

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

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*Data and text were in part based on a draft 'Scoping document: a review of viral hepatitis and HIV co-infection among injecting drug users and assessment of priorities for future activities' prepared by Nick Walsh and commissioned by the Department of HIV/AIDS, WHO, Geneva. The authors of this chapter would like to thank all those who reviewed and contributed to that document.*

## 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 [TDV]). 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 a2b expires in 2015 and Roche's patent on pegylated interferon a2a 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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