUs) <sup>51</sup> Nairobi (n = 94 current IDUs) <sup>52</sup>	Nairobi (n = 314 IDUs and non IDUs) <sup>52</sup>
Viet Nam	Hanoi, Viet Nam (n = 179 IDUs) <sup>54</sup> Northern Viet Nam (n = 309 IDUs) <sup>53</sup>	Northern Viet Nam (n = 309 IDUs) <sup>53</sup>
Italy	Reported as national figure <sup>55</sup>	n/a

n/a = data were not available

### **Box 3.1.1: Milestones on viral hepatitis**

#### **World Health Assembly (WHA)**

- Over the past two decades, the WHA has considered specific aspects of hepatitis prevention, including HBV vaccine integration into national immunisation programmes (resolution WHA45.17) and inclusion in outcome objectives of national cancer control programmes (WHA58.22),<sup>g</sup> HBV immunisation within the Global Plan of Action on Workers' Health 2008–2017, as well as safe blood supply, food safety and safe injections.
- As of 2007, more than 88% of Member States have introduced hepatitis B vaccine. Overall coverage with three doses of vaccine was 65%, and globally 27% of newborn infants received the birth dose of hepatitis B vaccine. This may change the dynamics of HBV among new cohorts of people who inject drugs in the coming years.
- In May 2009 Brazil, supported by China, Oman and Afghanistan, succeeded in adding viral hepatitis to the agenda of the 62nd annual WHA.<sup>103</sup> Brazil, Columbia and Indonesia then submitted a draft resolution on viral hepatitis, which was discussed at the WHO Executive Board meeting in January 2010.
- Most significantly, on 23 January 2010 the WHO Executive Board recommended to the 63rd WHA the adoption of resolution EB126.R16: Viral hepatitis,<sup>104</sup> which would direct the WHO Director-General to increase significantly WHO's focus on viral hepatitis and to encourage and support member states, donors and international organisations to do the same.

#### **World Health Organization (WHO)**

- The WHO has undertaken several activities in this area since identifying HBV as 'a primary candidate for elimination or eradication' in 1998.<sup>h</sup> For example, setting targets for the exclusive use of auto-disable syringes for all immunisation injections by 2003 and the reduction of chronic HBV virus infection rates to less than 2% among five-year-old children in the western Pacific region by 2012. In November 2008 WHO's Strategic Advisory Group of Experts on immunisation recommended that regions and countries develop goals for hepatitis B control.
- In 2009 WHO released a revised position statement for HBV vaccine use, which specifically advises targeting most-at-risk populations, including people who inject drugs, and recommends the offer of free or low-cost HBV vaccination to be made routinely available in health settings, such as NSPs and OST programmes.<sup>105</sup> In late 2009 the Regional Committee for the Eastern Mediterranean adopted a resolution calling for harm reduction, among other measures, for the prevention of hepatitis.<sup>106</sup>

#### **WHO, UNODC and UNAIDS**

- Vaccination, prevention and treatment of viral hepatitis are among the nine interventions recommended in guidelines for scaling up towards universal access.<sup>87</sup> The package of interventions has been endorsed within various multilateral fora and enshrined in the political declaration and plan of action of the Commission on Narcotic Drugs (the governing body of UNODC)<sup>107</sup> and an ECOSOC resolution in 2009.<sup>108</sup>

#### **UNAIDS Programme Coordinating Board (PCB)**

- In June 2009, at the 24th PCB meeting, the board called on 'UNAIDS to intensify its assistance to, and work with, all groups of civil society, including those affected by drug use and those that provide services to people who use drugs, aimed at advocating for anti-stigmatizing, anti-discriminating, and evidence-based approaches to HIV and Hepatitis C Virus (HCV) epidemics at national, regional and global levels'.<sup>109</sup>

#### **Civil society campaigns for access to HCV treatment**

- Civil-society-led advocacy campaigns have been driven by escalating concern at the numbers of people who inject drugs and people living with HIV co-infected with HCV. For example, the Asian Network of People Who Use Drugs (ANPUD), along with its allies and partners, plans to launch a regional HCV campaign in 2010. The campaign seeks the recognition by donors and governments of the need to include HCV treatment in Round 10 proposals to the Global Fund, in addition to the incorporation of HCV testing alongside HIV testing and price negotiations at national level for HCV treatment drugs, which are currently prohibitively expensive.<sup>110</sup>
- In addition, recent efforts have begun to investigate the possibility of pegylated interferon being included within UNITAID's patent pool, an initiative that aims to provide people in low- and middle-income countries with increased access to more appropriate and lower priced medicines.<sup>109</sup>

g At the time of writing, implementation of this resolution and its monitoring are still in progress.

h At the Conference Regarding Disease Elimination and Eradication as Public Health Strategies in Georgia, US.

## The way forward

The growing body of evidence and the increased morbidity and mortality due to viral hepatitis and HIV co-infections result in an urgent need to support the scale-up and implementation of a broad range of interventions to prevent and manage these co-infections among most-at-risk populations, particularly people who inject drugs.

The following actions are necessary for an effective response to viral hepatitis among people who inject drugs, people living with HIV and the wider population. Many of the interventions outlined below have long been advocated for in the HIV response.

### Strategic information

- Improve surveillance of viral hepatitis B and C and HIV among most-at-risk populations, disaggregating data by age, gender and risk behaviours.

### Health systems

- Increase awareness of viral hepatitis among health care workers.
- Decrease stigma towards and increase the willingness of health care workers to provide services to most-at-risk populations by addressing their beliefs about and attitudes towards these populations.
- Build the capacity of health care workers working with people who use drugs to provide viral hepatitis and HIV prevention, testing and diagnosis and treatment services.
- Ensure coordination of viral hepatitis services with HIV, TB and mental health and drug dependence treatment services for integrated treatment and care.
- Ensure meaningful involvement of drug user organisations in the design, implementation and monitoring and evaluation of prevention, treatment and care services.

### Prevention

- Increase knowledge about viral hepatitis and HIV transmission, the means of prevention and treatment options among people who use drugs.
- Increase the level of hepatitis A<sup>i</sup> and hepatitis B vaccination among most-at-risk populations.
- Advocate for and implement a comprehensive package of harm reduction interventions, including radically increasing coverage rates<sup>87</sup> for NSPs and OST in communities and closed settings, with the addition of other more specific interventions for HCV, such as reduction of alcohol consumption and the provision of other injecting paraphernalia such as tourniquets, filters and spoons.

### Treatment and care

- Increase the availability of viral hepatitis testing, particularly in conjunction with HIV treatment programmes working with people who use drugs.
- Ensure that HBV/HIV co-infected individuals taking ARV therapy are on a regimen with more than one ARV with anti-HBV activity (e.g. lamivudine [3TC] or emtricitabine [FTC] plus tenofovir [TDV]).
- Ensure that people who inject drugs and are living with HIV are screened for HCV prior to initiating ART and that they are monitored for hepatotoxicity.

- Advocate for and expand access to HCV therapy for people who inject drugs, people living with HIV and the wider population.
- Advocate for research into less costly and easier to administer drugs.
- Ensure that current drug use is not used as a contraindication for access to ART or viral hepatitis therapy.

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# 3.2: Enhancing synergy: Responding to tuberculosis epidemic among people who use drugs

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## Introduction

Tuberculosis (TB) is a major infectious disease responsible for over one million global adult deaths each year. These fatalities are preventable as TB is almost always curable if diagnosed and treated early. The estimated 15.9 million people who inject drugs around the world have a higher risk of developing TB than the general population. For the estimated 3 million people who inject drugs and are living with HIV, the risk is even higher. Prison populations, often including significant numbers of people who use drugs, are also at increased risk of developing TB. UN agencies recommend including TB prevention, diagnosis and treatment as part of an integrated and comprehensive harm reduction package inside and outside prisons. Attainment of international HIV/AIDS targets such as universal access and the millennium development goals will require the provision of TB services to marginalised groups such as people who inject drugs and prisoners.

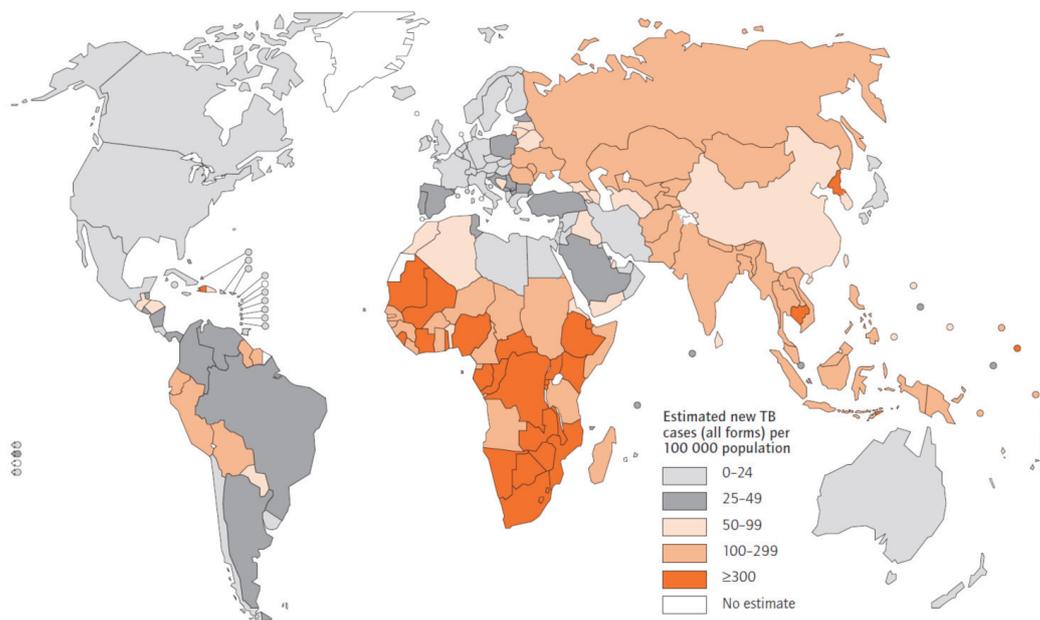
This chapter reviews the epidemiology of TB and the TB and HIV co-infection among drug-using populations and explores the international response in policy and implementation to address these epidemics. While TB services are being integrated into wider efforts to scale up HIV and harm reduction services in some countries, these are few and not proportionate to the scale of the problem. Access to harm reduction interventions and general health care for people who inject drugs remains low in most countries. For prison populations, access to these services is even lower. There is an urgent need for increased collaboration between TB, HIV, drug treatment and harm reduction services and health services in the criminal justice system in order to address this issue.

## TB and HIV co-infection among people who use drugs

TB is a mycobacterial infectious disease spread from person to person by droplet transmission through the lungs (e.g. when coughing). Transmission does not result in disease in nine out of ten people who are infected, so that around one-third of the global population is infected with 'sleeping' or latent TB and for most of them nothing else happens. Only one in ten people with latent infection will develop TB disease during their lifetime. However, among people with compromised immune systems, such as those living with HIV, one in ten TB infections each year will result in development of the disease.

TB disease affects and destroys mainly the lungs, but may also spread to other parts of the body such as lymph nodes, bones and kidneys. Symptoms usually develop gradually during the course of the disease and include coughing (for more than two weeks), fever, night sweats and weight loss. In approximately half of the cases (less if HIV co-infected), TB can be diagnosed by examining sputum stained with a dye under a microscope, a test that has been used for over a century. Where sputum examination is negative, diagnosis is more difficult, requiring a clinician's decision to treat based on clinical signs and symptoms, aided where available by culture of sputum or other tissues, X-rays and other tests. Line-probe assays and LED microscopy are exciting recent developments with the potential to increase early diagnoses from sputum examinations. However, a diagnostic point of care test that reliably distinguishes TB infection from disease, and diagnoses this disease correctly every time, remains elusive.

**Map 3.2.1: Estimated TB incidence rates in general population per 100,000, 2008**



Accurate diagnosis and treatment of TB is literally a matter of life or death. If left untreated, over half of people with TB will die within two years and one-third will develop chronic debilitating symptoms. For people living with HIV, the death toll rises to over 80% within a year. HIV-related TB is more difficult to diagnose, as immuno-suppression also suppresses symptoms and signs. Only around one-third of HIV-positive TB patients can be diagnosed by sputum microscopy, making the role of a symptom-based clinical diagnosis even more important in the case of people living with HIV. Actively screening for TB, early TB treatment or TB prevention using isoniazid preventive therapy (IPT) and infection control measures, in addition to the early provision of antiretroviral therapy (ART) and co-trimoxazole preventive treatment (CPT), are therefore lifesaving interventions among people living with HIV.

The treatment of drug-sensitive TB involves four drugs, usually given in combination tablets for a period of up to six months, with patient support from health workers, community or family to ensure treatment adherence. Drug-resistant tuberculosis requires a two-year treatment with more expensive drugs, which also cause more side effects.

### **The extent of the TB epidemic**

Worldwide, more than nine million people develop TB every year. In 2008 the estimated global TB incidence rate was 139 per 100,000 population, which equates to 9.4 million (range: 8.9–9.9 million) new TB cases.<sup>1 2</sup>

The TB epidemic increased during the 1990s and has only recently peaked. The 2008 figures show an 11% and 40% increase in TB incidence rates and TB cases respectively in comparison with 1990 estimates. This global increase in rates was largely the result of increases in the Sub-Saharan African and Europeana regions and was mainly due to the HIV epidemic. The HIV epidemic in Europe has been primarily driven by injecting drug use. In Sub-Saharan Africa, mirroring the HIV epidemic, TB incidence and death rates have

a This refers to the European region as defined by the WHO, which corresponds to Europe and Eurasia in this report.

doubled and the numbers of TB cases and deaths have tripled in comparison with estimated figures in 1990. Globally, incidence rates have been declining slowly since 2004, by less than 1% annually, although the number of TB cases is still rising as a result of increases in population size. More than half (55%) of the estimated number of TB cases in 2008 were in Asia, followed by Africa (30%). Alongside HIV, TB is the leading cause of adult death from infectious disease. In 2008 the number of deaths estimated to have occurred from TB without HIV was 1.3 million and a further 520,000 TB deaths were related to HIV.<sup>1</sup> TB causes one-quarter of the 2.1 million annual deaths among the 33.4 million people living with HIV.<sup>1 3</sup>

TB rates are high among people who inject drugs, a situation primarily linked to the high rates of HIV in this group. However, drug use was identified as a risk factor for TB even before the HIV epidemic.

### **TB and people who use drugs**

Although there is a lack of global data, the available research suggests that TB presents a major challenge for people who use drugs. Studies among HIV-negative drug users from the United States and Europe suggest a rate of TB between six and ten times that of the general population. For example, in a study from 1973 (prior to the impact of the HIV epidemic) carried out in New York in twenty methadone treatment centres, researchers found a TB disease prevalence rate among drug users of 1,372 per 100,000 citywide against a general population rate of 86.7 per 100,000.<sup>4</sup> In Amsterdam some fifteen years later, a study found that the incidence of TB in HIV-negative drug users was 180 per 100,000, six times higher than in the overall Amsterdam population in the same period.<sup>5</sup>

Both injecting and non-injecting drug use is associated with elevated TB infection rates. Approximately half the people who inject drugs (both those living with HIV and those not) in a Spanish study tested positive for TB infection.<sup>6</sup> A study from the US also showed crack cocaine users to be at an equally high risk for TB

**Table 3.2.1: Summary of data from ten countries with 70% of global total of injecting drug users (IDU) living with HIV**

Name of country	Number of people who inject drugs <sup>32</sup>	HIV prevalence among people who inject drugs <sup>32</sup>	Number of IDU living with HIV	Percentage of global total number of IDUs living with HIV	Proportion of IDUs living with HCV	Incident TB rate per 100,000
Russia	1,825,000	37.15%	677,988	22.6%	68-95%	110
Brazil	800,000	48%	384,000	12.8%	40-70%	48
US	1,857,354	15.57%	289,190	9.6%	35%	4
China	2,350,000	12.3%	289,050	9.6%	61%	98
Ukraine	375,000	41.8%	156,750	5.2%	70-90%	102
Indonesia	219,130	42.5%	93,130	3.1%	60-98%	228
Thailand	160,528	42.5%	68,224	2.3%	90%	142
Kenya	130,748	42.9%	56,091	1.9%	42%	353
Viet Nam	135,305	33.8%	45,733	1.5%	10-81%	171
Italy	326,000	12.1%	39,446	1.3%	42-90%	7
<b>TOTAL</b>	<b>8,179,065</b>		<b>2,099,602</b>	<b>70%</b>		

infection as people who inject drugs.<sup>7</sup> Rates of TB infection were found to be similar among HIV-positive and HIV-negative injecting drug users in a two-year prospective study. The rate of development of TB in HIV-negative injecting drug users also appears to be higher than the rate of TB in the general population.<sup>8</sup>

TB prevalence rates vary greatly between countries and this variation is likely to be reflected in TB rates among drug using populations. Figure 3.2.1 shows the national variations in rates of TB in 2007, with a twentyfold difference in rates between the US (4/100,000) and China (98/100,000), both countries with sizable numbers of people who inject drugs (see Table 3.2.1).<sup>9</sup>

Using the mid-point estimates of data gathered by the Reference Group to the UN on HIV and Injecting Drug Use,<sup>10</sup> ten countries (see Table 3.2.1) with almost half of the global number of people who inject drugs, also have over two-thirds (70%) of the global estimated numbers of injecting drug users living with HIV. The overall TB rate in the people who inject drugs in these countries would be somewhere between 700 and 1,220 per 100,000, assuming that TB rates in HIV positive people are twenty-five times higher than the background population rates, and taking the rates of HIV-negative drug users as between one and ten times the background population rates of TB. Overall there would be between 54,000 and 90,000 TB cases annually among the seven million drug users in these countries. The general population TB rates in these countries vary between 4 and 353 per 100,000.<sup>11</sup> More data are needed on TB rates among drug users in these countries, especially those with high rates of TB, in order to improve the estimation of the burden of TB disease in drug users.

Several factors are likely to increase the vulnerability to TB infection of people who inject drugs, including high rates of incarceration, homelessness and poverty. The rates of TB disease in prisons can be more than thirty times higher than those outside prisons.<sup>13</sup> Poor nutrition associated with heavy drug use is also likely to add to susceptibility to TB. Although all these factors are

important contributors to the overall rates of TB in drug users, it is the presence of HIV that is the most important contributing factor to the TB epidemic among this population.

### ***TB and HIV co-infection among people who inject drugs***

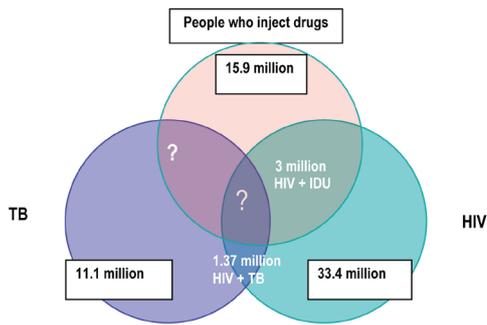
TB prevalence rates among people living with HIV are twenty to thirty times higher than among people who are HIV-negative. This is due to the increased risk of progression from TB infection to TB disease: from one in ten during a lifetime in HIV-negative people to one in ten annually for people living with HIV.

There is some evidence that the relative risk of TB may be elevated among HIV-positive drug users compared with the general population. The relative risk of developing TB in people living with HIV (as compared with the general population) in countries where HIV infection is primarily linked to drug use is 27.6 versus 20 in those countries with generalised epidemics.<sup>1</sup> This is most likely because vulnerable populations, such as people who use drugs, have TB exposure factors in addition to HIV that increase their level of TB, relative to the country population they come from.

In 2008 there were an estimated 1.37 million new cases of TB and 520,000 TB deaths among all people living with HIV.<sup>1</sup> There are no data on what proportion of this is related to drug use. However, if the rate of TB among people living with HIV who inject drugs is assumed to be the same as that among other people living with HIV, it would suggest that perhaps as many as 140,000 cases of TB (5 per 100 injecting drug users) with 52,000 deaths (2 per 100 people who inject drugs) occurring annually among the more than three million people living with HIV who inject drugs.

Projecting from what is known about the estimated interactions between the TB and HIV epidemics and their relationship with injecting drug use, the gaps in knowledge are in the estimated numbers of drug users who have TB and HIV-related TB (see Figure 3.2.2).

**Figure 3.2.2: The interaction between TB, HIV and injecting drug use**



Estimate of number of people with TB<sup>1</sup>  
 Estimate of number of people living with HIV<sup>2</sup>  
 Estimates of numbers of people who inject drugs<sup>9</sup>

TB is a leading cause of death among injecting drug users living with HIV. Globally, approximately 520,000 people died from HIV-related TB in 2008, which was nearly one in three TB deaths (29%). TB also contributed to 26% of the estimated HIV deaths occurring globally. Both all-cause and TB-associated mortality rates are several-fold higher among injecting drug users living with HIV than in other people living with HIV.<sup>14 15</sup>

Data from Ukraine, where the HIV epidemic is largely among people who use drugs, suggest high death rates from HIV due to TB. A retrospective study showed TB to be the leading cause of death among people living with HIV, accountable for approximately 58% of all causes of death in people living with HIV in Ukraine.<sup>16</sup> Reports from TB registers in Latin American countries, where much HIV-related TB is found among drug-using populations, show that 20% of TB patients living with HIV and undergoing treatment died. This rate was approximately five times higher than the rate of death in TB patients without HIV (4%) and occurred in countries with a comparatively high ART coverage among people living with HIV.<sup>b</sup>

### Hepatitis C and TB

The majority of people who inject drugs are living with hepatitis C virus (HCV) (see Chapter 3.1 on viral hepatitis). In the nine countries that are home to half of all people who inject drugs, the prevalence of HCV is very high (see Table 3.2.1). It appears that over two-thirds of all people who inject drugs are living with HCV, regardless of their HIV status. The estimates of HCV prevalence among drug users living with HIV are even higher.<sup>17</sup>

Data on the proportion of people who inject drugs who have co-infection with HCV and TB are not available. However, the majority of people who inject drugs living with TB, regardless of their HIV status, will also have HCV. People co-infected with HCV should not be denied lifesaving TB treatment and ART, although more careful monitoring of hepatic side effects is needed during the treatment of TB and HIV and during concurrent treatment for HCV.<sup>18</sup>

## The threat of multidrug-resistant TB

Multidrug-resistant tuberculosis (MDR TB) is TB that has developed resistance to some or all drugs used in treatment, usually as a result of poor treatment in the past. Globally, approximately 500,000 cases are estimated to exist. Effective treatment of MDR TB takes longer and is more expensive than that of treatment-sensitive TB.

The evidence for increased risk of MDR TB in people who use drugs is indirect. There are no studies that have directly measured the prevalence of MDR TB in drug users. As mentioned above, there is a link between higher rates of MDR TB and prison populations. There is also a growing evidence base for the link between HIV and MDR TB, and this also applies to drug users with HIV.<sup>19</sup> Major outbreaks of MDR TB in congregate settings such as prisons or health institutions have occurred repeatedly, especially among people living with HIV.

Published literature over the last two decades suggest that institutional outbreaks of MDR TB primarily affect people living with HIV, with a significantly higher mortality rate and short survival period.<sup>20 21</sup> The outbreaks were largely linked to poor infection-control practices and occurred before the availability of ART.<sup>19</sup> However, the initiation of ART does not necessarily improve survival time, with mortality rates of over 80% within weeks of MDR TB detection.<sup>22</sup>

One hospital outbreak in Portugal in the 1990s was among drug users living with HIV.<sup>23</sup> Data from this outbreak showed that among the ninety-five cases of HIV-related MDR TB, most people died before the diagnosis could be established. Epidemiological data from DNA fingerprinting analysis supported the conclusion that the transmission of MDR TB occurred among injecting drug users living with HIV who were exposed to infectious TB cases on open wards in the HIV unit. Improved infection control measures on the HIV unit and the use of empirical therapy with six drugs, once patients were suspected to have TB, reduced the incidence of MDR TB from 42% of TB cases in 1996 to 11% in 1999.

People who use drugs need to have access to treatment for MDR TB. Places where drug users congregate, including prisons and health care settings for substitution therapy or drug treatment, need to implement airborne infection control measures in order to counteract the risk of person to person transmission of TB, including MDR TB.

<sup>b</sup> This information is derived from unpublished data from 2007 in the WHO Global Tuberculosis Database.

### **Prisons and TB**

The problems of TB and HIV among people who inject drugs are intensified by incarceration. There are between eight and ten million people in places of detention in the world. Because many people are detained for short periods of time, the actual numbers who pass through prisons and places of detention each year is many times higher. Detainees are often housed in overcrowded facilities with inadequate ventilation, hygiene and sanitation. The food that is provided can be unappealing and nutritionally inadequate. Health services may be weak or absent. The vast majority of prisoners and detainees around the world have no access to harm reduction measures or condoms, despite evidence that sex and drug use occur within these institutions across the globe. Such conditions are ripe for the outbreak of epidemic diseases, including TB and HIV (see Chapter 3.5 on prisons).

Much higher levels of active TB disease, thirty times or more, are reported within prisoner and detainee populations compared with those outside prisons.<sup>24</sup> Some prison programmes have found high levels of MDR TB, up to one-third of all cases.<sup>25</sup> A study from the Samara region in Russia reported TB rates of 37.3% in prison, twice as high as in the civilian population.<sup>26</sup> High rates of TB in prisons and places of detention are made worse by late diagnosis and inadequate treatment of infectious cases, due to lack of adherence or treatment support, high transfer rates of prisoners and gaps in continuity of care upon release. Prison health is often forgotten or given a low priority.

It needs to be remembered that the problem of TB and poor health of prisoners and detainees will not stay confined to prisons. Prison staff and visitors should be considered part of the prison population with respect to the transmission of infectious diseases such as TB. Prison health must be seen as a public health concern and health systems should be coordinated to ensure continuity and equivalence of care. This is most evident in the spread of MDR TB, an increasingly recognised threat to effective TB control.

## **The global policy response to TB**

Since the early 1990s, the provision of high-quality Directly Observed Treatment Short-Course (DOTS) has been central to responding to TB epidemics around the world. This requires the provision of services for early detection and diagnosis of TB through quality-assured bacteriology, followed by standardised TB treatment with supervision and patient support, using an effective drug supply, with monitoring and evaluation, including treatment outcomes and impact measurements.

*The Stop TB Strategy*, published in 2006 by the WHO, lays down additional elements for a comprehensive framework for TB control, including the involvement of all care providers, empowering people living with TB and communities, the treatment of MDR TB and TB/HIV co-infection and addressing highly vulnerable groups such as prisoners and people who use drugs.<sup>27</sup>

*The Global Plan to Stop TB*, published by the Stop TB Partnership (a global and multisectoral alliance of partners fighting TB), provides a budgeted work plan and lays down targets and milestones to achieve the millennium development goals related to TB.<sup>28</sup> People who use drugs are one of the groups that may not be easily reached through routine TB services alone, and the high proportion of drug users living with HIV also need the TB/HIV services detailed in the policy for TB/HIV collaborative services.<sup>29</sup> This highlights the need for TB patients to be screened for HIV and for the provision of HIV services, including early co-trimoxazole and ART for those TB patients living with HIV. For people living with HIV, it recommends regular screening for TB, provision of IPT and infection control measures in all congregate settings and especially in health facilities treating people living with HIV.

WHO, UNAIDS and UNODC have identified the key elements of the harm reduction package and include TB as one of the key areas to be addressed.<sup>30</sup> The three agencies also recognised that the provision of services for TB and HIV among drug users required additional guidance and, in 2008, collectively launched policy guidelines for the integrated delivery of TB and HIV services for injecting and other drug users.<sup>17</sup> This guidance makes thirteen recommendations in support of improving integrated services, providing a package of care and overcoming barriers to its implementation (see Figure 3.2.3). The guidelines are intended for people providing services for the population of drug users who have the most problematic patterns of use and who have the greatest risk of HIV and TB. These are people who use opiates, cocaine or amphetamine-type stimulants in a dependent or harmful way, in particular those who inject.

The guidelines recommend that services should have a more coordinated response to the needs of people who use drugs. Services should provide access to prevention, treatment and care services at all entry points. This requires collaborative planning between HIV, TB, specialist drug services and the criminal justice system. In particular, health services should provide treatment adherence support for people who use drugs. Co-morbidities, such as HCV, should not be a barrier to TB and HIV treatment services. Prisoners living with HIV, TB or drug dependency need to have the same access to treatment and care as people outside prisons, as should drug users who are migrants, homeless or otherwise marginalised. In addition, continuity of care on transfer in and out of places of detention is essential.

The guidelines were launched at the International AIDS Conference in Mexico City in 2008 and are available in Russian, Chinese and Spanish. Since their launch, they have been deliberated on at global workshops involving activists, programme managers of TB/HIV, health in prison, harm reduction and drug treatment services from high-burden countries, and are informing the implementation of services locally.<sup>17</sup>

**Figure 3.2.3: Recommendations from the policy guide for integrated TB and HIV services for injecting and other drug users**

<b>A</b>	<b>Joint planning service providers</b>
	<ol style="list-style-type: none"> <li>1. National local coordination body</li> <li>2. Plans with roles and responsibilities and monitoring and evaluation</li> <li>3. Human resources and training available</li> <li>4. Support to operational research</li> </ol>
<b>B</b>	<b>Package of care</b>
	<ol style="list-style-type: none"> <li>5. TB infection control plans in care settings</li> <li>6. Case finding protocols at services that people who use drugs attend</li> <li>7. Treatment services for TB and HIV available</li> <li>8. Isoniazid preventive therapy (IPT) available for TB prevention</li> <li>9. HIV prevention available (harm reduction package)</li> </ol>
<b>C</b>	<b>Overcoming barriers</b>
	<ol style="list-style-type: none"> <li>10. Integrated services (link TB/HIV treatment with harm reduction)</li> <li>11. Equivalence of care in prisons</li> <li>12. Adherence support measures</li> <li>13. Comorbidity not to be used to withhold treatment</li> </ol>

## TB services for people who use drugs

A total of 5.7 million incident TB cases were notified by national TB control programmes globally in 2008. This amounts to 62% of all estimated TB cases worldwide. These are being treated by national TB programmes using DOTS, with an average cure rate of 86%.<sup>1</sup> It is not known what proportion of people who use drugs globally have had TB diagnosed or treated successfully. There is evidence that drug users make poor use of general health services. US data suggest that a substantial proportion of injecting drug users living with HIV receive their HIV diagnosis late and have a lower chance of survival than people who acquired the virus via another transmission route.<sup>31</sup>

As recently as 2005 in Eastern Europe and Central Asia, people who inject drugs accounted for over 70% of HIV cases but represented only 24% of the people receiving ART.<sup>32</sup> Data collected for the WHO's universal access report in 2009 suggest that of 92 low- and middle-income countries that reported information on programmes and policies targeting injecting drug users, only 30 were providing needle and syringe programmes in 2008, 26 reported providing opioid substitution therapy (OST) and 26 reported access to HIV testing.<sup>33</sup> With regard to the prevention, diagnosis and treatment of TB in services aimed at people who inject drugs, a ratio of two to one countries replied that these were not available to drug users.<sup>32</sup>

Much more needs to be done to integrate TB and HIV services with those aimed at people who use drugs. As shown elsewhere in this report, there has been increasing focus on people who inject drugs within recent years and the scale-up of key harm reduction interventions such as OST programmes has been reported in many countries, including China, Vietnam and Indonesia, with a gradual move towards integrating these with HIV services. Integration with HIV and TB services is not yet the norm, although examples of good practice have been reported from countries such as Spain, Brazil and Ukraine.

### Integration of HIV/TB services for people who use drugs in Ukraine

With more than 1.5% adult HIV prevalence, Ukraine has been hard hit by the Eastern European HIV epidemic, largely driven by unsafe injecting drug use. The epidemic has had high mortality rates, with TB being the major cause of mortality among people living with HIV. The positive news is that Ukrainian civil society and government have made great progress in building a strong network of harm reduction services and providing HIV prevention, care and treatment to thousands of people with Global Fund to Fight AIDS, Tuberculosis and Malaria and state funding. However, despite the rapid scale-up of ART (from reaching 200 people in 2003 to approximately 10,000 out of 43,000 people living with HIV in 2008), TB has continued to be a major cause of mortality even for people receiving ART.

In order to support drug users in using services, civil society organisations, in collaboration with the Ministry of Health, are working to expand the provision of OST to over 150 sites, including TB centres, TB hospitals and ART clinics. New models of integrated care are being developed, such as 'one-stop shops' with multidisciplinary teams licensed to provide OST, DOTS treatment of TB and ART, as well as the provision of social support and low-threshold services integration. At least five of these pilot sites were operating by 2009.

Efforts are also under way to draw the prison services into the integrated treatment scale-up. The state of HIV services in the prison system has been lacking, quality drug treatment is more the exception than the rule and TB is widespread, with high rates of MDR TB, poor treatment access, lack of adherence and/or lack of social support. Using Global Fund Round 6 funding, prisons are being encouraged to set up harm reduction services integrated with HIV and TB treatment services.

## Next steps and recommendations

TB and HIV services are slowly scaling up in many countries, often alongside harm reduction services such as OST programmes, but there is a need to increase service cross-referral and integration.<sup>13</sup> This should be accompanied by the documentation of best practice in the provision of training and development of integrated services for TB/HIV and drug treatment/harm reduction, including collaboration with the criminal justice system.

Routine data on health service utilisation and outcome monitoring of people who use drugs is severely lacking and is needed for the planning and management of services, as well as for advocacy. This shortfall needs to be addressed through surveys and routine data collection.

Increased resources and political commitment for scaling up integrated services for people who use drugs, including TB, is essential. Drug user and harm reduction activists need to become more vocal in demanding access to these services.

The Global Fund is an increasingly important funding source for TB and HIV programmes, particularly for people who inject drugs. The international harm reduction community, including civil society and government, must take the opportunity the Global Fund provides to catalyse engagement in the provision of integrated services for drug users.

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# 3.3: Neglected infections, real harms: A global scoping of injection-related bacterial infections and responses

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## Introduction

Injecting drug use has been reported across the globe, with an estimated 16 million people injecting drugs worldwide.<sup>1</sup> Research on infectious diseases related to injecting drug use has focused mainly on blood-borne viral infections such as human immunodeficiency virus (HIV) and hepatitis C virus (HCV), with bacterial infections receiving much less attention.<sup>2</sup> However, these infections are an important contributor to ill health among people who inject drugs and can result in severe and sometimes fatal complications.<sup>3</sup>

Bacterial infections due to injecting drug use can occur at injection sites or elsewhere on the body. Those affecting the skin and soft tissues include bacterial infections that cause the accumulation of pus (abscesses) or tenderness, swelling and redness (cellulitis) at or near injection sites. Infections elsewhere in the body include those infections causing illness away from injection sites (distal infections) such as infection of the heart lining (endocarditis) and infections that are more widespread or affect the body as a whole (systemic illnesses) such as blood poisoning (septicaemia).<sup>3</sup>

The focus of this chapter is on infections around injection sites, principally those infections of the skin and soft tissues that lead to symptoms such as abscesses or cellulitis. These infections most frequently occur at actual injection sites, but they can also develop close to injection sites. As most people who inject drugs do so into their limbs, these infections are often reported on the arms, shoulders (deltoids), legs or buttocks.<sup>3,4</sup>

This chapter will examine the current state of knowledge on the extent, risk factors and responses to bacterial infections at injection sites. As there is little published work on these infections in low- and middle-income countries, the focus will be on developed countries. However, these infections are likely to cause significant problems among people that inject drugs in all countries.

### **Glossary:**

**Inflammation** is an area of redness and swelling that is usually warm and tender.

**Abscesses** are an accumulation of pus in addition to inflammation. Abscesses on the skin often result in lumps that are sometimes called boils.

**Cellulitis** is inflammation of the skin, or the tissue immediately below the skin, which usually begins as a small area of inflammation and then gets bigger.

**Infective endocarditis** is an infection of the lining of the heart and/or valves.

## Causes of injection site infections

Injection site infections are due to infection with a range of aerobic and anaerobic bacteria. The latter are bacteria that grow in the absence of oxygen, and so can infect damaged tissues. They tend to cause more severe infections, with one group of such bacteria, the clostridia, typically producing powerful and potentially lethal toxins. However, infections of injection sites are

mostly due to aerobic bacteria (which need oxygen to grow) such as staphylococcal or streptococcal species or to several types of bacteria (i.e. polymicrobial with a mix of bacteria that may include both aerobes and anaerobes).<sup>3</sup>

Injection site infections arise from contamination of the injecting equipment or the drug solution with bacteria. This usually occurs in one of four ways:

1. Bacteria from an individual's natural skin flora enter the body during the injecting process.
2. Contamination of the injecting equipment whilst preparing the drug(s) for injection.
3. The re-use of injecting equipment.
4. Contamination of the drug(s) with material from the environment containing bacteria, or their spores, during manufacturing, bulking up ('cutting') or distribution. Bacterial spores are small, hardy reproductive bodies that can remain viable for a long time in the environment. They can survive the heating involved in preparing some drugs for injection.<sup>5</sup>

## Complications of bacterial infections of injecting sites

Injection site infections can result in a range of complications, which may cause more serious illnesses and even death. These complications can be either local (at or near the injection site), distal (affecting another part of the body) or systemic (affecting the whole body).

Local complications include the spread of the infection to the surrounding tissues, resulting in, for example, infection of joints (septic arthritis),<sup>3,6</sup> infection of the bone (osteomyelitis)<sup>3,6</sup> or infection of the blood vessels producing blood-filled bulges (aneurysms).<sup>3</sup> Others include the development of persistent skin ulcers.<sup>3</sup>

Reported distal complications of injection site infections include infective endocarditis (infection of the lining of the heart or valves)<sup>7</sup> and abscess of the spine or brain.<sup>6</sup> Others include infections of bones and joints away from the injection site.<sup>3</sup> The most commonly reported and serious complication related to injection site infections is, however, infective endocarditis.<sup>7</sup>

Some species of bacteria produce poisons (known as toxins), some of which cause very severe illnesses. The most commonly reported injecting-related infections that produce powerful toxins are caused by clostridia. Clostridia are anaerobic bacteria that form spores that can survive in the environment for many years. These spores may then contaminate drugs and cause infection. These bacteria cause localised infections, but the powerful neurotoxins they produce cause systemic illnesses, which can be fatal. The two most widely reported are wound botulism (*Clostridium botulinum*) and tetanus (*Clostridium tetani*). The toxins that these organisms produce cause progressive paralysis and may result in respiratory failure and death.<sup>6,8</sup>

Other injection site infections can also produce powerful toxins. These include another serious, often fatal, infection due to a spore-forming bacteria, anthrax, although this is very rare.<sup>9,10</sup>

The complications of injection site infections vary in their severity, however, many could be averted by the prompt diagnosis and management of the initial infection.<sup>8</sup>

## Extent of injection site infections

Studies have found considerable variation in the extent (prevalence) of symptoms of bacterial infections at injection sites. Overall, studies suggest that the prevalence of the common symptoms of these infections, such as abscesses or cellulitis, is in the range of 6% to 36% amongst people who inject drugs.<sup>11 12 13 14 15 16 17 18 19</sup> Some of this variation will reflect the different definitions of infection and the different periods used in these studies.

**Table 3.3.1: Summary of studies reporting on the prevalence of injection site infections**

Study Design	City, Country	Setting	Outcome	Source
Cross-sectional, baseline for cohort	Vancouver, Canada	DCR	22% self-reported abscess(es) during the previous six months	Lloyd-Smith et al. (2005) <sup>12</sup>
Cohort	Vancouver, Canada	DCR	6% to 10% reported a current injection site infection	Lloyd-Smith et al. (2008) <sup>24</sup> ; Lloyd-Smith (2009) <sup>2</sup>
Cross-sectional	Seven locations, England	Community recruited	36% self-reported abscess(es) or open sore(s) during the previous year	Hope et al. (2008) <sup>14</sup>
Repeated cross-sectional, over three years	Multiple sites, England, Wales and Northern Ireland	Recruited through a range of specialist services	35% in 2006, 37% in 2007 and 34% in 2008 self-reported abscess(es) or open sore(s) during the previous year	Hope et al. (2010) <sup>23</sup>
Cross-sectional	Six locations, Australia	NSP and community	7% self-reported abscess(es) and 7% cellulitis during the previous year	Dwyer et al. (2009) <sup>13</sup>
Cross-sectional	Multiple cities, Australia	NSP users	27% self-reported ever having an abscess	Topp et al. (2008) <sup>15</sup>
Cross-sectional	Sydney, Australia	DCR	6% self-reported ever having an abscess or skin infection	Salmon et al. (2009) <sup>18</sup>
Cross-sectional	Tijuana, Mexico	Community recruited	20% self-reported abscess(es) during the previous six months	Pollini et al. (2010) <sup>19</sup>
Cross-sectional	San Francisco, US	Community recruited	32% had a current abscess, 4% had cellulitis and 14% had both	Binswanger et al. (2000) <sup>17</sup>
Cross-sectional (associated with a cohort)	Baltimore, US	Community recruited	11% reported abscess(es) during the previous six months	Vlahov et al. (1992) <sup>25</sup>
Prospective cohort	Amsterdam, Netherlands	Recruited through a range of services	Incidence of self-reported abscess(es) was 33 per 100 person-years	Spijkerman et al. (1996) <sup>16</sup>

The various studies that have reported on the prevalence and the rate of occurrence (incidence) of these infections in people who inject drugs are summarised in Table 3.3.1. The incidence of these infections is not easy to measure, but in a prospective cohort study (a study that followed a group of people who inject drugs over time) undertaken in Amsterdam between 1986 and 1994, the incidence of skin abscesses was reported to be as high as 33 per 100 person-years at risk through injecting.<sup>16</sup>

There has been little examination of trends in the prevalence of injection site infections over time. A US study of records from San Francisco General Hospital found an indication of increased use of hospital services for injection site infections, with Emergency Department use for these rising from 1,292 cases in 1996/7 to 2,619 in 1999/2000.<sup>20</sup>

In the UK there has been a marked rise in the number of hospital admissions of drug users with skin and soft tissue infections. For example, admissions due to skin abscesses of the central part of the body (trunk) and groin increased from 92 in 1997/8 to 613 in 2003/4, an increase of 566%.<sup>21</sup> During this same period, reports of severe group A streptococcal infections among people who inject drugs in the UK increased from less than ten in the mid-1990s to 143 in 2004.<sup>22</sup> More recent studies in England, which looked at the prevalence of symptoms of injection site infections among community-recruited samples of people who inject drugs, indicated little overall change in prevalence, with approximately one-third reporting symptoms in both 2004 and 2008.<sup>14 23</sup>

Canadian examinations of the occurrence of injection site infections among participants in a study in Vancouver during 2004 and 2005 found that the proportion reporting a current infection was fairly consistent over this period, fluctuating between 6% and 10%.<sup>24</sup>

Overall, the data suggest an increase in more severe infections among people who inject drugs in some developed countries.

## Factors associated with infections and symptoms

Injection site infections have been associated with a number of individual, behavioural and environmental factors. The behavioural factors are principally concerned with hygiene, injection practice and the drug solutions injected. These factors include:

- 1. Injection hygiene.** Inadequate cleaning of the hands or the sites used for injection,<sup>11 12 13 25</sup> drawing blood back into the syringe repeatedly,<sup>26</sup> sharing filters<sup>23</sup> and needle and syringe re-use<sup>11 14 18</sup> have all been associated with higher levels of infection. These practices can result in bacterial contamination of the injecting equipment or the drug solution being injected. Bacteria are then able to enter the body through the injection process and cause infection.
- 2. Injection frequency.** More frequent injection<sup>14 15 16 18 23 27</sup> has been associated with infection. This may be because repeated injecting at a single body site causes cumulative damage to skin and soft tissue, and results in increased susceptibility to infection.
- 3. Skin and muscle popping.** Subcutaneous injecting, more commonly referred to as 'skin popping',<sup>11 17</sup> has been associated with infections. Injecting into the skin or

muscle (intramuscular injecting or 'muscle popping') may provide a greater opportunity for infection as it can cause localised tissue damage. This damaged tissue creates a niche environment in which bacteria could grow that would not be created by injecting into a vein.<sup>28</sup> Damaged tissues may well provide an anaerobic environment suited to the growth of toxin-producing bacteria.<sup>29</sup> Some people choose to inject under the skin or into muscle because this is their preferred route or because damage to their veins has made intravenous injection difficult. However, many injections under the skin or into muscle may be accidental as a consequence of missing a vein.<sup>30</sup>

- 4. Body sites used for injection.** The occurrence of injection site infections has been associated with the body site that is used for injection, with sites other than the arms often associated with infection.<sup>12 14 23 27</sup> This might be because some sites, such as the groin (femoral vein), are likely to be harder to clean, or to keep clean, than other sites.
- 5. The drug(s) injected.** The drugs used by people who inject vary in availability, purity, form and across geographical settings. The risk of developing an injection site infection has been found to vary according to drug or drugs being injected.<sup>11 14 16 18 23</sup> Speedball (a combination of heroin and cocaine) injecting has been associated with injection site infections in San Francisco and Amsterdam.<sup>11 16</sup> A similar association has been found with the injection of opiate-stimulant combinations in the UK.<sup>23</sup> Cocaine injecting has been associated with such infections in Vancouver.<sup>12</sup> The injection of black tar heroin has been associated with developing wound botulism in the US.<sup>31</sup> The drugs used and the substances used to dissolve them (including any contaminants present in these) may have damaging effects on the skin and underlying tissues,<sup>3</sup> and so compound the tissue damage from injecting. Cocaine, for example, has been associated with causing the constriction of blood vessels.<sup>32</sup> Heroin base and crack-cocaine, unlike the salt forms, are not readily soluble in water. These are typically prepared for injection by being heated with an organic acid such as ascorbic or citric acid. The use of these compounds to dissolve drugs can result in an acidic drug solution, which can cause tissue damage particularly if injected under the skin or into muscle. The resulting damaged tissue may provide an environment that is especially favourable for the growth of anaerobic bacteria.<sup>29</sup>

Other factors associated with higher levels of bacterial infections include:

- 1. Length of time injecting and age.** The numbers of years injecting and the person's age have both been associated with injection site infections: being older<sup>13 14 15</sup> and injecting for longer<sup>17 18 23</sup> are both linked with higher levels of infection. A possible explanation for this is that veins may become hardened after many years of repeated injecting, resulting in increased occurrences of missing the vein, the need to inject in sites that are difficult to keep clean (such as the groin) or switching to injecting under the skin or into muscle. Conversely it has been suggested that inexperience could lead to a higher level of infections, possibly due to a less developed injecting technique, causing greater tissue damage, or assistance from others, increasing the risk of contamination.<sup>6</sup>

2. **Poor housing conditions and homelessness.** Individuals who are homeless or living in temporary accommodation (such as hostels) have been reported to have higher levels of injection site infections.<sup>24</sup> Injecting in public places, such as the street, has also been associated with the development of these infections.<sup>13 18</sup> The environments in which people live and inject may promote poor hygiene<sup>33</sup> or risky injecting practice, such as rushing the process. For example, people who inject in public places may have no access to clean water or may inject into a higher risk body site (i.e. using the groin for a 'quick fix' when injecting in public places or when it is cold).<sup>34</sup>
3. **Gender.** A number of studies have found that women injectors experience higher levels of injection site infections than men.<sup>8 12 14 15 18 23 24</sup> It has been suggested that this might reflect biological differences between men and women, such as women having smaller, less easily accessible veins, possibly resulting in them more frequently missing the vein and thereby increasing their risk of developing an abscess.<sup>2 15</sup> However, there is little anatomical evidence to support this.<sup>15</sup> There are other factors that may play a role. For example, women are more likely than men to report having assistance with injecting,<sup>35</sup> which may place them at an increased risk of an injection that misses the vein. In addition, the process of assistance itself may result in contamination of the injecting equipment. Gendered social roles and power dynamics within sexual relationships may also play a role, as these have been reported to have an impact on HIV-related risk behaviours.<sup>36</sup>
4. **Sex work.** Several studies have found that involvement in sex work is associated with developing injection site infections.<sup>12 16 18 19</sup> It has been suggested that this association may be due to sex work being a marker of greater social marginalisation or a street-based lifestyle which could increase risk.<sup>18</sup>
5. **Viral infections.** Higher levels of injection site infections have been reported among people living with HIV<sup>12 16</sup> and people living with hepatitis C,<sup>14 15</sup> conditions which increase peoples' susceptibility to other infections or reduce their ability to fight an infection.

A few studies have also reported other associations. For example, recent research from Mexico found associations between having an abscess and smoking methamphetamine, and also with negative experiences of policing.<sup>19</sup> Such associations, which have not been reported in other studies, may be specific to the particular setting.

Whilst the majority of the studies discussed above are from high-income countries, the factors related to these infections in developing and transitional countries are likely to be very similar. Factors such as injection hygiene and poor housing and homelessness may be more of an issue among people who inject drugs in low- and middle-income countries. In addition, the high prevalence rates of viral infections such as HIV and viral hepatitis among injecting populations in many countries may also increase their susceptibility to injection site infections.

## Harm reduction responses and the prevention of injection site infections

The prevalence of injection site infections can be reduced by harm reduction interventions that target key risk factors. These interventions should consider the needs of different groups who may be more vulnerable to harm, such as the homeless, women

and older long-term injectors. Such interventions include needle and syringe programmes (NSP) and opioid substitution therapy (OST), both of which are recommended by United Nations guidelines as part of a key package of interventions for people who inject drugs.<sup>37</sup> Easy access to NSP can prevent infections by providing access to sterile injecting equipment and alcohol wipes for cleaning injection sites and by giving advice on hygienic and safe injection technique. OST has been shown to be effective in preventing transmission of blood-borne viruses.<sup>38</sup> The availability of prescribed oral substitute drugs such as OST can also prevent injection-related infections if the dose given is sufficient to end the need to inject illicit drugs on top.<sup>39</sup> Thus, harm reduction interventions can play a key role in the reduction of these infections among people who inject drugs.

Harm reduction interventions that encourage routes of use other than injecting – known as 'route transition interventions' – have also been proposed and piloted, however, further evaluation is needed to determine whether they will be of benefit.<sup>40</sup> For example, providing sheets of aluminium foil to promote the smoking of drugs such as heroin as an alternative to injecting has been proposed,<sup>41</sup> and foil packs designed for use in such an intervention have been developed.<sup>42</sup> Smoking or inhaling drugs rather than injecting them would prevent bacterial infections of injection sites. However, smoking is closely associated with other well-documented harms, including lung damage. Furthermore, some spore-forming bacteria, including anthrax, can be found in drugs and could cause infection if smoked or inhaled.<sup>9</sup>

Harm reduction and route transition interventions have the potential to reduce the extent of injection-related bacterial infections. However, these interventions, even if extensively adopted, are unlikely to prevent all such infections and health services will still need to respond to these infections.

## Health care utilisation in response to injection site infections

People who inject drugs may find it difficult to access health care due to marginalisation and stigma. Some may attempt to self-treat symptoms, for example incising and draining an abscess.<sup>4</sup> <sup>19</sup> People may also delay accessing health care due to prior bad experiences or difficulties in seeking traditional primary care services. As a result people who inject drugs may be more likely to make use of hospital Emergency Departments, both due to ease of access and because the delay in seeking health care has meant the illness now requires urgent attention.

Treatment for injection site infections often involves a range of procedures, including incision and drainage, application of dressings and administering antibiotics either by intravenous injection or orally.<sup>46</sup> Treatment of people who inject drugs can be complicated by other diseases such as HIV infection.<sup>6</sup> In addition, treating an infection or a complication may require long periods of time in hospital. Lengthy hospital stays may be difficult for people who are regularly injecting drugs and if they do not receive appropriate medical management (i.e. OST) they may leave hospital early, against medical advice, and not complete the treatment.

Studies looking at the health problems that lead to people who inject drugs presenting at Emergency Departments have found that injection site infections are often the most common reason for attending. Studies in North America found that abscesses and

cellulitis, two of the most frequent symptoms of injection-related infections, were the most common diagnoses among people who inject drugs who visited Emergency Departments, and they were also the most common reasons for their hospitalisation.<sup>43,44</sup> For example, a study undertaken in Vancouver found that 17% of all Emergency Department visits and 18% of all hospitalisations among a community-recruited sample of people who inject drugs were due to skin abscesses and cellulitis.<sup>43</sup>

A US cohort study of people who inject drugs who sought treatment between May 2001 and May 2002 from a hospital in Washington State found that 40% of those who attended the Emergency Department for an injection site infection were admitted to the hospital.<sup>45</sup> Two-thirds presented with an abscess (69%), with one-quarter of these abscesses requiring drainage in an operating theatre. One-tenth of the abscesses had been drained previously, either spontaneously (i.e. bursting) or by self-incision and drainage.

The health care costs associated with injection-related bacterial infections are likely to be substantial. A number of US studies have estimated the costs associated with hospital treatment and found these to be high. A 1980s study looking at hospital use for abscess care over a twelve-month interval found that the average length of hospitalisation was 12.4 days, at an average cost of US\$10,651, and that the estimated annual cost of treating abscesses among people who inject drugs at the hospital was US\$6.9 million.<sup>46</sup> A review of patient records from 1998 at Rhode Island Hospital found that 45% of the admissions among a sample of HIV-negative people who inject drugs were due to injection site infections or their complications, with these accounting for almost all the injection-related problems found; the injection-related infections were significantly more costly than the other admissions (US\$13,958 vs US\$7,906).<sup>47</sup> A study of hospital records from San Francisco General Hospital found that skin incision and drainage was the most common primary procedure on all inpatient records of those admitted for injection-related infections, with approximately one-quarter of the cases having multiple admissions within a year; the injection site infections at this hospital resulted in inpatient-related treatment charges that averaged US\$9.9 million per fiscal year between 1996 and 2000.<sup>20</sup>

A community-recruited study of people who inject drugs undertaken at seven locations in England in 2004 found that 36% reported having either an abscess or an open wound at an injection site in the previous year.<sup>14</sup> This study collected data on the use of health services in response to these symptoms, and estimated the national health care burden using standard costs. Injection site infections in England were found to cost between UK£15.5 and UK£47 million per annum in 2006. Overall health care costs related to problematic drug use, both injecting and non-injecting, in England had been estimated to be approximately UK£500 million per annum in the financial year 2003/4, with UK£25 million of this due to blood-borne viruses (HIV, hepatitis B and C) among people who inject drugs.

A study undertaken in three Australian states (Queensland, New South Wales and Victoria) estimated the cost of non-viral injecting-related injuries and disease to be AUS\$19.9 million in the 2005/6 fiscal year.<sup>48</sup> Of this amount, AUS\$8.7 million was incurred by community-based services, AUS\$2.8 million by Emergency Departments (due to over 60,000 visits) and AUS\$8.3 million was due to hospital admissions, accounting for between approximately 8,500 and 14,000 bed days of care.

The existing literature suggests that injection site infections and their complications place a considerable burden on health care systems in high-income countries. Whilst no scientific literature was identified for other countries, these infections are likely to pose a significant challenge to low- and middle-income countries. Preventive activities and supporting prompt access to health care when symptoms appear could substantially reduce bacterial infections of injection sites and the associated costs for health care systems.

## Community-based health care services for injection site infections

As noted above, people who inject drugs often seek medical attention for injection site infections and other health issues at hospital Emergency Departments rather than within a primary care setting, and may even attempt self-treatment. Thus, care may be more costly than necessary.<sup>19</sup> In response, a number of community-based approaches that aim to reduce use of Emergency Departments and hospital inpatient care have been reported. As these services are oriented towards people who inject drugs, they can provide a tailored service responding to their specific needs.

The Integrated Soft Tissue Infection Services Clinic in San Francisco was established to provide coordinated surgical intervention, substance use counselling and social services for those presenting at a public hospital with soft tissue infections.<sup>44</sup> This clinic was found to be valuable and cost effective, resulting in a 47% decrease in surgical service admissions, a 34% reduction in inpatient acute care bed days and a 71% reduction in operating room procedures in its first year of operation. There was also a 34% reduction in Emergency Department visits. Overall, the clinic was estimated to have saved over US\$8.75 million in costs related to injection site infections, which represented a 45% reduction in the costs of treating these infections. This clinic shifted care from a mainly inpatient-based approach to one with a focus on outpatient-based provision that integrated a range of services.

Another example of effective treatment for injection site infections is the community-based Wound and Abscess Clinic located in an NSP in Oakland, US.<sup>49</sup> This clinic is provided by a multidisciplinary team who offer care for injection site infection integrated with referrals to other services in a dedicated space in the service. In 2000 this clinic was reported to have an average cost per individual treated of US\$5 (excluding overhead costs), substantially lower than equivalent hospital costs, which averaged between US\$185 and US\$360 (including overheads, but not including medication and physician fees).

A number of studies on the impact of the Supervised Injection Facility (SIF), a drug consumption room (DCR) in Vancouver, Canada, have looked at injection site infections and health care seeking. One study found that the majority (65%) of visits to the nurse within the SIF were related to care for injection site infections and that those who were subsequently referred to hospital by the nurse were hospitalised for shorter periods than those accessing hospital by other routes.<sup>2</sup> This finding suggests that offering community-based, easily accessible, nurse-provided services may promote more prompt health care seeking and so reduce the levels of severe infections or complications that may result in hospitalisation.

The community-based health care studies reported in the scientific literature have all been undertaken in high-income countries. The barriers (including cost, distance, exclusion criteria, stigma and discrimination) faced by people who inject drugs in accessing health care are often greater in low- and middle-income countries.<sup>50</sup> So although there are very limited data, it may be that the severity of complications, mortality and morbidity associated with injection-related bacterial infections are greater in these settings. The provision of community-based services offering treatment for injection-related bacterial infection has been noted in a number of countries including low- and middle-income countries. For example, it is reported that an abscess management service is provided by the drop-in centres for people who use drugs in Myanmar<sup>51</sup> and by the CARE organisation in Dhaka, Bangladesh.<sup>52</sup>

Published studies on interventions focusing on injection site infections are few in number and further development and evaluation work is clearly needed. The findings of these few studies, however, do indicate that community-based services such as NSPs and DCRs could have a substantial impact on reducing harm from these infections. They also indicate that the development of nurse-led services for injection site injuries and infections can be effective in improving prompt health care seeking and in reducing expensive complications. These services could possibly be integrated with community-based blood-borne virus (i.e. HIV and viral hepatitis) testing and vaccination clinics, and existing community-based clinics providing these services could be developed at relatively low cost to also provide injection site infection care.

## Conclusion

Injection site infections are common among people who inject drugs and can have severe complications that may, albeit infrequently, be fatal. The bacterial contamination leading to these infections may arise from the individual's skin flora during injection, contamination of the injecting equipment during the preparation and injection of the drug, re-use of injecting equipment or contamination of the drug(s) during their manufacture or distribution.

Studies from several high-income countries suggest that the prevalence of these infections varies, with between one in twenty and one in three people who inject drugs reporting injection site infections each year. This variation, in part at least, reflects differences in the methods used by the studies. However, it could also reflect global variations in the patterns of drug use and in the responses to this issue. Higher levels of infections have been associated with a number of factors including poor injection hygiene, frequent injection, injecting under the skin or into muscle, the use of certain body sites for injection, the use of certain drugs, having been injecting for a long time, poor housing conditions and having a blood-borne viral infection. The risk of bacterial infections could be reduced by addressing these factors through, for example, reducing injecting under the skin or into muscle, avoiding use of excessive acid to dissolve drugs, not re-using equipment, and cleaning skin with alcohol before injection. Preventive interventions should aim to address these factors through the provision of advice and the full range of injecting-related equipment. This could be readily achieved through easy-to-access NSPs, as has been recommended.<sup>37,53</sup> Access to OST can also help if a sufficient dose of the substitute drug is

given to prevent the need to inject illicit drugs on top. Route transition interventions to encourage the use of drugs by routes other than injecting may also have a role to play in reducing the harm from bacterial infections of injection sites, although further examination and evaluation is needed.

The excessive costs often associated with injection-related bacterial infections can be prevented by interventions aimed at providing people who inject drugs with timely and appropriate care. A small number of interventions that aim to make accessing such care easier have been assessed and found to be successful in reducing health care costs.<sup>44,49</sup> Whilst further research and intervention trials are needed to identify and evaluate the most appropriate interventions, work undertaken so far suggests that low-threshold community-based interventions, such as nurse-provided clinics in DCRs or NSPs, are likely to be effective.<sup>44,46</sup> The provision of assessments of injection site infections and access to care for these has been recommended as a core component of fixed site needle exchange provision by the National Institute of Health and Clinical Excellence in the UK.<sup>53</sup>

There is a noticeable absence of scientific studies on bacterial infections among people who inject drugs in low- and middle-income countries. This may indicate that little research has been undertaken in this area or that what has been undertaken has not been published or is not easily identified (i.e. in grey literature or from small sections of publications focusing on other topics). Services addressing these infections have been reported in a number of low- and middle-income countries, and these infections will occur among all populations of injectors to varying extents. Infections in countries with less developed health care systems may present an even greater burden than they do in high-income countries.

People who inject drugs are vulnerable to many infections, including those due to a wide range of bacteria. Bacterial infections introduced through the injection process are a common cause of illness among injectors and can result in considerable harm and health care costs. The occurrence of such infections can be reduced by improving injection hygiene and practice using harm reduction approaches, and the complications can be minimised by improving prompt access to health services. The scaling up of harm reduction interventions, such as NSPs and the provision of OST, could have a significant impact in reducing these infections and the harm that they cause.

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# 3.4: Speeding up the response: A global review of the harm reduction response to amphetamines

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## Introduction

Amphetamines, or 'amphetamine-related drugs', are stimulants with the temporary effect of increasing the activity of the central nervous system, producing effects similar to adrenaline. Although some amphetamines are prescribed, this chapter will explore the harms associated with the illicit use of certain amphetamines. Despite heavy media coverage of amphetamines and increased research attention in some countries, the harm reduction response remains underdeveloped when compared with the response to opiates and injecting-related harms. Programmes do exist and new guidance is being compiled, but there is a need for evaluation, further documentation of experiences and expansion of effective interventions. This chapter will discuss the emerging responses to amphetamines-related harms and consider the next steps for the international harm reduction community.

### Definitions and effects

Amphetamine, methamphetamine, methcathinone and cathinone, the four drugs discussed in this chapter, stimulate the central nervous system and cause the rapid release of dopamine and other neurotransmitters. They can produce feelings of energy, confidence, alertness, well-being, talkativeness and increased sex drive. They increase blood pressure, heart rate and other metabolic functions, and decrease appetite.<sup>1</sup>

Methamphetamine has stronger subjective effects, or a more intense high, than amphetamine.<sup>2</sup> Cathinone is the active substance in fresh khat, a North African shrub whose leaves have been chewed for centuries for their mild stimulant effect.

The differences between cathinone and methcathinone are similar to those between amphetamine and methamphetamine: methcathinone is stronger than cathinone and produces similar but more intense effects, including a sense of invincibility, energy and increased sexuality and talkativeness. Euphoric effects are often more pronounced than with amphetamine or methamphetamine, leading some to compare cathinone and methcathinone to cocaine. Negative effects are similar to those caused by amphetamine and methamphetamine. Cathinone or methcathinone can be addictive and cause problems similar to those produced by long-term or heavy use of amphetamine and methamphetamine.<sup>3</sup>

Although amphetamines are often grouped with ecstasy in the category 'amphetamine-type stimulants', this chapter will limit its scope to amphetamine, methamphetamine, cathinone and methcathinone. The chapter excludes ecstasy in part because of the dramatic differences in patterns of ecstasy use. People who use ecstasy are less likely to become dependent on it and are much less likely to inject or smoke it, reducing the frequency of harms associated with these routes of administration.

For simplicity, the plural term 'amphetamines' will be used to refer to the four amphetamine-like drugs discussed here. Individual drug names (e.g. the singular 'amphetamine') will be used to discuss issues specific to one drug, or when the research discussed refers to one drug rather than to the group.

## Overview of amphetamine use around the world

During the 1990s the global use and production of amphetamines increased significantly, receiving mounting attention from law enforcement agencies, the media, politicians, medical and social service providers and researchers.

In the context of continued efforts to reduce cocaine and heroin production, amphetamines have a clear advantage in the marketplace. Rather than being grown in the open over an extended period of time in specific climates, amphetamines can be manufactured relatively cheaply and easily from other chemical 'precursors' that are licit and often easily available. Amphetamines are produced in clandestine laboratories that vary widely in size and sophistication. In some regions, it is common for drug users to produce their own amphetamines at home. Amphetamines have the potential to yield huge profits, and production is even harder to measure and prevent than that of opium or coca. If a laboratory is identified by police, a replacement can quickly be set up in another location. When law enforcement succeeds in limiting certain precursors, manufacturers can use different ones or synthesise their own. For example, if access to the precursor pseudoephedrine is restricted, it can be replaced by another, more easily available medication that can also be used to produce amphetamines.<sup>4</sup>

From the user's perspective, amphetamines are often cheaper and more easily available than opiates or cocaine. They are popular in part because of their perceived functionality: many people use them to facilitate work, study, sex or weight loss.

### **Prevalence and patterns of use**

According to estimates from the United Nations Office on Drugs and Crime (UNODC), between 16 and 51 million adults used amphetamine-type substances in 2007; the wide range reflects the dearth of precise data on use.<sup>5</sup> Where available, prevalence estimates are based on household surveys, seizures and arrests by law enforcement agencies, treatment demand and other medical data, epidemiological research and anecdotal evidence. These methods are not, however, always reliable. Lab seizures and arrests reflect law enforcement priorities; treatment demand reflects accessibility and perceived effectiveness of treatment; household surveys tend to miss high-risk groups. Data collection methods vary dramatically from country to country, and some countries do not collect or analyse data at all. Internationally, large-scale epidemiological research is limited.

In its synthesis of international data on rates of drug use, UNODC uses the term 'prevalence' to mean use at least once a year, which can also be called 'annual prevalence'.<sup>6</sup> 'Regular use' is defined as use at least once within the last month.<sup>6</sup> Given the wide availability of licit and illicit amphetamines, their varied functions and forms and the large number of people able to use them occasionally without suffering severe drug-related harm, these definitions are problematic and provide a very limited understanding of the nature, severity and context of use. For example, people who snorted amphetamine at a party a single time are grouped with people who smoke methamphetamine in chronic binges, and students who take a pill once a month while writing a paper are grouped with people who inject multiple times a day.

'Heavy' use and 'binges', two terms used often in this chapter, are better indicators of problematic use of amphetamines and are much more closely correlated with severe harms. Heavy use is usually defined as several times a week or more over a sustained period of time, although studies may use varying definitions. A binge is characterised by periods of intensive use for a period of at least two days (often more), followed by a break.<sup>7</sup>

The Philippines, Australia, New Zealand, El Salvador, the United States, Estonia, Denmark and the United Kingdom report the highest prevalences of annual amphetamine use in their general populations.<sup>1</sup> Asia is home to almost two-thirds of the world's methamphetamine users, while Oceania has the highest regional prevalence of annual use.<sup>8</sup> After marked increases in the 1990s, use of amphetamines in the United States<sup>9</sup> and the European Union<sup>10</sup> seems to be stabilising or even decreasing. There appears to be little use of amphetamines in most countries of Latin America, where cocaine is more popular and more accessible.<sup>1</sup> Amphetamines use is low but appears to be increasing in the Middle East.<sup>4</sup> Almost no data is available from Africa, but methamphetamine now accounts for nearly half of drug treatment admissions in South Africa.<sup>11</sup>

When considering the use of methamphetamine, it is important to maintain a critical perspective on reports of increased use. In the United States, for example, methamphetamine has been the focus of exaggerated media claims about prevalence of use and effects on health and society. While it is true that there are a significant number of people who use methamphetamine in the US, rates of problematic use and treatment demand remain lower than those for cocaine or heroin and are a tiny fraction of the rates for alcohol or marijuana. Despite frequent statements in the media about the 'epidemic' of methamphetamine use, only 0.2% of Americans use methamphetamine once a month or more, and rates of use have not increased since 1999.<sup>9</sup> Treatment guidelines from Australia, a country with one of the world's highest prevalences of methamphetamine use, state that only 3% of methamphetamine users will use on a frequent, habitual basis.<sup>7</sup>

### **Forms and routes of administration**

Amphetamines are produced in pill, powder, crystalline and liquid forms. They can be swallowed, snorted, smoked, injected or inserted anally. The crystalline form (often called crystal meth, ice or glass) is most often smoked. It is usually more pure than other forms as it is difficult to produce crystals with impure materials.<sup>12</sup>

The relative popularity and availability of different forms of amphetamines vary according to region. In Asia, the main markets for crystal methamphetamine (shabu) are in Japan, the Philippines and Malaysia, and use is increasingly widespread in China. In Southeast Asia, methamphetamine pills (yaba or yama) were long the most popular form of amphetamines, but crystal methamphetamine produced in illicit commercial laboratories is growing in popularity. Asian use of methamphetamine has been intimately linked with economic growth and the demands placed on workers by a rapidly developing economy.<sup>13</sup> In the European Union, amphetamine use is more prevalent than methamphetamine use. Relatively high levels of methamphetamine use are reported only in the Czech Republic, Estonia and the United Kingdom. Use of crystal methamphetamine as opposed to other amphetamines is reported to be increasing in Australia and New Zealand.<sup>10</sup>

Commercially produced illicit drugs were rarely available in the Soviet Union, and users prepared their own amphetamines (usually called vint, pervitin or belyi) from locally available precursors. After the fall of the Soviet Union, users in Eastern Europe and Central Asia did not, for the most part, transition to commercially produced amphetamines. Instead, homemade methamphetamine, methcathinone or cathinone mixtures synthesised from ephedrine, pseudoephedrine, and, more recently, phenylpropanolamine remain the primary amphetamines in the region.<sup>14</sup>

Although it can be prepared in just forty-five minutes, methamphetamine production requires the greatest amount of time, skill and equipment, and it elicits a more toxic reaction. In contrast, methcathinone can be prepared in about twenty minutes.<sup>14</sup> Cathinone can be prepared in just a few minutes without heat, but homemade preparations appear to have weak effects that last as little as a few minutes. Though sometimes available as powder or crystals, these drugs usually come in liquid form, with a high volume required to obtain the desired effects. Users sometimes begin by drinking the solution, but often move to injecting after a period of use. The variety of precursors and cooking methods involved means that users and even cooks often do not know exactly what substance they are preparing and using.<sup>14</sup>

## Harms related to the use of amphetamines

### *Unwelcome side effects*

Amphetamines can cause anxiety, insomnia and aggression.<sup>15</sup> The use of very high doses of methamphetamine can cause chest pain, hypertension, tachycardia and other cardiac arrhythmias<sup>16</sup> and increase the risk of stroke, seizures, cerebral haemorrhage and death.<sup>17</sup> High doses, particularly in the context of repeated binges, can cause temporary psychosis that includes mood swings, visual, auditory and sensory hallucinations, paranoia, delusions, obsessive thought patterns, impulsivity and the potential for aggression.<sup>18</sup>

Heavy or long-time users often experience 'speed bugs', the feeling that insects are crawling under their skin. They pick at the bugs and sometimes try to cut them out, causing large wounds that may become infected and can even be fatal.<sup>19</sup> Psychotic symptoms usually subside with reduction of use, although this is not always the case for those predisposed to psychosis.<sup>20</sup>

Amphetamines can induce or exacerbate depression and anxiety disorders and trigger existing mental illnesses such as schizophrenia.<sup>21</sup> A study of people with pre-existing psychotic disorders found that those using amphetamines or cocaine at baseline were eight times more likely to commit suicide.<sup>22</sup> The paranoia, psychosis, fatigue and intense depression associated with amphetamine binges may prevent users from approaching service sites.<sup>23</sup>

Long-term use of methamphetamine can cause painful or irregular menstruation.<sup>24</sup> This can have important implications, as women users may assume they cannot become pregnant and stop using contraception or they may become pregnant without realising it until relatively late.

As methcathinone is metabolised, breakdown products are exuded from the skin. This can give chronic users a very unpleasant body odour.<sup>25</sup>

### *Withdrawal*

Withdrawal symptoms after long-term or heavy use of amphetamines can include fatigue, anxiety, irritability, depression, inability to concentrate, muscle aches, tremors, increased appetite and suicidality,<sup>15</sup> as well as insomnia, hypersomnia (excessive sleepiness), paranoia and aggression.<sup>26</sup> Methcathinone and cathinone withdrawal symptoms can also include a runny nose and nosebleeds, cravings for sweets, muscle spasms and joint pain.<sup>25</sup>

Withdrawal symptoms often subside after about a week, though the duration of typical withdrawal remains unclear. The length and severity of withdrawal varies depending on drug dose, purity and route of administration, as well as on the age and general health of the user.<sup>26</sup>

### *Neurotoxic effects and neurological damage*

A growing body of evidence has associated chronic methamphetamine use with persistent changes in neurotransmitter systems, although the functional results of these changes in humans are not yet clear.<sup>27</sup> They appear to cause depression in some people and to have negative effects on memory, attention and other cognitive functions, although cessation of use may result in a return to more normal neurotransmitter function.<sup>27</sup> High doses of amphetamines can cause permanent damage to the nerve endings of serotonin and dopamine neurons. This may become apparent only later in life, when this damage is augmented by age-related dopamine and serotonin neuron loss and manifests in disorders such as Parkinson's Disease or depression.<sup>27</sup>

In recent years, methcathinone use has been associated with Parkinsonism in Russia, Ukraine, Estonia and Azerbaijan.<sup>28</sup> It is assumed that this is due to toxic effects of the potassium permanganate (manganese) used to synthesise methcathinone and cathinone. It is not yet clear whether these symptoms resolve with cessation of use; the symptoms of some people exposed to high levels of manganese in the workplace continued to progress after exposure ceased.<sup>28</sup>

### *Mortality and overdose*

Mortality related to amphetamines is likely to be much lower than that related to opiates.<sup>29</sup> An Australian analysis of methamphetamine-associated deaths showed that only 17% were the direct result of methamphetamine toxicity alone, while combined drug toxicity was the cause of 51% of deaths. Opiates, benzodiazepines and antidepressants were the most common drugs present with methamphetamine. Levels of methamphetamine toxicity varied.<sup>30</sup> Opiates can cause respiratory depression that can lead to cardiac failure, whereas alcohol and methamphetamine increase blood pressure and thus the risk of cardiovascular crisis. Methamphetamine masks the effects of alcohol and opiates, allowing people to underestimate their intoxication and increasing the risk of accidents and overdose. Cocaine and methamphetamine taken together increase the risk of cardiotoxic effects from both drugs.<sup>31</sup> In the Australian study, underlying cardiovascular pathology was found in a substantial proportion of the deaths. Hyperthermia was also implicated in some deaths. It seems that mental illness is a significant factor

in methamphetamine-related deaths as 14% of total deaths and one-third of overdoses examined were determined to be suicides.<sup>30</sup>

## **Injecting**

The basic risks associated with injecting amphetamines are largely the same as those of opiate injecting, including HIV, hepatitis, endocarditis, abscesses, sepsis and collapsed veins. Injecting patterns, however, appear to differ somewhat. Whereas opiate-dependent people tend to inject a few times a day every day, provided that drugs are available, amphetamines users are more likely to have periodic binges of days or even weeks during which they inject many times a day. It should be noted, however, that this is not universally true: a US study found that daily methamphetamine injectors had an average of two injections per day.<sup>32</sup> Another US study found that methamphetamine users visited syringe exchanges less frequently and took larger numbers of syringes on a single visit, reducing opportunities to interact with them and offer additional services.<sup>33</sup> Some studies have shown that women and men who have sex with men (MSM) who inject methamphetamine are more likely to engage in high-risk sexual behaviours. That said, it is difficult to make generalisations, as studies have found substantial variations in patterns of use and risk behaviours among people who inject amphetamines.<sup>1</sup>

## **Smoking and snorting**

As compared with heavy opiate users, heavy users of amphetamines are more likely to smoke rather than inject, especially if they are using crystal methamphetamine. The dehydration caused by amphetamines use can cause users' lips to crack and bleed, making them more likely to contract and transmit infections via shared smoking paraphernalia. Smoking on foil or in a pipe can cause burns to the fingers and face, and using contaminated containers (e.g. paint cans) or inappropriate materials (e.g. plastic containers) can lead to inhalation of toxic fumes.<sup>34</sup> Straws used for snorting amphetamines can become contaminated with blood and thus transmit blood-borne viruses, notably hepatitis C.

## **Sexual risk**

Much of the discussion of amphetamines-related harm has focused on sexual risk-taking associated with methamphetamine use, especially among MSM. Studies, the majority of them from North America, Australia or Western Europe, have found conflicting evidence about a causal link between methamphetamine use and HIV. Though some have documented increased sexual risk behaviour among amphetamines users, it is difficult to untangle the relationship between amphetamines and sex.<sup>1</sup> Many people intentionally use the disinhibiting effects of amphetamines to facilitate sex, including high-risk sex. Amphetamines use is prevalent in many settings in which high-risk sex is already occurring, and people inclined to take the risk of drug use may also be inclined to engage in high-risk sex.<sup>1</sup> On the other hand, the confidence and impulsivity produced by amphetamines may make users more likely to forgo condoms or engage in other risk behaviours.

There is good reason to believe that amphetamines can increase the likelihood of infection during sex: they dry mucous membranes, decrease sensitivity of the genital and rectal areas and delay orgasm, increasing the risk of torn membranes vulnerable to infection.<sup>35</sup>

## **Risks for people living with HIV**

Research suggests that amphetamines use by people living with HIV is associated with increases in viral replication and viral load, even among people receiving antiretroviral therapy [ART]. It may also alter the metabolism of HIV medications and negatively affect HIV-related dementia.<sup>27</sup> The effects of methamphetamine may be stronger for people taking some protease inhibitors, especially ritonavir, which could increase the risk of overdose.<sup>36</sup> Frequent use of amphetamines has been linked to increased risk of lymphoma in people living with HIV.<sup>37</sup>

## **Amphetamines and pregnancy**

Use of amphetamines during pregnancy does not appear to cause congenital defects. It has been associated with elevated risks of heart defects<sup>38</sup> and cleft lip and palate<sup>39</sup> in studies in which the subjects used multiple drugs, confounding results. Use of amphetamines in pregnancy has also been correlated with low birth weight, premature birth, post-partum haemorrhage and retained placenta.<sup>40</sup> Large-scale studies of the effects of prenatal exposure to methamphetamine are in their early stages.

As with better-studied drugs such as cocaine and heroin, it is important to remember the complex of factors that affect the course of a pregnancy, and to be wary of blaming the drug itself for all negative outcomes. For example, poor nutrition, irregular sleep patterns, tobacco use, alcohol use and lack of access to prenatal care have a greater effect on pregnancy outcome than cocaine use in itself.<sup>41</sup> Heavy use of amphetamines often leads to poor nutrition, lack of sleep, increased tobacco use and difficulty planning ahead and keeping appointments, meaning that pregnant users are at risk for many of the factors that contribute to a high-risk pregnancy. Harm reduction measures to deal with this set of risks, along with drug treatment, are likely to be effective in improving pregnancy outcomes.

## **Production and environmental harms**

Illicit synthesis of amphetamines can be dangerous for cooks and the people around them. Chemical processes involved in the production of amphetamines require and produce flammable, carcinogenic, poisonous and caustic substances.<sup>42</sup> Some of these can cause explosions if managed improperly. These risks are greater if cooks have poor knowledge of chemical processes or if their judgement is impaired by drug use or other factors. Chemicals can spread into surrounding areas and contaminate soil and water. Proper clean up of methamphetamine labs is expensive, time-consuming and at times dangerous.<sup>42</sup>

## Harm reduction for people who use amphetamines

Harm reduction for people who use amphetamines follows the same fundamental principles as harm reduction for opiate users: meet users where they are, give them the information, means and opportunities for positive change and organise programmes around their needs rather than imposing external demands. Many aspects of harm reduction programmes for people who use amphetamines are identical to those of programmes for opiate users. These include provision of safer injecting supplies and accurate information; mobile services and outreach workers to access users unwilling or unable to come to a harm reduction site; engagement of active and former drug users as staff members, volunteers and advisors; and referrals and assistance in accessing other needed services.

Some harm reduction programmes, designed for and accustomed to work with opiate users, are daunted by the idea of working with amphetamines users. There are indeed some differences in basic needs. For example, in many settings users are more likely

to smoke amphetamines than opiates, and the psychological problems associated with heavy use can make them seem more 'difficult' than opiate users as clients. Use of amphetamines may lead to paranoia, confusion, impulsiveness and memory and attention lapses that make it challenging to counsel users. Finally, there is almost no access to pharmacological treatment for dependence on amphetamines. This can be disconcerting to providers accustomed to being able to offer treatments as straightforward and effective as methadone and buprenorphine.

Fortunately, experience from various countries has shown that harm reduction programmes can respond effectively to harms associated with the use of amphetamines. Table 3.4.1, developed using several existing resources,<sup>23 34 43 44 45 46</sup> presents key aspects of harm reduction interventions for people who use amphetamines. These approaches are useful not only for harm reduction service providers, but also for users, friends and family, and primary and emergency health care providers and law enforcement personnel in contact with people who use amphetamines. There may be a role for harm reduction service providers in training others to respond appropriately to amphetamines-related harms.

**Table 3.4.1: Responding to harms associated with the use of amphetamines**

Area	Behaviour	Harm	Harm Reduction Strategy
Hydration, nutrition and hygiene	<ul style="list-style-type: none"> <li>Forgetting to eat and drink</li> <li>Eating only junk food</li> <li>Not sleeping</li> </ul>	<ul style="list-style-type: none"> <li>Malnutrition and dehydration</li> <li>Increased risk of anxiety, paranoia and psychosis</li> <li>Decreased high, need for higher dose to achieve the same effects</li> <li>Intensified 'crash'</li> </ul>	<ul style="list-style-type: none"> <li>Provide water, juice and healthy food where possible, especially for homeless, marginally housed and impoverished users</li> <li>Stress the need to sleep or at least rest in a darkened room, eat healthy food (especially fruits and vegetables) and drink water regularly. Point out that these are not abstract health concerns, but have immediate positive effects on the experience of day-to-day use</li> </ul>
	<ul style="list-style-type: none"> <li>Forgetting to drink water and brush teeth</li> <li>Eating sugary foods</li> <li>Grinding teeth</li> </ul>	<ul style="list-style-type: none"> <li>Dry mucous membranes more vulnerable to infection</li> <li>Dental problems</li> </ul>	<ul style="list-style-type: none"> <li>Stress the importance of hydration and dental hygiene</li> <li>Distribute toothbrushes and toothpaste</li> </ul>
Moderating patterns of use	<ul style="list-style-type: none"> <li>Binges (heavy use over a period of days or weeks)</li> </ul>	<ul style="list-style-type: none"> <li>Increased risk of amphetamines-induced psychosis, as well as paranoia, anxiety and other health problems</li> </ul>	<ul style="list-style-type: none"> <li>Encourage users to plan for breaks in advance. Develop methods to help them keep track of how long and how much they have been using, take a break at the limit they have set for themselves, eat well before using and stay hydrated while using. When introducing and implementing these new plans it can be helpful for the user to have a 'harm-reduction buddy', someone they trust who can support their efforts</li> </ul>
	<ul style="list-style-type: none"> <li>Heavy use</li> </ul>	<ul style="list-style-type: none"> <li>Withdrawal and 'crashes'</li> </ul>	<ul style="list-style-type: none"> <li>Stress that depression, fatigue, moodiness and aches are a natural part of withdrawal and will pass with time</li> <li>Inform users that focusing on pleasant, distracting activities; keeping close to supportive people; and maintaining a healthy diet and routine will help them to manage withdrawal and crashes</li> <li>After the crash is over, help users develop their own strategies to reduce crashes, using the same tactics effective for episodes of paranoia and psychosis</li> </ul>

<b>Reducing harms related to modes of use</b>	<ul style="list-style-type: none"> <li>• Sharing injecting equipment</li> <li>• Sharing mouthpieces, including jagged ones</li> <li>• Smoking with toxic materials</li> <li>• Using pipes that can easily cause burns</li> </ul>	<ul style="list-style-type: none"> <li>• Risk of blood-borne diseases, lung damage, toxicity, cuts and burns</li> </ul>	<ul style="list-style-type: none"> <li>• Distribute sterile injecting equipment and information on safer injecting</li> <li>• Distribute glass stems with gauze or individual pipe tips</li> <li>• Teach users how to make safer pipes</li> <li>• Distribute lip balm and burn salve</li> </ul>
	<ul style="list-style-type: none"> <li>• Transition to smoking and injecting or to more potent forms (e.g. crystal meth)</li> </ul>	<ul style="list-style-type: none"> <li>• Dependence develops more quickly and is more severe among users who inject and who use more potent forms</li> <li>• Increased risk of blood-borne viruses</li> </ul>	<ul style="list-style-type: none"> <li>• Inform users who swallow or snort about the risks of injecting and smoking and about safer injecting and smoking techniques</li> <li>• Encourage users not to transition to a more intense route</li> <li>• Give users who inject or smoke appropriate information about safer methods and encourage them to transition to snorting or swallowing if possible</li> <li>• Inform users that smoking from a pipe produces a faster and more intense high than smoking on foil and inhaling smoke through a tube or smoking from a joint, and that switching to one of these methods is another harm reduction strategy</li> </ul>
	<ul style="list-style-type: none"> <li>• Injecting many times in one sitting</li> </ul>	<ul style="list-style-type: none"> <li>• Increased risk of vein and tissue damage, missed shots, infection and other injection-related harms</li> </ul>	<ul style="list-style-type: none"> <li>• Use a butterfly needle scheme, eliminating the need to enter the vein repeatedly and repeat the risk of associated harms. Distribute appropriate supplies and teach participants how to use them</li> </ul>
<b>Managing paranoia, delusions and anxiety</b>	<ul style="list-style-type: none"> <li>• Picking at 'speed bugs'</li> </ul>	<ul style="list-style-type: none"> <li>• Open wounds that can become infected</li> </ul>	<ul style="list-style-type: none"> <li>• Use measures described above to deal with delusions</li> <li>• It may be helpful to create non-invasive 'treatments' for the bugs to calm the user during acute episodes</li> </ul>
	<ul style="list-style-type: none"> <li>• Exhibiting signs of paranoia, delusions and/or acute anxiety</li> </ul>	<ul style="list-style-type: none"> <li>• Risk of harm to self or others</li> </ul>	<ul style="list-style-type: none"> <li>• Be calm and reassuring</li> <li>• Take user to a quiet, calming place and try to turn their attention to something else</li> <li>• Take users seriously and do not tell them that they are delusional as this can upset them more. Validate their experience while avoiding acknowledging that it is real (if you are certain that it is not)</li> <li>• Help users recognise the ways in which paranoia and anxiety are associated with patterns of drug use and with harms such as violence or arrest</li> <li>• Do not sit behind a desk, take notes or have the client face doors or windows</li> <li>• Apply cool compresses to the neck, underarms, backs of the knees and forehead to help lower body temperature</li> <li>• Provide plenty of hydrating fluids (nothing caffeinated or sugary)</li> <li>• If available, small doses of benzodiazepines can be helpful, as can 50–100 ml of diphenhydramine (Benadryl/Dimedrol)</li> <li>• When user is not high, discuss strategies to reduce the occurrence of anxiety, paranoia and psychosis, including diet, hydration, sleep, breaks, moderation of dose, routes of administration and setting</li> <li>• Users who are acutely psychotic or aggressive, appear to be a danger to themselves or others, or are experiencing symptoms of acute toxicity need medical attention. For psychological symptoms this includes benzodiazepines and, in acute cases, anti-psychotics. If vital signs are significantly elevated, an IV line, cardiac monitoring and emergency care may be needed. If appropriate, it is important to check for breathing and use rescue breathing if needed</li> <li>• Harm reduction providers should not risk their own safety if a situation appears to be dangerous</li> </ul>
<b>Managing harms of associated activities and 'functional' use</b>	<ul style="list-style-type: none"> <li>• Sexual risk</li> </ul>	<ul style="list-style-type: none"> <li>• HIV and STIs</li> </ul>	<ul style="list-style-type: none"> <li>• Provide free access to condoms, lubricant and information about STIs and HIV</li> <li>• Emphasise the special importance of using plenty of lubricant during long, dry or rough sex</li> <li>• Provide low-threshold access to HIV and STI testing and treatment, as well as to contraception and pregnancy testing and counselling</li> <li>• Understand and acknowledge the role that amphetamines play in the sexual lives of users. Rather than perceiving amphetamines as the sole source of risk, understand that many people use them to facilitate sexual activity. Discuss pleasure and functionality along with risk to allow more sophisticated strategies of risk reduction</li> <li>• Develop a sexual harm reduction plan in advance, discussing realistic ways to reduce sex-related harms in the context of users' lives</li> <li>• Talk not only about HIV and STIs, but also about sexual and physical violence, transactional and commercial sex, abusive relationships, housing and other issues intimately related to sexual risk behaviours. Addressing the context of sexual risk and developing a plan to make behaviours less dangerous is often the best way to support users in reducing risk</li> </ul>
	<ul style="list-style-type: none"> <li>• Using amphetamines to control weight</li> </ul>	<ul style="list-style-type: none"> <li>• Dependence, excessive weight loss, other harms associated with use</li> </ul>	<ul style="list-style-type: none"> <li>• Recognise that some people, especially women, use amphetamines to lose or control weight and fear gaining weight if they stop using</li> <li>• Discuss this fear with users and help them to develop a plan to prevent or manage weight gain, while exploring the issues underlying poor body image</li> </ul>
	<ul style="list-style-type: none"> <li>• Use of amphetamines for work or study</li> </ul>	<ul style="list-style-type: none"> <li>• Dependence, other harms associated with use</li> </ul>	<ul style="list-style-type: none"> <li>• Remind users that while amphetamines can initially help sustain attention and endurance for long periods of time, heavy use eventually makes it very difficult to complete a task, focus or behave appropriately in work or study settings</li> <li>• Organise separate support groups to respond more accurately to the needs of people who use amphetamines for different reasons. Truck drivers who use methamphetamine while working, for example, are likely to have very different concerns than teenagers who use it at raves or sex workers who use it to endure harsh working conditions</li> </ul>

## Drug dependence treatment

Because there is as yet no widely accepted medication-assisted treatment for amphetamines dependence and because the psychological side effects of heavy amphetamines use can make traditional drug treatment counselling methods impractical, it is sometimes believed that dependence on amphetamines cannot be treated. This is not true, though there remains a shortage of evidence-based treatment specific to amphetamines.

Evidence supports the effectiveness of behavioural interventions, particularly cognitive behavioural therapy and contingency management, and guidelines have been developed in Australia and the United States.<sup>47</sup> One model that has demonstrated success is the Matrix Model, which integrates cognitive-behavioural therapy, family education, social support and individual counselling in a non-confrontational, non-judgmental style reinforced by peers.<sup>48</sup> While some believe that the long-term psychological effects of heavy amphetamines use mean that users require long-term treatment,<sup>49</sup> others have found significant increases in abstinence following a session of motivational interviewing and behavioural therapy lasting only two to four hours.<sup>50</sup>

The stepped care approach is a way of adjusting interventions to the needs and motivation levels of individual clients. This approach begins with provision of the least intensive intervention and offers the possibility of scaling up into longer and more intensive ones. It has the added benefit of maximising resources by avoiding unnecessarily intensive interventions and thus increasing the number of people who can be provided with services.<sup>2</sup>

Pharmacotherapy for dependence on amphetamines is still in trial phases. In England, an experimental substitution treatment programme that prescribed a set dose of 30 mg/day of dexamphetamine sulphate found that half the subjects stopped injecting and the remainder reduced injection significantly; 85% had not used or shared injecting equipment after entering treatment.<sup>51</sup> Modafinil, bupropion and methylphenidate are also under investigation, but the results are not yet conclusive.<sup>52</sup>

## Next steps for reducing harms related to amphetamines use

The first priority for the international harm reduction community should be to support the development, evaluation and expansion of harm reduction interventions specific to amphetamines. Though the evidence base for these interventions is not yet as substantial as that for harm reduction interventions among opiate users, the positive experience of programmes in several countries suggests their value. Research on these interventions should be prioritised, but in the meantime it is important to expand the range of services available to amphetamines users and to work to reduce the spread of HIV and other harms in this group. Harm reduction providers in many countries have expressed their need for training on work with amphetamines users, and efforts should be made to make such trainings available as soon as possible. The experience and knowledge of service providers in countries such as the United States or Australia can be used to develop expertise in regions such as Eastern Europe, Southeast Asia or South Africa.

Next, treatment for amphetamines users needs to be demystified. There is significant research on treatment modalities and some guidelines already exist. Interventions specific to amphetamines should be implemented and evaluated in other regions, and international guidelines for treatment should be developed and promoted.

Service providers, researchers and policy-makers also need to consider the role of drug policy in harms related to amphetamines. On a macro level, it is clear that efforts to suppress one drug often lead only to the 'substitution' of another that is more easily or cheaply available.<sup>53</sup> For example, efforts to suppress opium production in Asia led to a boom in production of amphetamines.<sup>54</sup> Vigorous and even violent prohibition efforts succeeded only in replacing one drug with another that is equally or more harmful. This experience indicates the need to re-examine global drug policy.

On a more local level, experience in countries as varied as Australia and Ukraine suggests that attempts to control precursors of amphetamines can lead to increased harms associated with their use. Decreased availability of cold medicines has been linked to increased pharmacy break-ins in Australia<sup>55</sup> and to a shift in Ukraine to more neurotoxic preparations made using less tightly regulated precursors.<sup>56</sup>

Prohibition can push production, trafficking and use towards more potent, easily concealable and transportable forms of drugs.<sup>13</sup> More potent forms and more direct methods of administration – for example, injecting crystal meth instead of taking amphetamine pills – are more likely to cause dependence and other harms, including HIV infection. Moreover, punitive policies and law enforcement practices can push drug users to use quickly and wherever they can (e.g. in an alley), inhibiting their ability to practice harm reduction.<sup>53</sup> Policy-makers and advocates need to consider the consequences of prohibition and explore other methods of reducing problem drug use, notably drug treatment, harm reduction and evidence-based drug education targeted at high-risk groups. Further research on the relationship between drug policy, drug use patterns and associated harms would be useful in supporting more effective public-health-oriented drug policies.

Finally, service providers need to take into account the role of production methods in harms related to amphetamines. Especially in situations in which users produce drugs themselves, a change in production methods could reduce neurotoxic effects, environmental hazards and perhaps other harms. Region-specific research into drug production methods could give providers and users a better understanding of exactly what drug they are synthesising and its specific dangers. It would be useful to explore the possibility of developing harm reduction interventions related to production, as well as the legal, political or ethical questions that such interventions might raise.

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# 3.5: Out of sight, out of mind? Harm reduction in prisons and other places of detention

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*[B]y entering prisons, prisoners are condemned to imprisonment for their crimes; they should not be condemned to HIV and AIDS. There is no doubt that governments have a moral and legal responsibility to prevent the spread of HIV among prisoners and prison staff and to care for those infected. They also have a responsibility to prevent the spread of HIV among communities. Prisoners are the community. They come from the community, they return to it. Protection of prisoners is protection of our communities.*  
**United Nations Commission on Human Rights (1996)<sup>1</sup>**

## Introduction

The rates of HIV prevalence among prisoners and detainees<sup>a</sup> are significantly higher than those in the general population in many countries. Hepatitis C virus (HCV) prevalence rates are even higher than those of HIV. Since the early 1990s a number of countries have introduced HIV prevention programmes in prisons. However, many of them are small in scale and restricted to a few prisons and even fewer pre-trial detention facilities. Most also exclude necessary evidence-based interventions, in particular needle and syringe programmes (NSPs) and opioid substitution therapy (OST). Even where countries have adopted harm reduction in their responses to drug-related harms outside prisons, they often fail to do so in prisons and other places of detention. To date, only ten countries have NSPs operating in at least one prison and less than forty countries have some form of OST in at least one prison. There is therefore an urgent need to introduce comprehensive programmes and to scale them up rapidly.

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a Different jurisdictions use different terms to denote places for detaining people who are awaiting trial, who have been convicted or who are subject to other conditions of security and to describe the various groups of people who are detained. Here, the term 'prison' is used for all places of detention and the term 'prisoner' describes all who are held in such places, including males and females detained in criminal justice and prison facilities during the investigation of a crime, while awaiting trial, after conviction and before sentencing, and after sentencing. Although the term does not formally cover persons detained for reasons relating to immigration or refugee status, those detained without charge and those sentenced to compulsory 'treatment' and 'rehabilitation' centres as they exist in some countries, most of the considerations in this paper apply to them as well.

## Prevalence of HIV and HCV in prisons

HIV surveillance has been the most common form of HIV research in prisons, although this has largely been restricted to high-income countries. Data from low- and middle-income countries are more limited, tend to be varied and unsystematic and, in many cases, are not recent enough to provide an accurate picture of the current situation in prisons.<sup>2</sup> Even in high-income countries, the precise number of prisoners living with HIV is difficult to estimate. Rates of HIV infection reported from studies undertaken in a single prison or region may not accurately reflect HIV prevalence in all prisons or regions within a country.

More thorough and systematic research is needed to provide an accurate picture of the current situation of HIV in prisons. Nevertheless, existing reviews show that HIV infection is a serious problem that requires immediate action. In many prison systems, rates of infection are several times higher than in the community outside prisons and this is primarily attributed to injecting drug use prior to incarceration.<sup>3</sup> In other systems, elevated HIV prevalence rates reflect the high HIV prevalence rates in the general population.<sup>4</sup> Everywhere, the prison population consists of individuals facing greater risk factors for contracting HIV (and HCV and TB) than the general population outside prisons. Such characteristics include injecting drug use, poverty, alcohol abuse and living in medically underserved and minority communities.<sup>5</sup>

Studies have shown HIV prevalence ranging from zero in a young male offenders' institution in Scotland<sup>6</sup> and among prisoners in Iowa, United States,<sup>7</sup> to 33.6% in an adult prison in Catalonia, Spain,<sup>8</sup> to over 50% in a female correctional facility in New York

City.<sup>9</sup> As early as 1988 about half of the prisoners in Madrid<sup>10</sup> and 20% of prisoners in New York City tested HIV positive.<sup>11</sup> The highest HIV prevalence reported among a national prison population was in South Africa, where estimates put the figure at 41.4%.<sup>2</sup> Conversely, some countries report zero prevalence; most of these are in North Africa or the Middle East.<sup>2</sup>

HCV prevalence rates in prisons are even higher than HIV rates. A 2004 review of all published studies of HCV in prisons estimated that 30% to 40% of all prisoners in the US were infected with HCV.<sup>3</sup> While WHO estimates that about 3% of the world's population has been infected with HCV,<sup>12</sup> estimates of the prevalence of HCV in prisons range from 4.8% in an Indian jail<sup>13</sup> to 92% in two prisons in northern Spain.<sup>14</sup>

Within prison populations, certain groups have higher levels of infection. In particular, the prevalence of HIV and HCV infection among women tends to be higher than among men.<sup>4</sup>

## Drug use in prisons

Many prisoners have a history of drug use before they enter prison.<sup>15</sup> In 1999, 68% of all new prison admissions in the US tested positive for an illegal drug in urine screening<sup>16</sup> and similar findings have been reported across Europe,<sup>17</sup> North America and Australia.<sup>18</sup> In other parts of the world, the situation is less clear because of the lack of systematic research,<sup>19 20</sup> but in many countries histories of drug use among prisoners are common. In fact, a large percentage of prison populations around the world have been sentenced for drug-related offences. These may be crimes related to drug production, possession, trafficking or use or crimes committed to acquire resources to purchase drugs. Many prison systems have seen increases in their population (and consequent overcrowding) attributable in large measure to a policy of actively pursuing and imprisoning those dealing with and consuming illegal substances.<sup>21</sup>

For people who inject drugs, imprisonment is a common event; studies from a large number of countries report that between 56% and 90% of people who inject drugs are imprisoned at some stage.<sup>22 23 24</sup> Multiple prison sentences are more common for prisoners who inject drugs than for other prisoners.<sup>25</sup> The percentage of prisoners with a history of injecting drug use varies from prison to prison; studies have found, for example, that it was 11% in England,<sup>26</sup> but 64% in Australia.<sup>27 28</sup>

Some people who use drugs prior to imprisonment discontinue their drug use while in prison. However, many carry on using, often with reduced frequency and amounts,<sup>29</sup> but sometimes maintaining the same level of use.<sup>30 31</sup> Prison is also a place where drug use is initiated, often as a means to release tension and to cope with being in an overcrowded and often violent environment.<sup>32 33</sup>

Injecting drug use in prison is of particular concern given the potential for transmission of HIV and HCV. Those who inject drugs in prisons often share needles and syringes and other injecting equipment, which is a very efficient way of transmitting both viruses.<sup>34</sup> A large number of studies from countries around the world report high levels of injecting drug use, including among female prisoners.<sup>35 36</sup>

Although more research has been carried out on injecting drug use in prisons in high-income countries, studies from low- and middle-income countries have found similar results. In Iran, for example, about 10% of prisoners are believed to inject drugs while

incarcerated, with 95% reported to share needles.<sup>37</sup> Injecting drug use has also been documented in prisons in Eastern Europe and Central Asia,<sup>38 39 40 41 42</sup> Latin America<sup>43</sup> and Sub-Saharan Africa.<sup>44 45</sup>

## HIV and HCV transmission resulting from drug use in prisons

A large number of studies from countries in many regions of the world have reported HIV and/or HCV seroconversion within prisons, or have shown a history of imprisonment to be associated with prevalent and incident HIV and/or HCV infection among people who inject drugs.<sup>46</sup>

HIV infection has been significantly associated with a history of imprisonment in Europe (including among female prisoners) and also in the Russian Federation, Canada, Brazil, Iran and Thailand. Using non-sterile injecting equipment in prison was found to be the most important independent determinant of HIV infection in a number of studies.<sup>4</sup> The strongest evidence of extensive HIV transmission through injecting drug use in prison has emerged from documented outbreaks in Australia, Lithuania, the Russian Federation and Scotland.<sup>28 32 47 48 49</sup>

HCV infection by sharing of injecting equipment in prison has been reported in Australia and Germany.<sup>50 51 52</sup>

## Harm reduction in prisons: Implementation, evidence and guidance

There are evidence-based interventions that can be put in place to reduce drug-related harms within prison populations and a wealth of international guidance on implementation. In fact, it could be argued that it is even more important that these programmes reach prisoners and detainees, given their increased vulnerability to HIV and HCV infection, than people outside prison. Prison health programmes have the potential to reach vulnerable people with a broad range of services that they may not be likely to access outside prison.

**Table 3.5.1: Countries and territories with NSP or OST in at least one prison<sup>b</sup>**

Country/territory	Needle exchange in prisons	Opioid substitution therapy in prisons
ASIA		
India	x	✓
Indonesia	x	✓
Malaysia	x	✓
EASTERN EUROPE and CENTRAL ASIA		
Albania	x	✓
Armenia	✓	x
Belarus	✓	x
Croatia	x	✓
Czech Republic	x	✓
Georgia	x	✓
Hungary	x	✓
Kyrgyzstan	✓	x
Macedonia FYR	x	✓
Moldova	✓	✓
Montenegro	x	✓
Poland	x	✓
Romania	✓	✓
Serbia	x	✓
Slovenia	x	✓
MIDDLE EAST and NORTH AFRICA		
Iran	✓	✓
NORTH AMERICA		
Canada	x	✓
United States	x	✓
(Puerto Rico)	x	✓
OCEANIA		
Australia	x	✓
New Zealand	x	✓
SUB-SAHARAN AFRICA		
Mauritius	x	✓
WESTERN EUROPE		
Austria	x	✓
Belgium	x	✓
Denmark	x	✓
Finland	x	✓
France	x	✓
Germany	✓	✓
Ireland	x	✓
Italy	x	✓
Luxembourg	✓	✓
Malta	x	✓
Netherlands	x	✓
Norway	x	✓
Portugal	x	✓
Spain	✓	✓
Sweden	x	✓
Switzerland	✓	✓
United Kingdom	x	✓

<sup>b</sup> Inclusion in this table does not indicate scope, quality or coverage of intervention. In Georgia, methadone is currently provided for *detoxification* over a maximum period of three months and not for long-term maintenance; however, expansion to a maintenance programme is being considered.

## **Needle and syringe programmes (NSPs)**

The first prison NSP was established in Switzerland in 1992. Since then NSPs have been introduced in over sixty prisons in ten countries in Europe, Central Asia and Iran (see Table 3.5.1). In some countries, only a few prisons have NSPs, however, in Kyrgyzstan and Spain, NSPs have been rapidly scaled up and operate in a large number of prisons.<sup>c</sup>

Germany remains the only country in which prison NSPs have been closed. NSPs had been successfully introduced in seven prisons by the end of 2000 and other prisons were considering implementing them. However, six of the programmes have since closed as a result of political decisions by newly elected conservative state governments, made without consultation with prison staff. Since the programmes closed, prisoners have gone back to hiding and sharing injecting equipment, thus increasing the likelihood of transmission of HIV and HCV.<sup>53</sup> Staff have been among the most vocal critics of the decision to close down the programmes and have lobbied the governments to reinstate the programmes.<sup>4</sup>

In most countries with prison NSPs, implementation has not required changes to laws or regulations.<sup>d</sup> Across the eleven countries, various models for the distribution of sterile injecting equipment have been used, including anonymous syringe dispensing machines, hand-to-hand distribution by prison health staff and/or non-governmental organisation (NGO) workers and distribution by prisoners trained as peer outreach workers.<sup>54</sup>

Systematic evaluations of the effects of NSPs on HIV-related risk behaviours and of their overall effectiveness in prisons have been undertaken in ten projects. These evaluations and other reports demonstrate that NSPs are feasible in a wide range of prison settings, including men's and women's prisons and prisons of all security levels and sizes. Providing sterile needles and syringes is readily accepted by people who inject in prisons and contributes to a significant reduction of syringe sharing over time. It also appears to be effective in reducing resulting HIV infections.<sup>47</sup> At the same time, there is no evidence to suggest that prison-based NSPs have serious, unintended negative consequences. In particular, they do not lead to increased drug use or injecting, and syringes are not used as weapons.<sup>55</sup> Evaluations have found that NSPs in prisons facilitate referral of people who use drugs to drug dependence treatment programmes.<sup>56 57</sup>

Studies have shown that important factors in the success of prison NSPs include easy and confidential access to the service, providing the right type of syringes and building trust with the prisoners accessing the programme.<sup>47</sup> For example, in Moldova, a small number of prisoners accessed the NSP when it was located within the health care section of the prison, however, once prisoners could obtain sterile injecting equipment from fellow prisoners, trained to provide harm reduction services, the amount of equipment distributed increased significantly.<sup>58</sup>

Ultimately, since most prisoners leave prison at some point to return to their community, implementing NSPs in prisons will benefit not only prisoners and prison staff, but also society in general. Therefore, experts and UN agencies recommend that NSPs should be introduced in prisons and other places of detention. Following an exhaustive review of the international evidence, WHO, UNODC and UNAIDS recommend that prison authorities in countries experiencing or threatened by an epidemic of HIV infections among injecting drug users should introduce and scale up NSPs urgently.<sup>59</sup>

c A prison NSP has been introduced in a Portuguese prison but is currently not operating  
d In some former Soviet Union countries, regulations and later legislative changes were undertaken to allow for prison NSPs.

## **Bleach programmes**

Programmes providing bleach or other disinfectants for sterilising needles and syringes to reduce HIV transmission among people who inject drugs in the community were first introduced in San Francisco in 1986.<sup>24</sup> Such programmes have particularly received support in situations where opposition to NSPs in the community or in prisons has been strongest. By 1991 sixteen of fifty-two prison systems surveyed had made bleach or other disinfectants available to prisoners, including in Africa and Central America.<sup>60</sup> Today, bleach or other disinfectants are available in many prison systems, including in Australia, Canada, Indonesia, Iran and some systems in Eastern Europe and Central Asia.<sup>4 55</sup>

Evaluations of bleach programmes in prisons have shown that distribution of bleach or other disinfectants is feasible and does not compromise security. However, WHO concludes that the 'evidence supporting the effectiveness of bleach in decontamination of injecting equipment and other forms of disinfection is weak.'<sup>56</sup> While the efficacy of bleach as a disinfectant for inactivating HIV has been shown in laboratory studies, field studies cast 'considerable doubt on the likelihood that these measures could ever be effective in operational conditions.'<sup>56</sup> Moreover, studies did not find a significant effect of bleach on HCV seroconversion.<sup>61 62</sup> For these reasons, bleach programmes are regarded as a second-line strategy to NSPs. WHO, UNODC and UNAIDS recommend that bleach programmes be made available in prisons where 'authorities continue to oppose the introduction of NSPs despite evidence of their effectiveness, and to complement NSPs.'<sup>60</sup>

## **Opioid substitution therapy and other drug dependence treatments**

The first experimental OST programme in prison, offering methadone pre-release to prisoners in New York City, was initiated in 1968.<sup>63</sup> The early literature noted that, in addition to Rikers Island in New York,<sup>64</sup> over the next twenty years such programmes either existed or had existed at some point at a prison in California (Contra Costa County), in Rotterdam in the Netherlands, at Wolds Remand Prison in the United Kingdom<sup>65</sup> and in Denmark and Sweden.<sup>66</sup>

In Australia, a pilot pre-release methadone programme started in New South Wales in 1986 and was later expanded so that the pre-release programme became just one component of a larger prison methadone maintenance therapy (MMT) programme.<sup>67</sup> Initially, the programme focused on 'breaking the cycle of criminal activity associated with drug use.'<sup>67</sup> However, as early as 1987, it became the first prison MMT programme to move towards a HIV prevention strategy and to include the reduction of injecting heroin use and HIV and hepatitis B transmission among its objectives.<sup>67</sup>

Since the early 1990s, and mostly in response to raising HIV rates among people who inject drugs in the community and in prison, there has been a marked increase in the number of prison systems providing OST to prisoners. Today, prison systems in nearly forty countries offer OST to prisoners, including most systems in Canada and Australia, some systems in the US, most of the systems in the 15 'old' European Union (EU) member states,<sup>68</sup> Iran and Indonesia (see Table 3.5.1).<sup>4</sup> In Spain, according to 2009 data, 12% of all prisoners received MMT.<sup>69</sup> In most other prison systems, coverage is much lower.

OST programmes are also provided in some of the states that joined the EU more recently (including Hungary, Malta, Slovenia and Poland), although they often remain small and benefit only a small number of prisoners in need.<sup>69</sup> A few systems in Eastern Europe and Central Asia have also started OST programmes (such as Moldova and Albania) or are planning to do so soon.<sup>59</sup>

Reflecting the situation in the community, most prison systems make OST available in the form of MMT. Buprenorphine maintenance treatment is available in only a small number of systems, including in Australia<sup>70</sup> and some European countries.<sup>71 72</sup>

Generally, drug-free treatment approaches continue to dominate interventions in prisons in most countries.<sup>73</sup> OST remains controversial in many prison systems, even in countries where it is accepted as an effective intervention for opioid dependence outside prisons. Often prison administrators are not receptive to providing OST, due to philosophical opposition to this type of treatment and concerns about whether the provision of such therapy will lead to diversion of medication, violence and/or security breaches.<sup>74</sup>

A recent comprehensive review showed that OST, in particular with MMT, is feasible in a wide range of prison settings.<sup>75</sup> As is the case with OST programmes outside prisons, those inside prisons are effective in reducing the frequency of injecting drug use and associated sharing of injecting equipment, if a sufficient dosage is provided (more than 60 mg per day) and treatment is available for longer periods of time (more than six months) or for the duration of incarceration.<sup>60 76</sup>

A four-year follow-up study to a randomised controlled trial of MMT versus waiting list control in prison examined the longer term impact of MMT on mortality, reincarceration and HCV and HIV seroconversion. Retention in treatment was associated with reduced HCV infection, while short MMT episodes (less than five months) were significantly associated with greater risk of HCV.<sup>77</sup>

In addition, evaluations of prison-based MMT found other benefits for the health of prisoners participating in the programmes and for prison systems and the community. For example, reincarceration is less likely among prisoners who receive adequate OST, and OST has been shown to have a positive effect on institutional behaviour by reducing drug-seeking behaviour and thus improving prison safety.<sup>76</sup> While prison administrations initially raised concerns about security, violent behaviour and diversion of methadone, these problems have not emerged or have been addressed successfully where OST programmes have been implemented.<sup>47</sup>

WHO, UNODC and UNAIDS recommend that 'prison authorities in countries in which OST is available in the community should introduce OST programmes urgently and expand implementation to scale as soon as possible'.<sup>76</sup>

While OST has become increasingly available in many prison systems at least in part because of its potential to reduce injecting drug use and the resulting risk of spread of infection, other forms of drug dependence treatment have not usually been introduced in prison with HIV prevention as one of their objectives. Consequently, there is little data on their effectiveness as an HIV prevention strategy.<sup>76</sup> Nevertheless, good quality, appropriate and accessible treatment has the potential of improving prison security, as well as the health and social functioning of prisoners,

and may reduce reoffending. Studies have demonstrated the importance of providing ongoing treatment and support and of meeting the individual needs of prisoners, including female prisoners, younger prisoners and prisoners from ethnic minorities.<sup>76</sup> Given that many prisoners have severe problems related to the use of illegal drugs, it is unethical not to provide people in prison with access to a wide range of drug treatment options.<sup>77</sup>

WHO, UNODC and UNAIDS recommend that, in addition to OST, prison authorities provide a range of drug dependence treatment options for prisoners with problematic drug use, in particular for substances such as amphetamine-type stimulants. Given the lack of data, they recommend that evaluations of their effectiveness in terms of reducing drug injecting and needle sharing should be undertaken.<sup>76 78</sup>

While drug-free or abstinence-based treatment should be considered as a necessary component element of comprehensive prison drug services, such programmes alone are insufficient to address the multiple health risks posed by injecting drug use and HIV transmission in prisons.

The interventions detailed above are not the only ones that contribute to addressing HIV and HCV in prisons. International guidelines recommend they be implemented in conjunction with the following necessary elements of a comprehensive programme: HIV/AIDS education; voluntary and confidential HIV testing and counselling; condom provision; prevention of rape, sexual violence and coercion; and HIV care, support and treatment, including antiretroviral therapy (ART).<sup>4</sup>

## Effect of efforts to reduce drug supply in prisons

A broad range of search and seizure techniques and procedures are used by prison systems in an attempt to reduce the availability of drugs in prisons. These supply reduction measures include random cell searches, staff and visitor entry/exit screening and searches, drug detection dogs and other drug detection technologies, perimeter security measures and urinalysis programmes (often referred to as 'mandatory drug testing programmes' or MDT).<sup>79</sup>

Many prison systems, particularly in high-income countries, place considerable and growing emphasis on these measures to reduce the supply of drugs. In particular, urinalysis has been adopted as policy in several prison systems to reduce the use of and demand for drugs in prison. Urinalysis, combined with self-report surveys of prisoners, is also used to obtain an estimate of the extent of drug use<sup>80</sup> as well as to target programmes and treatment services.<sup>81</sup>

Despite substantial investments in drug supply reduction measures, there is no evidence that they lead to reduced HIV risk. Indeed, mandatory drug testing programmes may increase prisoners' risk of HIV infection. Implementing such programmes appears to contribute to reducing the demand for, and use of, cannabis in prisons, but has little effect on the use of opiates. In fact, there is some evidence that a small number of people switch to injectable drugs to avoid detection of cannabis use through drug testing. Given that smoking cannabis presents no risk of HIV transmission while injecting opiates presents a significant risk

of HIV and other health risks, the evidence that some prisoners switch from cannabis use to use of more harmful drugs by injecting is cause for concern.<sup>76</sup>

WHO, UNODC and UNAIDS recommend that 'improving the documentation and evaluation of supply reduction measures should be a priority for prison systems making substantial investments in such measures'. They further recommend that 'prison systems with MDT programmes should reconsider whether to include urinalysis testing for cannabis. At a minimum, they should make clear distinctions in punitive terms between those testing positive to cannabis and opiates.'<sup>76</sup>

## Taking action for prisoners: Conclusions and next steps

The importance of implementing HIV interventions, including NSPs and OST, in prisons was recognised early in the HIV/AIDS epidemic. After its first consultation on prevention and control of HIV in prisons in 1987,<sup>82</sup> WHO responded to growing evidence of HIV infection in prisons worldwide by issuing guidelines on HIV infection and AIDS in prisons in 1993. With regard to health care and prevention of HIV, the guidelines emphasise that 'all prisoners have the right to receive health care, including preventive measures, equivalent to that available in the community without discrimination, in particular with respect to their legal status or nationality'.<sup>79</sup>

Indeed, prisoners retain all rights that are not taken away as a fact of incarceration.<sup>83</sup> e Loss of liberty alone is the punishment, not the deprivation of fundamental human rights. Failure to provide access to evidence-based HIV and HCV prevention measures (in particular NSP and OST) to people in prison is a violation of prisoners' rights to the highest attainable standard of physical and mental health under international law, and is inconsistent with numerous international instruments dealing with the health of prisoners and with HIV/AIDS.<sup>84</sup>

This situation was recognised in the 2006 framework for an effective national response to HIV/AIDS in prisons, jointly published by UNODC, WHO and UNAIDS. The document emphasises that governments and the international community have much to do to meet their 'obligations on human rights, prison conditions, and public health' and states that preventing 'the transmission of HIV in prisons is an integral part of reducing the spread of infection in the broader society'.<sup>85</sup> It stresses that public health can no longer afford to ignore prison health. HIV interventions are feasible and effective in prisons and implementation of these interventions in prisons is an important component of national HIV/AIDS programmes that can no longer be neglected.

### Ensuring that prisoners are included in national scale-up efforts

Very little information exists about what is being done to ensure that prison systems are an integral part of national efforts to scale up access to comprehensive HIV prevention, treatment, care and support, and there are no published studies or even guidelines on this to date. Sustainable HIV prison programmes, integrated into countries' general HIV programmes or at least linked to them, are needed.

At the *international level*, initiatives to support scale-up efforts should include a component specific to prisons and pre-trial detention and ensure that:

- Prison systems (and pre-trial detention facilities) are included in technical assistance missions
- Data about access to HIV prevention, treatment, care and support and coverage in prisons are collected and published
- Best practice models are developed and disseminated
- The public health and human rights implications of inadequate efforts in prisons are brought to the attention of policy makers.

At the *country level*:

- Prison departments (and departments responsible for pre-trial detention facilities) should have a place within the national HIV coordinating committees and the country coordinating mechanisms that develop and submit grant proposals to the Global Fund to Fight AIDS, Tuberculosis and Malaria
- Prison issues should be part of the agreed HIV/AIDS action framework and monitoring and evaluation system
- Prison departments (and departments responsible for pre-trial detention facilities) should be involved in all aspects of scale-up of prevention and treatment, care and support, from funding applications (to ensure that funds are specifically earmarked for prisons) to development, implementation, monitoring and evaluation of roll-out plans
- The ministries responsible for health, the prison system and pre-trial detention facilities should collaborate closely, recognising that prison health is public health. Alternatively, governments could assign responsibility for health care in prisons and pre-trial detention facilities to the same ministries, departments and agencies that provide health care to people in the community.

Finally, at the *regional and local levels*, prisons and pre-trial detention facilities should:

- Form partnerships with health clinics, hospitals, universities and NGOs, including organisations of people living with HIV, to provide services for prisoners
- Develop integrated, rather than parallel, care and treatment programmes.

e This can be expressed as 'limited exceptionalism'. Significantly, a number of domestic courts have recognised this principle.

## **Undertaking broader prison reform**

Addressing HIV and HCV in prisons effectively cannot be separated from wider questions of human rights and prison reform. Prison conditions, the way in which prisons are managed and national policy all impact on HIV and HCV transmission in prisons.

Overcrowding, violence, inadequate natural lighting and/or ventilation and lack of protection from extreme climatic conditions are common in many prisons in many regions of the world. When these conditions are combined with insufficient means for personal hygiene, poor nutrition, limited access to clean drinking water and inadequate health services, the vulnerability of prisoners to HIV infection and other infectious diseases is increased, as is related morbidity and mortality. Sub-standard conditions can also complicate or undermine the implementation of effective responses to health issues by prison staff. Therefore, action to prevent the spread of infections in prisons and to provide health services to prisoners living with HIV and HCV is integral to – and enhanced by – broader efforts to improve prison conditions. Efforts to stop the transmission of HIV in prisons must start by making HIV prevention measures available, but should also include reforms aimed at addressing these underlying conditions.

Action to reduce the size of prison populations and prison overcrowding should accompany – and be seen as an integral component of – a comprehensive strategy to prevent HIV and HCV transmission in prisons, to improve prison health care and to improve prison conditions. According to UN agencies, this should include legislative and policy reforms aimed at reducing the criminalisation of non-violent drug offences and significantly reducing the use of incarceration for non-violent users of illicit drugs. Developing alternatives to prison and non-custodial diversions for people convicted of offences related to drug use would significantly reduce the number of people who use drugs who are sent to prison, the overall prison population and levels of prison overcrowding.<sup>86</sup>

Action to reduce the excessive use of pre-trial detention – the arrest and incarceration of people who have not yet been convicted of any crime – is also essential. Pre-trial detainees account for over one-third of all the people in prisons around the world. They are frequently held in overcrowded, substandard conditions without medical treatment or any measures for infection control. Incarceration exposes detainees to a range of health risks, including interruption of critically important medications to treat HIV, TB or drug dependence and exposure to new infections. As in prisons, drug use and sex occur in pre-trial detention centres, while tools to promote protection such as condoms, drug dependence treatment and sterile syringes are largely unavailable – even in jurisdictions where these measures are available in prisons. The health risks associated with pre-trial detention affect not only those detained but also societies at large, as people move between pre-trial detention and the community.<sup>86</sup>

International standards clearly state that pre-trial detention should be an ‘exceptional’ measure that is used sparingly. For health, human rights and prison reform advocates, it is imperative to advocate for programmes that provide safe alternatives to pre-trial detention for persons accused of low-level crimes, for effective disease prevention and treatment for those who must

remain in pre-trial detention and for better conditions while in pre-trial detention.

Finally, ‘in the medium and longer-term, transferring control of prison health to public health authorities could also have a positive impact.’<sup>87</sup> This recommendation recognises that health care in prisons can be delivered more effectively by public health authorities than by prison management, as long as sufficient resources are provided and freedom of action of the new prison health authorities is guaranteed.

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# 3.6: Underestimated and overlooked: A global review of drug overdose and overdose prevention

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## Introduction

There is a global epidemic of morbidity and mortality caused by drug overdose, primarily related to opioids. Where data are available, overdose is commonly the leading cause of death among drug users.<sup>1</sup> Overdose is a leading cause of death among all youth in some countries, and the leading cause of accidental death among all adults in some regions.<sup>2</sup>

A growing body of evidence demonstrates that targeted overdose programming can reduce overdose death rates. While the scale at which overdose programming is implemented is still limited, pilot programmes show that barriers to implementation can be overcome.

### **What is an overdose?**

Overdose happens when a person takes more of a drug or combination of drugs than the body can handle. As a consequence, the central nervous system is not able to properly control basic life functions. The person may pass out, stop breathing, have heart failure or experience seizures. Overdose can be fatal, although in a majority of cases it is not. Non-fatal overdose, which can be associated with several health harms, is also a cause for concern.

This chapter examines the epidemiology of opioid overdose, describes the different elements of overdose prevention programmes and outlines barriers to implementation.

## An overview of overdose epidemiology

Information on overdose mortality is collected through national reporting systems in some high-income countries. These rates are often expressed as the number of deaths per 100,000 in the adult population, thereby allowing comparison over time and between countries. Nevertheless, the different methods of ascertaining death and collecting data make international comparisons difficult. Definitions of overdose also vary, as do the individuals and agencies reporting the data and coding for cause of death or toxicology. Overdoses may not come to medical attention in many countries and it is presumed that data on overdose mortality in general suffer from considerable under-reporting.

Overdose mortality rates are also derived from research where cohorts of people who inject drugs are followed over time. These studies calculate annual death rates and the causes of death. Death rates are often expressed as deaths per 100 or 1,000 life years in order to allow comparison between studies and with death rates in non-drug-using populations. The latter comparison assesses 'excess mortality' (i.e. deaths attributed to drug use).

The United Kingdom and Australia have demonstrated epidemiologic coordination and reliable data collection on overdose. In the United States, national data are estimates, although several cities have recently made advances in data collection and selected national agencies are increasingly involved in data analysis efforts. Most other countries have limited national data on overdose, requiring alternative data sources and, frequently, expert opinion to estimate overdose.

Overdose data are limited by poor efforts to ascertain causes of death, concern from both witnesses and health care providers about police involvement, limited access to toxicological resources and inadequate collation of data across municipalities and countries. In Russia, overdose death data are available only for registered drug users, who represent approximately 20% of the drug-using population.<sup>1</sup> In some states in Eastern Europe and Central Asia, emergency departments and medical examiner's offices frequently do not record overdose as the cause of admission or death. This is due to a combination of lack of reimbursement for services, legal implications for patients and families and the social stigma of drug use.<sup>1</sup>

A few surveys have begun to characterise overdose in, for example, Iran, Viet Nam, Thailand and China. While overdose data from African states remains elusive, heroin and other injection drug use appears to have become increasingly prevalent in the region in recent years (see Chapter 2.9).

### Fatal overdose

Annual mortality rates among people who inject drugs are between thirteen and seventeen times greater than among their non-drug-using peers.<sup>3</sup> The leading cause of death among people who inject drugs in most countries is overdose.<sup>1 4 5 6 7 8 9 10</sup> Over half of deaths among heroin injectors are attributed to overdose,<sup>11</sup> far exceeding deaths due to HIV/AIDS or other diseases.<sup>7</sup> These trends hold true in the European Union<sup>12</sup> and the United States,<sup>13 14</sup> where drug overdose exceeds motor vehicle accidents as the primary cause of accidental death in sixteen US states.<sup>2</sup> Overdose remains a leading cause of death among Australian drug users.<sup>15</sup> It is the second leading known cause of death among drug users in Russia, at the highest rate documented in any country, and is a leading cause of death among drug users in most other Eastern European and Central Asian states for which any data are available.<sup>1</sup>

There is evidence to suggest that overdose death has been increasing in many countries over the past decade. For example, drug overdose deaths among adults in the US have risen from 4.0 per 100,000 population in 1999 to 8.8 per 100,000 (26,389 deaths) in 2006.<sup>16</sup>

A review of overdose in several Eastern European and Central Asian states found 17 overdose deaths (among medical examiner cases) in Latvia in 2007; 35 deaths (1.7% of autopsies) in Bucharest, Romania in 2006; 21 deaths (12.7% of ambulance calls for overdose) in Khorog, Tajikistan in 2006; and 57 deaths (9.4% of ambulance

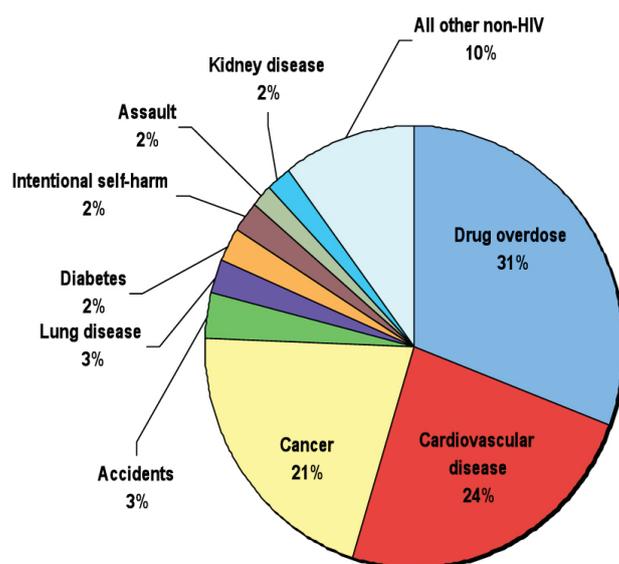
calls) in Bishkek, Kyrgyzstan in 2006.<sup>1</sup> Nonetheless, drug overdose is considered by expert opinion to be the leading cause of death among drug users in the last three countries.<sup>1</sup>

In Asia, one study in northern Thailand found a drug overdose death rate of 8.97 per 1,000 person-years among HIV-negative drug users between 1999 and 2002,<sup>17</sup> In Xichang City, China, another study found a heroin overdose death rate of 4.7 per 100 person-years among 379 people who injected drugs from 2002 to 2003.<sup>10</sup>

Little is known about the epidemiology of stimulant overdose, although data are slowly emerging.<sup>18 19</sup>

Drug overdose death rates are high among people living with HIV/AIDS and account for a substantial proportion of deaths among this population in countries with injection-driven HIV epidemics. Figure 3.6.1 displays non-HIV causes of deaths among all those living with HIV/AIDS in New York City.<sup>20</sup> In 2007 overdose was responsible for 21% of all deaths among people living with HIV/AIDS in Russia and was the second leading cause of death among people living with HIV/AIDS (after tuberculosis).<sup>21</sup>

**Figure 3.6.1: Non-HIV causes of death among all people living with HIV/AIDS, New York City 1999–2004**



**Table 3.6.1: Overdose mortality in selected countries/regions**

Country/Region	Number of drug overdose deaths	Rate per 100,000 person-years	Definition	Population	Year	Source
Russia	9,354	6.6	Opioid overdose	Registered drug users (14% to 20% of total drug user pop) / national population	2006	Koshkina, Petrozavodsk, Russia, 2008
US	18,304	6.2	Opioid overdose	National population over the age of 18	2004	MMWR 2007 56: 93–6
EU	7,557	4.4	Drug-related deaths (60% to 100% are opioid overdose)	National population aged 15 to 39	2005	EMCDDA Statistical Bulletin 2007
Australia	354	3.1	Opioid overdose	National population aged 15 to 54	2004	Opioid Overdose Deaths in Australia 2004

## Non-fatal overdose

In addition to the burden of overdose mortality, people who inject drugs experience a high prevalence of non-fatal overdose. Studies found that the proportion of people who inject heroin reporting at least one non-fatal overdose in their lifetime was 59% in sixteen Russian cities;<sup>22</sup> 48% in San Francisco;<sup>23</sup> 41% in Baltimore;<sup>24</sup> 42% in New York City;<sup>25</sup> 68% in Sydney;<sup>26</sup> 38% in London;<sup>27</sup> 30% in Bangkok;<sup>28</sup> and 83% in Bac Ninh, North Viet Nam.<sup>29</sup> Rates of non-fatal overdose within the previous twelve months range from 10% to 20%, with 12% of heroin users in Xichang City, China reporting at least one such overdose.<sup>30</sup> Non-fatal opioid overdose has been associated with numerous negative health outcomes, including pulmonary oedema, pneumonia, cardiac arrhythmia and cognitive impairment in between 5% and 10% of cases.<sup>31 32</sup>

## Risk factors for overdose

Following a relative hiatus in research during the 1980s, overdose has been increasingly studied over the last two decades. Investigations were initially most prominent in Australia in the mid-1990s, with researchers describing drug overdose in ways that have proven fairly consistent with reports from elsewhere.<sup>15</sup> <sup>26</sup> Based on reviews of medical examiner data, ambulance and emergency centre records and drug user surveys, overdose is believed to be primarily due to opioids, mostly injected, with death occurring most often among older users, although younger users may have more frequent non-fatal overdose events.<sup>33</sup>

The most notable risk factors for overdose among drug users are a prior overdose,<sup>34 35 36</sup> a recent period of abstinence (e.g. substance abuse treatment, incarceration, self-imposed abstinence)<sup>27 30 37 38</sup> <sup>39 40</sup> and concomitant use of other drugs including depressants (alcohol, benzodiazepines and barbiturates)<sup>41</sup> as well as stimulants.<sup>42</sup> HIV-positive status is associated with a two or three times increased risk of overdose death. Although the reason for this is unclear, it may be due to the presence of an HIV-related condition such as liver, pulmonary or systemic dysfunction.<sup>43 44 45</sup> While drug potency and impurities may contribute to overdose, variations in purity appear to account for only about one-quarter of variations in overdose mortality.<sup>46</sup>

### Who can overdose?

There are estimates of what constitutes a 'lethal dose' of a particular substance, but these can only really help to determine what might cause overdose for someone using it for the first time and without mixing it with other substances. For most people who use drugs, it can be difficult to predict how much of a certain drug, or combination of drugs, will lead to an overdose. Individual characteristics such as a person's weight, health, tolerance for a drug at a particular time, drug potency, route of administration and speed of use all play a role in determining how much a person's body can handle.

About two-thirds of people who inject drugs will experience an overdose at some time. Based on experience and estimates from developed countries, approximately one-half of overdoses will receive medical attention, while the other half will be managed by bystanders, with roughly 4% resulting in death.<sup>33</sup> If medical attention is received within a couple of hours of the overdose, most people will survive.<sup>40</sup> However, drug users may be reluctant to call for help due to fear of police attendance or perceived

mistreatment by medical personnel.<sup>22 40 47</sup> People who overdose and bystanders have in rare cases faced legal consequences. If reported by the media these cases can perpetuate fear and deter people from seeking assistance for overdose.<sup>48</sup>

## Regional variations

While the characteristics of overdose epidemiology are fairly well researched in many high-income countries, information is confined to anecdotal reports or small-scale surveys in much of the rest of the world. Factors that may influence overdose epidemiology in different settings include the types of drugs used and patterns of use, social support networks of drug users and the availability and accessibility of health care for people who use drugs. Further understanding of these factors and their influence on overdose risk in different settings would help to inform the planning and evaluation of overdose prevention programmes in community contexts.

In Eastern Europe and Central Asia, for example, there is wide variation in the availability of heroin versus other injectable opioids. Ukraine has a largely seasonal market for shirka, an injectable opioid produced from locally grown poppy, which may contribute to overdose as users' cycle in and out of opioid use. Drug users in this and other regions also frequently live at home and have close family relationships and so may benefit from overdose prevention programmes targeted at educating and distributing naloxone to family members.<sup>1</sup> Opium remains the dominant cause of overdose in Tehran, Iran<sup>49</sup> and is a major drug of choice in China<sup>10</sup> although overdose rates are unknown. The predominance of cocaine in Latin America and of amphetamine-type stimulants in much of Asia and parts of Eastern Europe is likely to have a significant effect on overdose incidence and mortality. It is also likely that limited availability of ambulances, delayed arrival of medical services and lack of availability of naloxone for use by medical personnel in many countries affects the morbidity and mortality of overdose.<sup>1</sup>

## An overview of overdose prevention programming

Overdose was not traditionally considered preventable. Over the past fifteen to twenty years, however, researchers and service providers have developed several strategies to reduce overdose incidence and mortality. Driven by experience and research findings, overdose prevention programmes generally include education and awareness building, efforts to create supportive public policy environments, first responder training and increasing the availability of naloxone, both as take-home doses for opioid users and for medical personnel in severely under-resourced settings.

Although not designed as overdose prevention programmes per se, opioid substitution (methadone and buprenorphine) maintenance services are strongly associated with reduced overdose.<sup>50 51 52</sup> For example, there was a 79% reduction in opioid overdose over the four years following introduction of buprenorphine maintenance in France in 1995.<sup>53</sup> Similarly, safer injection facilities in eight countries have overseen millions of injections and experienced no overdose deaths.<sup>54 55</sup> As overdose risk is higher among those who inject, efforts to encourage transition to other routes of administration<sup>56 57</sup> might prove useful in reducing overdose.

Since the late 1990s there has been an increase in overdose prevention programmes in many countries, particularly programmes targeting heroin and other opioid users. The majority of these programmes are run by non-governmental organisations, although government public health agencies have become increasingly involved in several EU countries. Current overdose prevention education aims to alter individual behaviours that increase risk of fatal overdose and to increase the likelihood that people who inject drugs recognise and properly respond to witnessed overdoses.<sup>58</sup>

### **What is an overdose prevention programme?**

An overdose prevention programme is any cooperative effort designed to give people who use drugs the skills and materials necessary to prevent overdose from occurring and to respond effectively to those that do occur. A programme may involve harm reduction, medical, criminal justice or any other professionals engaging with drug users, and necessarily involves people who use drugs as leaders. Programmes are usually, but not always, integrated with an array of other drug or HIV services. They operate on any scale and in any setting where there is an opportunity for reducing the experience of overdose or its impact.

Major elements of an overdose prevention programme may include:

**Community needs assessment:** Most programmes develop a needs assessment to understand the unique characteristics of overdose in that locality. This often involves surveys and focus groups with people who use drugs and a review of relevant scientific literature. Some programmes seek partnerships with political leaders, law enforcement personnel and/or emergency medical providers to create greater buy-in, improve the care that drug users receive and reduce the involvement of police when emergency assistance is requested.

**Education:** Most programmes provide face-to-face education and informational materials with the aim of reducing overdose frequency by educating people who use drugs about the risk factors for overdose in their region. Modifiable risk factors include advice about how to use drugs after a recent period of abstinence, such as incarceration, hospitalisation, detoxification or self-imposed abstinence, as well as problems with the concomitant use of other drugs with opioids, such as cocaine, benzodiazepines or alcohol.<sup>1</sup> Other major risk factors include previous overdose, older age and health status. Using alone, while not known as a risk factor for overdose, almost certainly increases the risk of fatality in the case of overdose and is a major issue for drug users who are socially isolated.<sup>59</sup> Educating people who use drugs on the risks of injecting versus other routes of administration such as smoking may also be useful in overdose prevention programmes.<sup>60</sup>

**Training:** Training people who may be present during an overdose (e.g. family or friends of drug users, or people working in places where overdose might occur) to identify and respond correctly to overdose is the most common approach employed in prevention programmes. Training is offered in a variety of settings and sessions may range in length from five minutes to three hours depending on the circumstances. Most programmes offer training for people who use drugs (as well as non-using friends or family) in identifying overdose based on breathing and response to stimuli, and teach participants how to respond to overdose with rescue breathing, a simple intervention that addresses the

primary cause of opioid overdose death – respiratory depression. Cardiopulmonary resuscitation (CPR) training can be important to managing stimulant or polydrug overdoses. Research has demonstrated that people who use drugs can learn first response and rescue breathing techniques and can remember what to do when asked at a later date,<sup>61 62 63</sup> and that bystander-administered CPR improves outcomes for heroin overdose victims.<sup>64</sup> If a programme distributes naloxone, training on its proper use must also be provided. It is also important to dispel incorrect beliefs and myths around overdose prevention and to identify what does not work.

**Naloxone distribution:** Naloxone distribution is the centrepiece of many programmes, mainly because of its capacity to overcome barriers to seeking medical care for overdose (fear of arrest, inadequate or disrespectful care etc.). Existing programmes have adopted a very wide range of distribution schemes, in part due to local regulations or other policies. However, the basic goal is to maximise the probability that naloxone will be in the hands of a trained responder who is present at the time of an overdose.

**Policy advocacy:** Advocacy goals often include legislative reform, improved collaboration with police and emergency medical providers and greater overdose awareness among professional and research bodies. Laws covering ‘good Samaritan’-type actions can be enacted that protect witnesses from prosecution when calling for help with an overdose and that protect individuals from liability for administering naloxone to others in the case of a suspected overdose. For example, police orders have been issued in Australia and elsewhere to restrict the role of police accompanying paramedics to an overdose incident and avoid arrests.<sup>40</sup> Advocacy has also been undertaken to encourage government agencies to take responsibility for oversight of national policy on overdose.

**Monitoring and evaluation:** While small or under-resourced programmes may avoid creating more work through data collection, most programmes routinely document basic demographic and overdose history data from their participants, as well as information on training, naloxone distribution and reports of overdose response from participants. As data on overdose is generally lacking, prevention programmes are often an important source of basic information that can inform research on viable intervention strategies and other aspects of overdose.

A recently launched website – [www.take-homenaloxone.com](http://www.take-homenaloxone.com) – provides information on existing naloxone programmes worldwide.

While overdose education is not new to harm reduction, the major innovation of recent programmes has been to put naloxone in the hands of opioid users and their friends and family in order to maximise the potential that the medication is available immediately at the scene of an overdose. Naloxone is uniquely effective at reversing opioid overdose, with response times of one to three minutes, no contraindications except for allergy and no well-established side effects distinct from the medical consequences of overdose itself. The effects of naloxone last for between thirty minutes and one hour, long enough for adequate metabolism of most short-acting opioids (including heroin) so that significant respiratory depression is unlikely to reoccur.

Naloxone can be administered intravenously, intramuscularly or subcutaneously with similar response times (due in part to the time required to find a vein).<sup>65</sup> Intranasal administration, through the use of atomisers, has emerged as a novel approach that avoids the distribution and use of needles and, according to several studies, is between 80% and 100% as effective as injected naloxone.<sup>66 67 68 69</sup>

### **What is naloxone?**

Naloxone, also known as Narcan and other brand names, is a medication used to reverse the effects of opioids, most importantly the respiratory depression that causes death from overdose. Naloxone is a pure opioid antagonist, meaning it 'kicks out' opioids from receptors in the body. It is safe, with no significant side effects and no potential for misuse. Naloxone is usually effective one to three minutes after intravenous, subcutaneous, intramuscular or intranasal administration. It is mainly available in a 0.4 mg/ml liquid formulation, with 1–2 ml considered a standard effective dose when injected, or slightly higher when administered intranasally.

The first large-scale effort at naloxone distribution began in 1997 through the Chicago Recovery Alliance, with similar programmes established around the same time in Berlin. Programmes were later set up in a number of other US cities and in the UK, Canada, Russia, Ukraine, Tajikistan, Afghanistan and elsewhere. Most recently, programmes have been launched in Georgia and Kazakhstan. More sporadic or semi-underground naloxone distribution has occurred in Cambodia, China, Thailand and other countries. Naloxone has been available over the counter at pharmacies in Italy since the 1980s. In Chicago, which is still home to one of the largest programmes, by May 2009 the programme had distributed over 11,000 naloxone kits and received reports from participants of more than 1,000 successful overdose reversals.<sup>70</sup> Newer and smaller programmes are also finding ways to scale up. In Russia, five pilot overdose prevention programmes trained more than 1,500 people who inject drugs in overdose prevention and response and distributed more than 6,000 doses of naloxone in 2009.<sup>71</sup>

Overdose prevention programming has been taken up in a much wider range of settings, including primary care medical clinics, HIV and homeless services, opioid substitution therapy programmes and prisons and jails. In the US, evidence to suggest that prescription opioid overdose death rates have risen to similar levels as heroin overdose prompted the launch of programmes,

including Project Lazarus in North Carolina and at least one arm of the US military, to develop education protocols to provide naloxone to patients receiving opioid prescriptions.

Though growing, the overall level of funding for overdose prevention programmes remains small. Early programmes were often initiated with private contributions. Today, funding for programmes is largely from government public health agencies in higher income countries, and from private and multilateral donor agencies in lower income countries. The Global Fund to Fight AIDS, Tuberculosis and Malaria, the largest single donor agency for HIV/AIDS programmes, has indirectly supported overdose prevention programming (including naloxone purchase) in Russia and Ukraine, where overdose is a significant health issue for people living with HIV/AIDS.

Interest in the evaluation of overdose prevention programmes has increased with the number of programmes, but research is still in the early stages. Although several qualitative studies<sup>58 72</sup> and small pilot evaluations suggest the effectiveness of naloxone distribution, there are no definitive studies demonstrating effectiveness and no formal cost-benefit analyses. Importantly, no study has shown a statistically significant association between overdose prevention programmes (including naloxone distribution) and population-level reductions in overdose mortality.

Obstacles include weak or inconsistent data collection, which means that there are often no reliable baseline data and that officially reported data on overdose may not be comparable from one location to another or over time. Research funding has been scarce, such that most studies have been relatively small-scale collaborations between overdose programmes and researchers, or limited to documenting basic overdose history data and self-reported overdose reversals by programme participants. Moreover, experimental study designs with control groups not receiving naloxone raise substantial ethical questions. Finally, overdose death is a 'statistically rare event' that varies over time for reasons that are not yet clear. Therefore, large studies are required to investigate an impact on mortality rates. Case-control studies may prove more feasible.

Nonetheless, existing data are promising. Ample data demonstrate the acceptability of naloxone distribution for service providers and drug users.<sup>73 74 75 76 77 78</sup> Programmes in the US and the UK have been shown to be effective at teaching people who use drugs how to prevent and manage overdose.<sup>79 80 81 82</sup> Ecological data suggest a reduced level of overdose fatality in some locations during a period of naloxone distribution.<sup>83 84</sup> Programmes in the US and UK, which routinely record the number of naloxone kits distributed and the number of clients reporting use of naloxone to save a life, generally report that between 10% and 20% of kits result in a 'save', almost all of which were considered appropriate uses by programme staff.<sup>1</sup> New research efforts include the N-ALIVE study in the UK, which is evaluating naloxone dispensing to prisoners.<sup>85</sup>

In the absence of more compelling evidence of effectiveness, many people, including some within the harm reduction movement, remain sceptical and caution against the wider roll-out of overdose prevention programmes, particularly with regard to resource issues related to the expense of naloxone. Others feel that better data are not necessary to support naloxone

distribution programmes. Many providers and advocates have lost clients and friends to overdose and believe – much as syringe exchange advocates did in the 1980s – that research may lag behind service.

## Barriers to overdose prevention services

Several important policy and logistical barriers have slowed the wider adoption of overdose prevention programmes around the world. Major barriers include poor commitment from public health agencies to reduce overdose-related mortality, lack of investment in systematic data collection on overdose mortality, poor health care systems and, in particular, emergency health care provision, poor availability of naloxone, the prioritisation of law enforcement over public health and more broadly a lack of public support for drug user health initiatives.

**Government commitment:** Few governments have established drug overdose to be within the remit of a specific agency. As a result, overdose prevention programming is often overlooked. In low- and middle-income countries, where available, programmes form small components of HIV programmes and are often funded by international donors.

**Data collection:** Overdose data are inadequate in most countries and almost non-existent in many others. Greater investment in the systematic collection of data on overdose mortality and the characteristics of overdose is necessary to provide a clearer picture of its impact on people who use drugs, particularly in low- and middle-income countries. This information is also important to inform overdose prevention programmes that are tailored to the particular communities they serve.

**Emergency health care services:** While emergency health care and hospital-based overdose care are available in many countries, several factors can impede access for people who use drugs, including distance, inadequate number of ambulances and limited access to naloxone for medical providers.<sup>1</sup> Naloxone may not be carried in ambulances, or may be restricted to specialised ambulances, in major city centres. Medical services are often state-funded, although in some countries patients give ‘tips’ for service or have to pay for fuel costs. While police may or may not be involved in emergency medical services, fear of police involvement is a major deterrent to calling for emergency assistance in all countries that have been studied. Some countries, such as Kyrgyzstan and Romania, require witnesses to drug use to contact police.<sup>1</sup>

**Naloxone availability:** Although naloxone is on the World Health Organization Model List of Essential Medicines, in some countries it is not registered as a medication at all or is available in extremely limited fashion. Even in countries where naloxone is available, some emergency medical services do not carry the drug. Overdose programming in Tajikistan has included providing naloxone to emergency health care and hospital staff, leading to an impressive reduction in mortality among those overdoses attended to by medical professionals in Khorog.<sup>1</sup>

In some locations, several issues have combined to increase the cost of naloxone. In the US, for example, Hospira became the only manufacturer of the naloxone solution in 2007 and naloxone

prices for harm reduction agencies roughly doubled over the following year. Hospira, as well as most European manufacturers, also relies on a single source, a German corporation called Mallinckrodt, for naloxone powder base. Quotas on the availability of noroxymorphone, naloxone’s opioid precursor, may also keep prices unnecessarily high. Elsewhere, there is also local naloxone production, notably in countries with indigenous legal opium manufacture (e.g. India and Ukraine). While the US Food and Drug Administration approved injectable formulations of naloxone in 1971, no device has been approved for intranasal administration in the country, which limits insurance reimbursement opportunities.

**Law and policy:** Overdose is rarely addressed in policy documents and prevention of overdose is frequently not a priority for policy makers. Laws and policies related to overdose often appear contradictory in that overdose bystanders or medical providers may be legally obligated to report overdose to police, while people who use drugs are simultaneously promised access to medical services. Naloxone distribution for use by non-medical people is probably legal in the US,<sup>74</sup> has been legal in the UK since 2005 and is either legal or likely to be tolerated in many other countries. Nonetheless, health care providers not accustomed to harm reduction approaches may desire formal support for overdose prevention practices.<sup>78</sup> Several US states, including California, Connecticut, New York, New Mexico, Massachusetts and Washington, are at the forefront of developing and harmonising laws and policy to support overdose prevention. This includes laws that protect witnesses who call emergency services, laws that explicitly authorise use by non-medical people of naloxone for opioid overdose and laws and policies establishing funding streams for overdose prevention research and programming.<sup>84</sup>

## Conclusion

Drug overdose is a major and longstanding source of morbidity and mortality throughout much of the world. The situation has worsened in many countries over the past twenty years. Although governments have long ignored the subject, service providers and researchers have determined overdose to be largely preventable and have identified several approaches to achieve reductions in medical complications and death. Community-based programmes have emerged to reduce overdose and are often incorporated into other low-threshold drug services and primarily based on the distribution of naloxone. An increasing number of studies are attempting to evaluate the effectiveness of these interventions. Policy changes to improve overdose management and access to emergency medical care have proved possible in several locations and should be a priority in many others. Although current investment in overdose prevention and management remains grossly inadequate to address the number of lives being lost, a vibrant field of intervention and research has emerged that promises to reduce the losses suffered worldwide by people who use drugs and their friends and families.

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# 3.7: Bridging the gap: An analysis of global spend and resourcing need for harm reduction

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## Introduction

Twenty-five years into the response to HIV among people who inject drugs, considerable progress has been made. The techniques to prevent the spread of HIV infection among people who inject drugs are well known and well tested and HIV-related harm reduction has been shown to work in a wide range of settings.

The international community has endorsed the HIV-related harm reduction package. The effectiveness of the comprehensive package of HIV prevention – including opioid substitution therapy (OST), outreach, needle and syringe programmes (NSPs), education and sexual risk interventions for people who inject drugs – has been well established and evaluated in high, middle and low income countries.<sup>1</sup> Numerous reviews, including an extensive assessment by the US Institute of Medicine,<sup>2</sup> have concluded that the scientific literature is clear that OST, access to needles and syringes and outreach are effective at decreasing drug-related risk behaviours.

The international community has also endorsed universal access to prevention, treatment and care for all people affected by HIV/AIDS, including people who inject drugs,<sup>3</sup> and there have been major increases in the allocation of resources to fight HIV.<sup>4</sup>

However, notwithstanding this progress, people who inject drugs in the majority of countries do not get access to the prevention tools and services that they need and to which they are entitled.<sup>5</sup> Despite the international commitment to universal access, resourcing for harm reduction remains entirely inadequate to

meet the needs of people who inject drugs worldwide. IHRA considers that \$160 million<sup>a</sup> is a plausible estimate of the money spent on HIV-related harm reduction in low and middle income countries in 2007.<sup>6</sup> Amounting to less than three US cents per day per injector in these countries, this response is clearly insufficient. It also means that the biggest investors in harm reduction are people who inject drugs. The expenditure on harm reduction supplies (e.g. needles and syringes) and on drug treatment mainly comes from drug users' out-of-pocket expenses rather than from harm reduction services.

This chapter examines expenditure on harm reduction, how far this expenditure falls short of need and the implications of the shortfall for the international community, for national governments, for donors and for the future shape of harm reduction.

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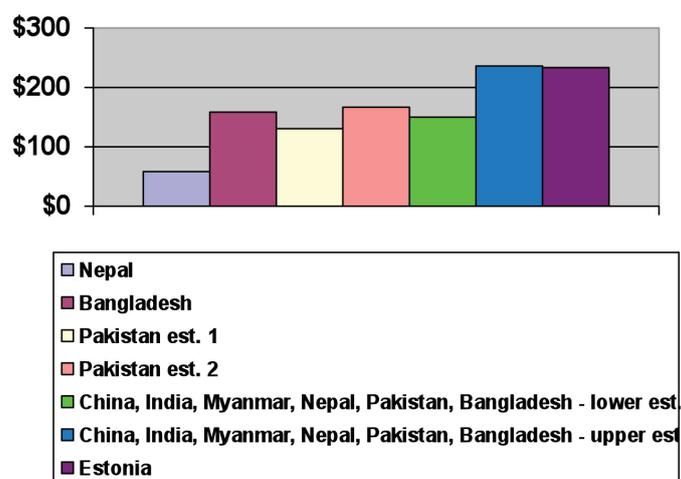
<sup>a</sup> All \$ figures are US dollars.

### A low-cost, high-impact intervention

- Prevention of HIV infection is cheaper than treatment of HIV/AIDS. The Commission on AIDS in Asia concluded that the comprehensive package of HIV harm reduction interventions costs approximately \$39 for every disability-adjusted life year saved, considerably less than anti-retroviral treatment, which costs approximately \$2,000 per life year saved.<sup>7</sup>
- The benefit return for methadone maintenance treatment is estimated to be around four times the treatment cost. According to the US National Institute on Drug Abuse, 'Research has demonstrated that methadone maintenance treatment is beneficial to society, cost-effective, and pays for itself in basic economic terms.'<sup>8</sup>
- NSPs directly averted an estimated 32,050 new HIV infections and 96,667 new hepatitis C infections in Australia between 2000 and 2009. For every dollar invested in needle and syringe exchange, more than four were returned in health care savings.<sup>9</sup>

Based on these figures, it is reasonable to estimate that the cost per injector per year in low income countries is approximately \$100 for NSPs and \$500 for OST. These figures are not normative and not intended to be used for budget planning purposes.

Figure 3.7.1: Examples of unit costs for NSPs<sup>12</sup>



## The cost of harm reduction

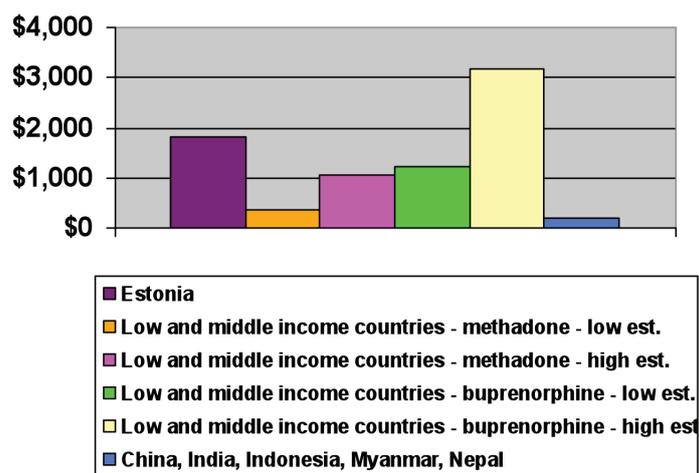
There has been insufficient research done on the costs of harm reduction interventions across an adequate range of countries. Although in theory the information needed should be relatively easy to access from programme budgets, in practice there are a number of difficulties in calculating costs.

Take the example of NSPs. It is difficult to assess their costs because of the range of delivery systems: pharmacies, vending machines, outreach and specialist exchange programmes, each with its own specific associated cost. Also, most needle and syringe exchanges provide a mix of services: they often deliver information materials and voluntary HIV counselling and testing, and may also offer social support, legal advice and referral to treatment. As well as the costs of the needles and syringes, there are the costs of set-up, staffing, premises, overheads and ensuring local political and community support.

Likewise, OST can take place in a range of settings from specialist units through to primary care, each with staff at different levels of cost and each offering various services in addition to methadone treatment. While these services are usually delivered through government health systems in high income countries, civil society organisations are often the primary providers of harm reduction in low and middle income countries.

Despite these inherent difficulties, some costings are provided in the resource needs estimates developed by UNAIDS,<sup>10</sup> the Commission on AIDS in Asia<sup>7</sup> and the UN Regional Task Force on Injecting Drug Use and HIV/AIDS for Asia and the Pacific.<sup>11</sup> These suggest that the cost of delivering NSPs for each injector reached in drop-in and outreach programmes ranges between \$51 and \$235 per year (see Figure 3.7.1). The annual costs for OST range from \$132 to \$1,811 (see Figure 3.7.2). Higher costs reflect higher labour costs and treatments using buprenorphine, which is comparatively expensive.

Figure 3.7.2: Examples of unit costs for OST<sup>12</sup>



## Estimating the total resources needed for harm reduction

UNAIDS makes estimates of the total global and country resources needed for HIV prevention based on the size of the target population, the unit cost of each intervention and the level of coverage required (see Figure 3.7.3).

**Figure 3.7.3: Calculating resource needs estimates**



This equation is easy to understand and has simple inputs. More sophisticated resource models can be developed, but given the generally low expenditure on harm reduction that is reported, the simple resource needs model is adequate for present purposes.

The size of the target population can be estimated using a variety of research methods. Most countries lack good knowledge of the size of the target population and therefore the best estimates for the numbers of people injecting drugs are reported by the Reference Group to the United Nations on HIV and Injecting Drug Use.<sup>13</sup>

There has been considerable debate about the level of coverage required for effective HIV prevention. The original idea of '60%' coverage came from vaccine programmes, which do not require 100% coverage in order to provide a good level of population immunity. Public health specialists have argued, based on epidemic modelling studies, that less than 100% coverage is needed in order to prevent epidemics. Expert consensus, although arguably based on limited evidence and analysis, is that NSPs need to cover 60% of the population and OST programmes need to cover 40% of the population. These are the figures used in UNAIDS resource needs estimates.<sup>14</sup>

This then poses the problem of how to measure coverage. Coverage is the proportion of a population needing a service that has access to that service. The WHO, UNAIDS and UNODC target-setting guide defines coverage of NSPs as the number of people who inject drugs who have had access to a programme at least once a month or more in the past twelve months.<sup>15</sup> Other measures might, for example, be the percentage of injections that are covered by using a sterile syringe.

It is clear that, for many reasons including logistics, access and appropriateness of interventions, 100% coverage will not be reached. However, it is important to recognise that the way in which 'universal access' is interpreted by UNAIDS falls far short of the 2006 declaration of commitment on HIV/AIDS. The implications of this declaration are that *all people who inject drugs should have access to HIV prevention, treatment and care.*<sup>3</sup> Given the fundamental commitment of the UNAIDS programme to human rights, all vulnerable people have the right to have access to HIV interventions. A 'right to health' approach therefore expects that every member of the target population should have access to essential medicines and to harm reduction services.

### **Refinements to resource needs estimates<sup>16</sup>**

Resource needs estimation models could also take into consideration:

- Economies of scale: The cost of going to scale may not be a simple replication of the costs of small projects on which the unit costs are often derived. Scaling up and bulk purchasing can lead to cost savings.
- Combined delivery: There can be savings where two or more services are provided in the same place, hence reducing overhead costs.
- Interaction effects within harm reduction services: There can be interactions between different interventions, where, for example, the successful delivery of needles and syringes significantly reduces health burden and hence other health care costs.
- Interaction effects within health and community delivery systems: Where, for example, investment in primary care reduces the need for outreach and community services, or vice versa; or where investment in OST strengthens other aspects of primary care by enhancing staff competency.
- Cost-effective allocation: The simple model assumes no priorities between interventions. However, some will be more cost-effective than others and may need to be put in place first. In resource-constrained settings, priority might be given to establishing low cost/high effectiveness interventions.

### **Estimates of the resources needed**

Applying the resource needs model to all populations, the UN estimates that the total global resources needed for HIV/AIDS between 2009 and 2013 would be almost \$200 billion to achieve universal access, and \$140 billion for slower scale-up to achieve universal access by 2015.<sup>10</sup>

For people who inject drugs, UNAIDS uses the 60% target for NSPs and 40% target for OST. Based on this, UNAIDS estimates that the resources needed for needle exchange and OST are \$2.13 billion in 2009 and \$3.29 billion in 2010. These figures exclude the resources required for anti-retroviral treatment, care and support. The UNAIDS estimates are equivalent to an average per injector of \$170 in 2009 and \$256 in 2010.

## Estimating global spending on harm reduction

There is no simple, accurate source of information on how much is being spent on harm reduction. Despite the establishment of mechanisms for global resource tracking, harm reduction is relatively invisible in national and international budgets. This may be indicative of the lack of attention to the issue of resourcing for harm reduction by advocates, national governments and international agencies.

The UNAIDS Resource Tracking, Resource Needs and Costing Team collects information from donors and national governments and aims to track money from source to spend. Although the National AIDS Spending Assessment (NASA) specifies detailed budget

lines, including harm reduction, these often remain unused in the reports and it is generally not possible to analyse resource allocation within a country according to specific prevention activities.

More detailed information about harm reduction expenditure has to be gained directly from donors, such as the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM), bilateral national donors and large philanthropic donors, as well as from implementing agencies. As there is no existing database of harm reduction donors or harm reduction programmes, it is only possible to come to informed estimates through the use of personal contacts within donor countries and agencies and by cross-checking with implementing agencies in receipt of funds, a process that inevitably fails to identify some donors.

IHRA's main sources of information included personal contacts, project reports, financial reports and the websites of multilateral agencies and country and philanthropic donors. The data were of variable availability and quality and attempts were made, where possible, to cross-check information and to compare estimates with those of others and against country-level estimates. All estimates were referred to donors for checking.

In collecting information on global resourcing, 'HIV-related harm reduction' was defined as comprising the comprehensive package of interventions including needle exchange, OST, outreach, voluntary testing and counselling, access to primary health care and prevention of sexual transmission. As the objective was to identify spending on frontline HIV prevention – in other words how much of the money was actually going to HIV prevention services for people who inject drugs – attempts were made to exclude spending on antiretroviral treatment, research and capacity building. In practice, however, it is often impossible to disentangle expenditure in this manner.

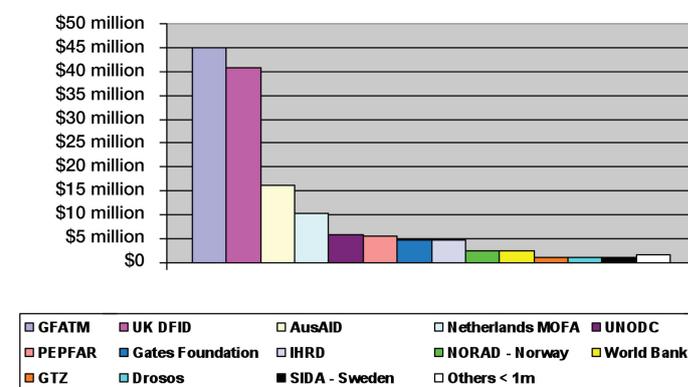
#### Problems in gaining information on expenditure

- Donors not making budgeted information available in the public domain.
- Countries not keeping central records of international spending.
- Lack of functional budgets, i.e. budget lines specifying HIV prevention activities.
- Harm reduction expenditure subsumed under broader budgets, such as HIV/AIDS or development.
- Donors moving from earmarked funding to global budget support.
- Different definitions of HIV prevention and harm reduction.
- Where HIV expenditures are identified, a lack of disaggregation of prevention resources to different populations.
- Lack of disaggregated expenditure according to capacity building, care, treatment, support and impact mitigation, as well as direct services.
- Lack of clarity between financial commitments and actual disbursements.
- Differences in accounting years.
- Potential double counting, where resources are reported both by donor agencies and sub-recipients.
- Lack of reporting of 'out-of-pocket' expenditure on harm reduction by people who inject drugs.

The funds that IHRA identified are shown in Figure 3.7.4. There is room for error in these estimates. In many cases, budgets were unclear, necessitating judgments about, for example, the proportion spent in each year and the allocation of expenditures specifically for HIV-related harm reduction within larger budgets. As a result the figures probably underestimate domestic expenditure (i.e. expenditure from national governments). However, many of the budgets were likely to have lower harm reduction components than those in these estimates.

While the assumptions used in estimating expenditure are open to challenge, this only points to the need for better data collection globally and it is fair to assume that errors resulting in over- or under- estimation will cancel out each other. Specific sums reported may be contested, but it is unlikely that any major sources of funding have been overlooked.

**Figure 3.7.4: Estimated expenditure on harm reduction interventions, 2007<sup>12</sup>**



#### Estimated total expenditure

It is cautiously estimated that approximately \$160 million was invested in HIV-related harm reduction in low and middle income countries in 2007, of which \$136 million (90%) was from international donors.

There is little evidence to suggest that this sum has increased since 2007. In some countries, expenditure on harm reduction might have decreased as many projects initiated within the last decade are coming to an end. The estimate of \$160 million is plausible when compared with the spend in countries where harm reduction budgets were able to be identified, most of which were countries with higher than usual investment.

The \$160 million estimated expenditure equates to \$12.80 per injector per year in low and middle income countries, or three US cents per day. This figure is calculated by dividing the global spending by the estimated 12 million people who inject in low and middle income countries. \$12.80 per injector compares with an estimated per capita spend of \$25 per person in Ukraine, \$13.50 in the Russian Federation, \$62.50 in Vietnam and \$141.60 in Taiwan.<sup>6</sup>

This estimate of \$160 million exaggerates the actual amount of funding for frontline services and interventions. Given the early state of implementation of harm reduction in many countries, much of the resourcing goes into capacity building and advocacy.

Many large programmes funded by bilateral donors target both general populations and vulnerable sub-populations. Even where harm reduction is identified, the total budgets reported often do not include a breakdown of what is spent on each activity, for example on OST or NSPs. In a few cases, spending on particular activities could be identified. For example, it is estimated that approximately one-third of the funding from the German GTZ and the Dutch Ministry of Foreign Affairs goes on direct health services; the equivalent proportion is approximately 30 to 60% for AusAID.<sup>6</sup>

Given the lack of resource tracking for harm reduction, there remains room for error in these estimates. For the reasons identified above, these figures probably overestimate the amount spent. But even if they underestimate global spending by a factor of two or three (which is unlikely) it does not change the conclusion that the amount of money invested in harm reduction is extremely low.

**Figure 3.7.5: Estimated total harm reduction expenditure, 2007**

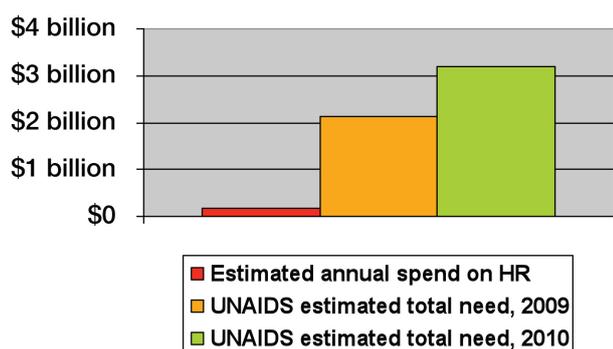


On the basis of expert advice from HIV researchers, three cents a day is less than the amount many drug users themselves will be spending on needle and syringes and other harm reduction commodities including drug treatment.

## The gap between spending and need

While there are challenges in accurately determining spending levels, the huge gap between the estimated need and the estimated spend overshadows any measurement errors (see Figure 3.7.6). The \$160 million spent on harm reduction in 2007 was a mere 7% of the \$2.13 billion estimated by UNAIDS as necessary in 2009 to address HIV prevention among people who inject drugs. And it was only 5% of the \$3.2 billion UNAIDS estimates to be needed in 2010.

**Figure 3.7.6: The harm reduction resource gap**



The annual spend of \$12.80 per injector is low in comparison with the indicative unit costs of providing needles and syringes (approximately \$100 per person per year) or methadone (approximately \$500 per person per year). It is much less than the UNAIDS resource needs calculations, which indicate that approximately \$170 and \$256 per injector per year should be spent in 2009 and 2010 respectively.

Comparing the current estimated spend with the estimated need, the resources required for HIV prevention for people who inject drugs are between fourteen and twenty times greater than the resources currently allocated.

## What can be done?

There are many things that can be done.

The many obstacles to scaling up HIV-related harm reduction for people who inject drugs have been well documented in the *Global State of Harm Reduction* and elsewhere. HIV prevention for injecting drug users is unpopular. Implementing harm reduction, both establishing it to begin with and then delivering it with good coverage, requires many obstacles to be overcome. These obstacles frequently go hand in hand with a lack of investment. Often the demand for harm reduction services does not exist at a high level within countries and is insufficiently vocalised by civil society organisations.

### Obstacles to harm reduction

- Ignorance of governments and public health officials.
- Antipathy to drug users by governments and professional elites.
- Massive over-investment in criminal justice approaches to drugs and drug users at the expense of health investment.
- Legal barriers to harm reduction interventions in many countries, which prevent NGOs from operating, make needle and syringe exchange illegal or forbid the prescribing of methadone or other opioid substitution therapies.
- The marginal and undervalued place in society of people who use drugs and, by association, those who choose to work with them.

Funding for harm reduction must be made proportionate to need or to funds going into HIV prevention. Based on evidence of the lack of coverage and the concomitant resources, a conservative guideline for donors is that around **20% of total global funds allocated for HIV prevention for low and middle income countries should go into harm reduction.**

The limited number of donors who fund harm reduction is a notable barrier. The main international donors for harm reduction – the United Kingdom, Australia and the Netherlands – between them accounted for \$67.4 million in 2007 (42% of the donor funding identified). This amount is greater than that provided by the Global Fund. Clearly there is an urgent need for more wealthy countries to fund harm reduction. In this regard, the potential for the US President's Emergency Plan for AIDS Relief (PEPFAR) to openly and directly fund specific harm reduction interventions now that US policy against needle and syringe exchange has been removed is a welcome development.

### Recommendations

1. More global resources are needed for harm reduction.
2. Resources for harm reduction and HIV services for people who use drugs should be proportionate to need within countries.
3. Donors should set targets for the proportion of spending going to HIV-related harm reduction, with 20% of total global funds allocated for HIV prevention for low and middle income countries going to harm reduction.
4. Global expenditure on harm reduction must be properly monitored by UNAIDS and by NGOs.
5. Better estimates are required on the resources needed for harm reduction.
6. New ways of delivering harm reduction services may be needed.
7. More resources are required to advocate for and create demand for harm reduction via the Global Fund's community system strengthening and/or establishing a global community fund for harm reduction.

There needs to be a significant increase in allocations to harm reduction within country budgets. National governments have typically been unwilling or unable to provide their own resources, although there are notable exceptions. Malaysia, for example, where approximately 70% of HIV infections between 1997 and 2005 were related to unsafe injecting, committed \$150 million in 2005 for harm reduction programmes including OST and NSPs.<sup>17</sup>

Taiwan introduced a harm reduction programme in 2005, including OST and NSPs, and in 2007 doubled the national HIV/AIDS prevention budget to \$8.5 million.<sup>18</sup> By July 2006 every city and province was distributing free needles to drug injectors. The number of syringes distributed increased to four million in 2007. OST was scaled up into a national programme in 2009.

Domestic allocations to harm reduction need to be tracked – even if they are only of symbolic significance – as they indicate political will and commitment to harm reduction.

Another barrier of note is that few philanthropic donors fund harm reduction or are able to identify harm reduction expenditure within their budgets. The Bill and Melinda Gates Foundation funds only two major projects that include harm reduction: the Avahan Project in India and the China HIV Prevention Programme. \$4.8 million was identified as being spent on harm reduction in these projects in 2007. This amounts to 0.001% of the annual Gates Foundation budget for 2008/9 and 1.96% of the total HIV grants for 2006 to 2009.

There is clearly room for current donors – both national governments and philanthropic organisations – to invest more of their budgets in harm reduction, and also for more donors to begin funding. However, achieving this will require a concerted advocacy effort, most likely led by current donors.

There is also the need to address the apparent under-performance of the Global Fund, which spent an estimated \$45 million on harm reduction in 2007 and an estimated \$180 million over the period from 2004 to 2008. These figures compare poorly with Global Fund spending on HIV/AIDS of \$1 billion in 2007, \$1.6 billion in 2008 and \$2.8 billion in 2009.<sup>19 20</sup>

The difficulty is that the Global Fund responds to country-level demands. How then should the international community, which resources the Global Fund, deal with the problem of countries that ignore drug users in their bids or underplay the significance of HIV/AIDS and drug use? There are a number of things that can be done to draw attention to drug use issues, such as requiring all applications to be firmly based on epidemiological and resource needs, according to an agreed methodology, so as to ensure that the needs of the most-at-risk groups are properly reflected in bids.

The Global Fund is committed to the involvement of civil society organisations in the response to HIV/AIDS. However, many civil society organisations find it difficult to engage with Global Fund bids through the national country coordinating mechanism. The Global Fund can do much more to publicise the issue of the under-resourcing of harm reduction through its work with civil society organisations and Global Fund grant writers. The demand for harm reduction expenditure has to be encouraged.

## The need for advocacy for harm reduction

The current resource gap is so huge that resource mobilisation is unlikely to occur unless there is strong advocacy for harm reduction resources at national, regional and global levels. Unfortunately, harm reduction frontline organisations and harm reduction advocacy organisations are themselves seriously underfunded.

Only a handful of NGOs are funded for advocacy at the international or regional levels. In this respect, the recent consultation by the Global Fund on a community system strengthening framework is a welcome development.<sup>21 22</sup> For harm reduction NGOs, this means not only the provision of direct services to drug users, but also the possibility of funding to strengthen community organisations and to create a conducive legal and policy framework for effective harm reduction delivery.

Much support will be needed to enable harm reduction and drug user groups involved in advocacy to access these funds and negotiate their place in national Global Fund financed programmes. Harm reduction organisations are currently small and in a vicious circle as they lack the capacity to bid for the funds that would eventually increase their capacity.

There are other barriers preventing the development of effective regional and international advocacy for harm reduction. Many donors are often unenthusiastic about funding advocacy and prefer to direct their resources to frontline services. In addition, funding restrictions on national and philanthropic donors frequently prevent monies going to international or regional organisations. Large donors also often lack provision for handling the relatively small amounts of money required by small organisations.

There is an urgent and time-limited need to fund harm reduction advocacy so that the demand for harm reduction funding can be enhanced. An emergency Community Fund for Harm Reduction would provide resources to help organisations build their capacity, strengthen their voices and bid for harm reduction resources. Building harm reduction capacity and strengthening advocacy is also a means for increasing political commitment.

Many donors are shifting from earmarked funding to general budget support. In other words, they are becoming less interested in funding monies earmarked for specific diseases, such as HIV/AIDS, and more interested in funding health services and strengthening general budget support to poor countries. This encourages country ownership and allows countries to set their demands. However, the downside is that if a country is not interested in specific diseases or population groups, they are cut out of bids for funding at the national level.

A shift to general budget support, and the Global Fund's emphasis on responding to demand, clearly means that advocates have to be funded to ensure that marginalised groups get their share of funds.

The difficulty in obtaining high-quality information on harm reduction and expenditure from otherwise well-intentioned donors is perhaps symptomatic of the lack of attention given to this area. Significant improvements can be made to the NASA as there are serious discrepancies between country-level data and information about actual budgets.

Donors' difficulties in providing accurate information suggest that there is a need for a specialist global resource-monitoring system to track harm reduction expenditure. This would not require a huge amount of resources. It is a specialist activity that may be difficult to subsume within UNAIDS. Indeed, although it is the role of UNAIDS to monitor global spending and to encourage donors and countries to better report spending according to agreed criteria and functional budget lines, this activity should not be left to UN agencies alone.

There is a clear role for civil society to be involved in the process of resource tracking, to establish databases on the harm reduction programmes that are funded and to use this information to advocate for more resources. Such a framework would increase donor accountability and is potentially of value to donors themselves in improving coordination and avoiding duplication. It might also go some way to avoiding the funding gaps that so often arise between funding rounds.

Linked to this, there is a need for better estimates of resource needs so as to advocate for and allocate resources more efficiently on the basis of need, rather than on donor idiosyncrasies. Current resource needs estimation tends to be too global (as in the case of UNAIDS) or only patchily available at the national level (as in the work of the Commission on AIDS in Asia). A more transparent discussion about the interventions included in resource needs models, better information on unit costs and more data for more countries are required.

Given the huge gap in funding, it is not unreasonable to question whether needs will ever be fully met. It is difficult to imagine that donors will be sufficiently animated to increase their funding tenfold or twentyfold to bridge the current gap.

Serious discussion within the public health and harm reduction community is therefore required about the best way to deliver harm reduction services.

Currently, given the current low scale of harm reduction activity, a scale-up to high levels of coverage tends to be done by the multiplication of specialist NGO-led micro projects, for example moving from a few needle and syringe exchanges to many. Furthermore, the specialist nature of these services means that harm reduction projects are mainly delivered by civil society and community organisations.

There is, however, a need to explore different ways of delivering harm reduction services. For example, needle and syringe access can be increased by changing legislation about access and sale of needles and syringes in pharmacies. In this manner, not all countries need go through the route of specialist needle and syringe exchanges, but might instead jump straight to wider scale distribution through pharmacies or ordinary shops.

Another model of service delivery involves integrating harm reduction into general health and social welfare systems, whereby it becomes part of the responsibility of ordinary health and welfare systems to address harm reduction issues and to have harm reduction activities. This in part reflects the emphasis of some donors in shifting from donor-driven earmarked financing towards general budget support.

Australia and European countries with well-established harm reduction programmes have already taken significant steps towards integrating harm reduction into primary care and other community-led services. However, there are risks in this approach. The jump to integration, or to general budget funding, might backfire and exclude the very type of civil society organisations and input that are needed in the response to HIV/AIDS.

Currently there is no centre of excellence within the UN system or within academic institutions with the global analytic capacity to explore how harm reduction should be delivered. As the end of the third decade of harm reduction approaches, greater capacity to critically explore new models of harm reduction service delivery is certainly required. The comprehensive package alone may no longer deliver what is needed.

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