

GUIDANCE ON PREVENTION OF VIRAL HEPATITIS B AND C  
AMONG PEOPLE WHO INJECT DRUGS

2012





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## ABBREVIATIONS AND ACRONYMS

AIDS	acquired immunodeficiency syndrome
ART	antiretroviral therapy
CDC	Centers for Disease Control and Prevention
CI	confidence interval
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HBV	hepatitis B virus
HBcAb	hepatitis B core antibody
HBsAg	hepatitis B surface antigen
HCV	hepatitis C virus
HCVAb	hepatitis C antibody
HDSS	high dead-space syringe
HIV	human immunodeficiency virus
HR	hazard ratio
HTC	HIV testing and counselling
IDU	injecting drug use
LDSS	low dead-space syringe
mhGAP	Mental Health Gap Action Programme
NGO	nongovernmental organization
NSP	needle and syringe programme
OHCHR	Office of the United Nations High Commissioner for Human Rights
OR	odds ratio
OST	opioid substitution therapy
PICO	Population, Intervention, Comparison and Outcomes
PLHIV	person living with HIV
PrEP	pre-exposure prophylaxis
PWID	people who inject drugs
RR	relative risk
STI	sexually transmitted infection
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNODC	United Nations Office on Drugs and Crime
WHO	World Health Organization

## EXECUTIVE SUMMARY

The “silent epidemic” of viral hepatitis affects a large part of the world’s population without due attention from the health sector. Now, however, co-infection with HIV and viral hepatitis is increasingly recognized as a considerable public health problem.

It is estimated that 240 million people are chronically infected with hepatitis B (HBV) and 170 million are chronically infected with hepatitis C (HCV). These numbers far exceed the number of people living with HIV, estimated at 34 million.

People who inject drugs (PWID) are a key population affected by HBV and HCV. There are approximately 16 million people who inject drugs in 148 countries (1). In 2011 it was estimated that 1.2 million people who inject drugs are infected with HBV and 10 million people who inject drugs are infected with HCV (2).

Around the world, the prevalence of HBV among people who inject drugs correlates with the prevalence in the general population. The highest prevalence rates of HBV among the general population and people who inject drugs are found in Asia. On average, HCV prevalence among people who inject drugs is higher than 50% in most countries of the world, between 60% and 80% in 25 countries, and above 80% in a further 12 countries (2). The largest populations of injecting drug users live in China (HCV prevalence estimated at 67% of people who inject drugs), the Russian Federation (73%) and the United States (72%).

The global response to viral hepatitis B and C has been poor. For people who inject drugs, HBV and HCV are most commonly transmitted by sharing contaminated injecting equipment. Despite the recommendation to implement needle and syringe programmes as a key public health measure (3), many countries with injecting drug use do not provide these programmes, and coverage levels are generally not sufficient in countries that do provide sterile injecting equipment. It is estimated that globally only 22 syringes are provided per year per person who injects drugs (4).

Although the HBV vaccine is inexpensive, safe and effective, vaccination rates for HBV among people who inject drugs are lower than in the general population. There is a need to improve HBV vaccination rates in people who inject drugs. There is currently no vaccine for HCV; hence, there is an urgent need to identify additional measures to prevent transmission of HCV in this population.

## Guidance on prevention of viral hepatitis B and C among people who inject drugs

This *Guidance on prevention of viral hepatitis B and C among people who inject drugs* is the first step in the provision of comprehensive guidance on viral hepatitis surveillance, prevention and treatment by the World Health Organization. These recommendations are based on systematic reviews of scientific evidence, community values and preferences and implementation issues. Although the focus of this guidance is on low- and middle-income countries, this guidance applies equally to high-income settings.

The *WHO, UNODC, UNAIDS technical guide for countries to set targets for universal access to HIV prevention, treatment and care for injecting drug users (4)* presents a comprehensive package of interventions for HIV prevention, treatment and care for people who inject drugs. This document has helped to achieve global consensus with high-level political bodies, the United Nations, donor agencies and civil society organizations on adopting a public health response that best addresses HIV in countries facing epidemics of injecting drug use. The nine interventions of this package (see box) are also relevant to the prevention of viral hepatitis, in particular the first two, needle and syringe programmes and opioid substitution therapy.

### The nine interventions in the comprehensive package

- 1 needle and syringe programmes
- 2 opioid substitution therapy and other drug dependence treatment
- 3 HIV testing and counselling
- 4 antiretroviral therapy
- 5 prevention and treatment of sexually transmitted infections
- 6 condom programmes for people who inject drugs and their sexual partners
- 7 targeted information, education and communication for people who inject drugs and their sexual partners
- 8 vaccination, diagnosis and treatment of viral hepatitis
- 9 prevention, diagnosis and treatment of tuberculosis.

In addition to confirming the importance of implementing the comprehensive package of interventions, and most importantly NSP and OST, this guidance provides the following recommendations:

**Recommendation 1:**

It is suggested to offer people who inject drugs the rapid hepatitis B vaccination regimen.\*

**Recommendation 2:**

It is suggested to offer people who inject drugs incentives to increase uptake and completion of the hepatitis B vaccine schedule.†

**Recommendation 3:**

It is suggested that needle and syringe programs also provide low dead-space syringes for distribution to people who inject drugs.‡

**Recommendation 4:**

Psychosocial interventions are not suggested for people who inject drugs to reduce the incidence of viral hepatitis.

**Recommendation 5:**

It is suggested to offer peer interventions to people who inject drugs to reduce the incidence of viral hepatitis.

\* A higher dose HBV vaccine should be used with the rapid regimen; standard and rapid regimens should be offered to PWID, with first priority given to delivery of the first dose and then to completion of three doses.

† This recommendation is conditional on local acceptability and resource availability; vaccinations should be provided at a location and time convenient for PWID.

‡ Syringe programmes should offer all types of syringes appropriate for local needs.

## Summary of recommendations

### Hepatitis B vaccination

HBV vaccination is inexpensive, safe and effective. The standard schedule for HBV vaccination is at 0, 1, and 6 months, while the rapid schedule is at 1, 7, and 21 days. By 2008, 177 countries had incorporated HBV vaccination into their national schedule of childhood immunizations. An estimated 69% of the 2008 birth cohort received three doses of the vaccine. The implication of this high immunization rate is that HBV vaccination for people who inject drugs and other high-risk groups is a time-limited challenge, as new cohorts of people who inject drugs increasingly will have been immunized at birth. Nevertheless, in many parts of the world HBV

vaccination rates among people who inject drugs are low, for a variety of reasons including cost, access and the unsettled lives of many people who inject drugs. Systematic reviews examined HBV vaccine completion and uptake when the rapid HBV vaccine schedule is offered and, separately, when incentives are offered. Evidence showed that both the rapid schedule as well as providing incentives to people who inject drugs helped increase uptake and completion of HBV vaccination. Vaccination should be provided at a location and time convenient to PWID.

### **Type of syringes**

Low dead-space syringes (LDSS) are designed to reduce the amount of blood remaining in the syringe after completely pushing down the syringe plunger. LDSS commonly have a non-detachable needle joined directly to the syringe barrel. The amount of blood remaining in a LDSS after pushing down the syringe plunger and rinsing the syringe is up to 100 fold less than that in an ordinary syringe with high dead space. Studies have shown that this difference in dead space reduces the survival of HCV and HIV in blood remaining in syringes. The implication is a potential reduction in risk of HCV and HIV transmission when syringe-sharing takes place. The evidence for the effectiveness of LDSS in reducing HCV transmission among people who inject drugs was reviewed. Given the limited literature available, HIV transmission was interpreted as a proxy for HCV transmission. The evidence indicated that providing LDSS leads to a reduction in the transmission of HIV and HCV and that needle and syringe programmes should provide LDSS in addition to other types of syringes appropriate for local needs.

### **Psychosocial interventions for viral hepatitis B and C prevention**

Psychosocial interventions, also known as behavioural interventions, aim to change behaviour through the exchange of information, typically led by a clinician or educator. They include, but are not limited to, brief interventions, motivational interviewing, cognitive behavioural therapy, contingency management and self-help groups. Psychosocial interventions are used as therapy in a number of health disciplines, including the treatment of substance use disorders. Based on the results of systematic reviews, psychosocial interventions cannot be suggested as a core intervention because no evidence was found that they reduce rates of viral hepatitis transmission.

### **Peer interventions**

Peer interventions—initiatives that include peers in service delivery, also termed peer-based or peer-driven interventions—are often an aspect of outreach initiatives. Peer interventions for people who inject drugs are common in many parts of the world where there is injecting drug use. The evidence of the effectiveness of peer interventions to reduce HBV and HCV transmission as well as to change injecting and sexual risk behaviour was reviewed. In contrast to other psychosocial interventions, delivered by health workers, evidence showed that interventions delivered by peers were effective in reducing transmission of viral hepatitis.

## **Principles and implementation**

The principles for this guidance, and for working with people who inject drugs, are the protection of human rights, access to health care, access to justice, acceptability of services, health literacy and integrated service provision. Interventions must be acceptable and appropriate for people who inject drugs. Consultation and cooperation with drug user groups is important when designing and implementing services.

This guidance should be implemented in phases, consistent with the level of resources available. Consideration should be given to building awareness of this guidance among health-care workers and people who inject drugs. For the implementation of these guidelines, the local context of health systems, prevention services and community involvement should be considered.

## **Next steps**

This guidance will be updated in future in accordance with WHO policy. In addition, WHO is currently developing guidance on viral hepatitis surveillance, guidance on hepatitis C treatment and guidance on the management of HIV in the context of co-infection with viral hepatitis and HIV.

Multisectoral engagement is needed to increase the uptake of viral hepatitis prevention and treatment initiatives by people who inject drugs. There is a high prevalence of disease co-morbidity among people who inject drugs. The need for coordination between HBV and HCV intervention programmes and HIV, TB, mental health and drug dependence treatment services as well as harm reduction services for people who inject drugs cannot be overemphasized.

# 1. INTRODUCTION

This document is the first step in the provision by the World Health Organization (WHO) of comprehensive guidance on viral hepatitis surveillance, prevention and treatment. It provides recommendations on the prevention of viral hepatitis B (HBV) and viral hepatitis C (HCV). The recommendations are based on a summary and grading of the scientific evidence, the values and preferences of community representatives, implementation issues inclusive of resource implications, and discussion of key research questions. Although the focus of this guidance is on low- and middle-income countries, this guidance applies equally to high-income settings.

The evidence base for HCV prevention is not as strong as that for prevention of HIV and HBV, and it is generally recognized that guidance on HCV prevention is insufficient at a global level. At the same time, the field of hepatitis C research is rapidly changing. These recommendations will be updated in the future, in accordance with WHO policy, to reflect new developments.

WHO has already developed guidance for effective drug dependence treatment and for HIV prevention, treatment and care for people who inject drugs (PWID). In 2009 global consensus was reached on a public health driven comprehensive package of nine interventions that best address HIV in countries facing epidemics of injecting drug use (3) (see box).

## **The nine interventions in the comprehensive package are:**

- 1 needle and syringe programmes
- 2 opioid substitution therapy and other drug dependence treatment
- 3 HIV testing and counselling
- 4 antiretroviral therapy
- 5 prevention and treatment of sexually transmitted infections
- 6 condom programmes for people who inject drugs and their sexual partners
- 7 targeted information, education and communication for PWID and their sexual partners
- 8 vaccination, diagnosis and treatment of viral hepatitis
- 9 prevention, diagnosis and treatment of tuberculosis.

This comprehensive package has been endorsed at the highest political level, including by the United Nations Economic and Social Council (5). Despite global endorsement, implementation and coverage of specific interventions related to injecting drug use, in particular needle and syringe programmes (NSP) and opioid substitution therapy (OST), can be improved in many countries.

The interventions defined for HIV in the comprehensive package are also relevant for the prevention of other bloodborne viruses, including HBV and HCV. Given the burden of disease related to viral hepatitis infection, more specific guidance is needed.

## 2. SCOPE AND OBJECTIVES

The scope of this document is to recommend public health interventions to prevent viral hepatitis B and C among PWID. The target audience includes health professionals, policy-makers, national programme managers, researchers, nongovernmental organizations, community and civil society organizations and PWID. These guidelines may also be of interest to international funding agencies, the scientific media and advocates.

The objective of this guidance is to raise awareness on how to prevent HBV and HCV infection among PWID and to provide a tool for policy-making and advocacy as well as clinical guidance for front-line health professionals.

The guidelines are intended to provide countries and programmes with evidence-based recommendations to accomplish the following objectives:

1. underline the importance of the comprehensive package for HIV prevention, treatment and care for PWID and its relevance for preventing viral hepatitis transmission, in particular with needle and syringe programmes and opioid substitution therapy (6);
2. increase uptake and completion of hepatitis B vaccination among PWID;
3. provide information on potential advantages to and encourage the provision of low dead-space syringes within broader needle syringe programmes for PWID;
4. provide clarity concerning the limited effectiveness of psychosocial interventions as a solitary intervention in preventing hepatitis transmission;
5. support peer-based initiatives in programmes working with PWID.



## 3. BACKGROUND

It is estimated that 240 million people are chronically infected with HBV and 170 million are chronically infected with HCV (7-9). These numbers far exceed the number of people living with HIV, estimated at 34 million (10).

Co-infection with viral hepatitis and HIV is increasingly seen as a major public health problem: Chronic hepatitis B virus (HBV) infection affects 10% of people living with HIV worldwide, with great variability among geographical regions depending on the nature of the epidemic and other factors. Chronic hepatitis C virus (HCV) infection affects 20% of people living with HIV worldwide, with the majority living in low- and middle-income countries. Among PWID who are living with HIV, approximately 75% are co-infected with HCV (11,12).

The major modes of viral hepatitis transmission include unsterile medical injections, blood transfusions, sexual intercourse and injecting drug use (1, 13-16). HCV, however, is rarely transmitted sexually. In more recent years, as increased screening of blood products and the use of sterile equipment for medical injection has reduced transmission via these routes, injecting drug use has become proportionately more important as a vector for viral hepatitis transmission.

Both HBV and HCV can cause acute inflammatory hepatitis that can result in fulminant liver failure. Chronic infection can result in liver fibrosis and ultimately cirrhosis and hepatocellular carcinoma—conditions resulting in increased mortality (17,18). Both HBV and HCV can complicate HIV treatment, and HCV can accelerate the progression of HIV disease (19-26).

### 3.1 Viral hepatitis and injecting drug use

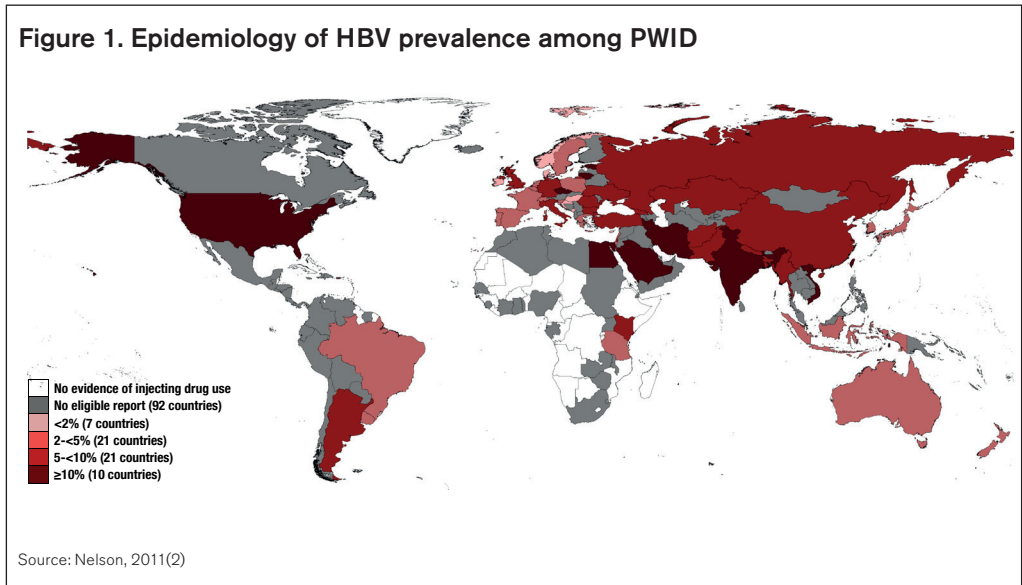
Injecting drug use is a major cause of morbidity and mortality worldwide. It is estimated that, globally, there are 16 million PWID (range: 11 million to 21.2 million), and injecting drug use is reported in at least 148 countries (1). HBV, HCV and related diseases are endemic among PWID (2). To date, however, the urgency of preventing HIV among PWID has overshadowed the epidemic of viral hepatitis.

#### 3.1.1 Hepatitis B

In 2011 it was estimated that approximately 1.2 million PWID were living with chronic hepatitis B, as indicated by hepatitis B surface antigen (HBsAg), while nearly 6.4 million were positive for hepatitis B core antibody (HBcAb), indicating exposure to the virus (2).

The main mode of HBV transmission varies among countries depending on the endemicity of the virus. In highly endemic settings (e.g. much of Asia and Africa), perinatal and horizontal routes are responsible for most transmission, and 70–90% of the adult population has serologic evidence of prior infection. Countries with intermediate endemicity have a mix of perinatal, horizontal, sexual and health-care-related transmission. In countries with low

endemically, most new infections occur among young adults and are acquired sexually or through injecting drug use (27,28).



HBV infection is measured in two ways: as exposure to the virus (HBcAb) and as chronic infection (HBsAg). HBsAg prevalence data on chronic infection in PWID have been recorded in 59 countries, with 73% of the global PWID population. The prevalence of HBsAg in PWID correlates with the prevalence in the general population, with the highest prevalence in endemic areas of Asia (Figure 1) (2).

HBcAb prevalence data for exposure to HBV are available for 43 countries, with 65% of the global PWID population. Although the prevalence of HBcAb varies widely among countries, in general it is much higher than the prevalence of HBsAg (2).

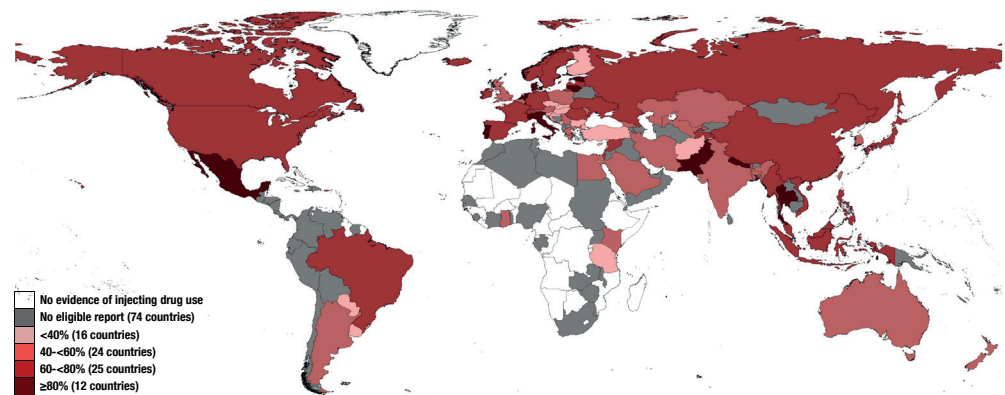
### 3.1.2 Hepatitis C

It is estimated that, globally, 10 million PWID are infected with HCV, as indicated by the presence of the HCV antibody (HCVAb) (2). For PWID, sharing contaminated needles and syringes is the most common mode of HCV transmission. Sharing other equipment such as spoons and filters is also associated with HCV transmission (29,30). HCV is substantially more infectious than HIV, and many PWID are repeatedly exposed to HCV. This results not only in higher incidence rates but also in reinfection after clearance of HCV (31-33).

HCV is more difficult to transmit through unprotected sexual intercourse than is HIV (34-37). There is evidence that, among people who are co-infected with HIV and HCV, traumatic sexual practices or ulcerative STIs are conducive to sexual transmission of HCV (38-42).

Data on hepatitis C prevalence among PWID has been recorded in 77 countries and territories, which account for 82% of the global estimated population of PWID (2). The incidence of HCV among PWID is higher in low- and middle-income countries than in high-income countries (43). The largest populations of PWID live in China (HCV prevalence estimated at 67% of PWID), the Russian Federation (73%) and the United States (72%). On average, HCV prevalence among PWID is higher than 50% in most countries, between 60% and 80% in 25 countries, and above 80% in a further 12 countries (2). The prevalence of HCV among PWID is shown in Figure 2.

**Figure 2. Epidemiology of HCV prevalence among PWID**



Source: Nelson, 2011(2)

Prevalence rates of HCV in prisons and other closed settings (like those of HIV and TB) are higher than in the community. In most countries PWID constitute a large proportion of the incarcerated population. Risk practices such as sharing injecting paraphernalia and non-sterile tattooing often occur in closed settings due to limited access to sterile equipment (44).

The epidemiology of HCV/HIV co-infection is less well understood. HIV/HCV co-infection is common among HIV-infected PWID—close to 100% in a number of countries (45-48). The epidemiology of co-infection generally follows that of HIV in PWID, with some exceptions (45-48).

## 4. METHODOLOGY

### 4.1 WHO guideline development process

WHO uses the GRADE approach (Grading of Recommendations Assessment, Development and Evaluation) for the development and review of recommendations (49). The initial steps entail identifying key topics, formulating the Population, Intervention, Comparison and Outcomes (PICO) questions, scoping the literature to identify whether evidence reviews exist or recent evidence can be obtained, developing a comprehensive search strategy and identifying and retrieving relevant evidence, including evidence concerning both benefits and harms (50).

Outcome frameworks are developed to ensure that outcomes are selected in a transparent and comprehensive manner and prior to reviewing the evidence. Each framework describes all possible pathways, starting with the intervention, going through the intermediate outcomes and leading to the important outcomes.

The first step of the GRADE approach is to rate the quality of evidence for each PICO question by outcome (51). This step entails consideration of study limitations, inconsistency, indirectness, imprecision and other limitations (50). The quality of the evidence is then graded as high, moderate, low or very low. A standardized table, the GRADE evidence table, presents the quantitative summary of the evidence and the assessment of its quality.

The second step of the GRADE approach is to move from “evidence to recommendation” for each of the PICO questions. This includes consideration of the quality of evidence, the balance of benefits and harms, community values and preferences and resource use. These factors affect both the recommendation's direction (for or against) and its strength (strong or conditional). Decision tables summarize these factors.

### 4.2 Viral hepatitis guideline development process

The WHO Department of HIV/AIDS led the development of these guidelines with the oversight of the WHO Guideline Review Committee. In 2010 a scoping exercise was carried out to review the literature and identify key programmatic issues related to viral hepatitis transmission among PWID (52). A subsequent expert consultation with civil society representatives and the Cochrane Collaboration Drug and Alcohol Review Group was held in September 2010 to formulate the PICO questions. Three systematic reviews were later conducted to address these questions using the GRADE methodology. A series of semi-structured interviews with service providers and PWID was carried out in late 2011 to obtain their perspectives, values and preferences on the draft recommendations for prevention of viral hepatitis in PWID.

A technical consultation was held in Geneva, Switzerland, in February 2012 to reach consensus on the recommendations on prevention, surveillance and HIV management in patients with viral hepatitis-HIV co-infection.\*

The expert panel included public health professionals, clinicians, academics, programme managers, implementers, civil society representatives and a GRADE methodologist. Appropriate geographical and gender representation was considered. The three systematic reviews on prevention in PWID were presented and discussed. The multidisciplinary expert panel assessed the evidence, risks and benefits, and values and preferences for each recommendation. The expert panel determined the direction of the recommendations and strength of the evidence. Consensus was reached for all decisions. By consensus, one of the original PICO questions, "Should motivational interviewing versus no motivational interviewing be used in people who inject drugs?", was dropped.

The expert panel noted the general low quality of evidence and the need for further research in the area of HBV and HCV prevention among PWID. Consequently, the expert panel developed a series of research questions that should be addressed in the future.

A draft version of the guidance was circulated among the expert panel members and external peer reviewers for feedback. The coordinators of the process incorporated comments from internal and external peer reviewers to finalize the guidelines.

A revision of these guidelines is planned for 2016, before which plans will be developed for quality evaluation of these guidelines, their usefulness and their impact. Recommendations from the forthcoming guidance on the surveillance of viral hepatitis will be incorporated into the quality evaluation. Complete details of the systematic reviews and all annexes are available online at [http://www.who.int/hiv/pub/guidelines/hepatitis\\_annex/en/](http://www.who.int/hiv/pub/guidelines/hepatitis_annex/en/).

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\* The process details for the surveillance and treatment components of the meeting are separate from this document and will be published elsewhere at a later date.

## 5. GUIDING PRINCIPLES

The overall framework for the development of these guidelines is based on human rights principles reflected in a number of international agreements (53, 54). Stigma and discrimination remain significant problems for people living with HIV and for people who inject drugs. It is essential that this document adhere to basic tenets related to self-determination, privacy, informed decision-making and protection.

### 5.1 Human rights

Fundamental to the development of these guidelines is the protection of human rights for people who inject drugs. Legislators and other government authorities should establish and enforce antidiscrimination and protective laws, derived from international human rights standards, in order to eliminate stigma, discrimination and violence faced by PWID and to reduce their vulnerability to infection with viral hepatitis and other bloodborne infections (54).

### 5.2 Access to health care

Access to health care is a universal and basic human right. It includes the right of individuals who use drugs to have access to appropriate health care without discrimination. Nonetheless, access to health care is not equitable. PWID are particularly vulnerable to poor access for many reasons, including stigma and discrimination, high incarceration rates, poor health literacy and low socioeconomic status. In addition, PWID have high rates of poor health no matter the context, including high rates not only of HIV and viral hepatitis but also of TB and other acute and chronic medical conditions. They are also more likely to have poor access to adequate shelter and food security.

Health-care providers and institutions should serve PWID based on the principles of medical ethics and the right to health (55). Health services should be accessible to PWID. For instance, the location and opening hours should be convenient for PWID. The recommendations in this guidance can be effective only with implementation on a wide scale. Poor access to these interventions will impede their impact on the prevalence of viral hepatitis among PWID and on public health in general.

### 5.3 Access to justice

Access to justice is particularly relevant to PWID, given their high rates of contact with law enforcement services due to the illegality of drugs and of drug injection in many countries. Access to justice includes freedom from arbitrary arrest and detention, the right to a fair trial, freedom from torture and cruel, inhuman and degrading treatment and the right, even in closed settings (56), to the highest attainable standard of health.

Drug use has legal implications in many jurisdictions. As a consequence, the incarceration rates of PWID are high in many countries. For those not incarcerated, regular contact with law enforcement agencies is common. The protection of human rights, including the rights to

employment, housing and health care for PWID, requires the collaboration of law enforcement agencies, including those responsible for the management of closed settings, with health-care agencies. Detainment in closed settings should not impede the right to maintain dignity and health (55).

#### **5.4 Acceptability of services**

Acceptability of services is a key component of effectiveness. Interventions to reduce the burden of viral hepatitis among PWID must be acceptable and appropriate to recipients in order to enlist their participation and ensure their retention in care. Although services working with PWID often apply appropriate models of service delivery, expertise in viral hepatitis is often lacking. Conversely, services specializing in viral hepatitis may not necessarily be acceptable to drug users. Hence, there is a need to build service capacity on both fronts. Adequate consultation with drug users' organizations and including drug users (known as peer workers) in service delivery are effective ways to work towards this goal.

#### **5.5 Health literacy**

PWID often lack sufficient health and treatment literacy, and this lack may impede their informed decision-making on drug use and health-seeking behaviour. Health services should regularly and routinely provide evidence-based health and treatment information to PWID, including information about viral hepatitis, its prevention and care and treatment options. Correspondingly, health services should strengthen providers' knowledge and capacity to prevent and to treat viral hepatitis in PWID.

#### **5.6 Integrated service provision**

PWID commonly have multiple co-morbidities and poor social situations. For example, HIV, viral hepatitis and other infectious diseases are prevalent in PWID, as are mental health conditions. PWID are also less likely to be employed or to have stable social relationships or adequate incomes. Integrated services provide the opportunity for patient-centred prevention, care and treatment for the multitude of issues adversely affecting PWID. In addition, integrated services enhance the likelihood of improved communication among, and thus of better care by, the different service providers working with PWID. Thus, wherever possible, service delivery for PWID should be integrated. When integrated service provision is not possible, strong links among health services working with PWID should be established and maintained (57).

## 6. RECOMMENDATIONS

WHO has synthesized the evidence on a range of interventions for HIV prevention, treatment and care for PWID in the Evidence for Action Series (58), which focuses on a public health approach to HIV and drug dependence. In 2009 the *WHO/UNODC/UNAIDS technical guide for countries to set targets for universal access to HIV prevention, treatment and care for injecting drug users* (3) defined and presented a comprehensive package of nine interventions. This technical guide has been endorsed by high-level political bodies including the UN General Assembly (59), the Economic and Social Council (60), the UN Commission on Narcotic Drugs (61), and the UNAIDS Programme Coordinating Board (62). In addition, donor agencies including the Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Fund) and the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) support this framework.

The interventions that have proved effective to prevent HIV are also of the utmost importance to prevent other infectious diseases in PWID, including viral hepatitis. In particular, the provision of sterile injecting equipment aims to prevent transmission of bloodborne viruses and has been demonstrated to be even more crucial for the prevention of HCV than of HIV (63, 64). Opioid substitution therapy (OST) for people dependent on (injecting) opioids has proven to reduce the prevalence and frequency of injecting and thereby to reduce transmission of HIV and viral hepatitis (65). In addition, OST has been shown to be an effective way to engage people in addressing other health needs, i.e. assisting with adherence to treatment and facilitating access to the health system (66-68).

Despite general recognition of its effectiveness and high-level endorsement of this comprehensive package, some countries resist implementing these public health interventions, while in other countries the accessibility and coverage of these interventions are still too low to have an impact on the prevalence of HIV and viral hepatitis (69). Variation in coverage occurs not only among countries but also within countries, in particular in prisons. Increasing the implementation and coverage of these services is crucial to curbing the spread of viral hepatitis (63).

### 6.1 Hepatitis B vaccination

The HBV vaccine, which became commercially available in 1981, is safe, effective and relatively inexpensive. It produces an immune response adequate to protect against infection in close to 100% of children and about 95% of adults, lasting at least 10 years (70). The risk of acute infection is very low in fully vaccinated individuals. As a result of the preservation of the anamnestic (immune memory) response and apparent immunoprotection, there is no need to administer a booster in routine immunization programmes (8).

The standard vaccination schedule for infants and unvaccinated adults is 0, 1, and 6 months, while the rapid schedule is 1, 7 and 21 days. Rapid vaccination schedules may confer immune response similar to that provided by the standard schedule (71-74) while facilitating higher



completion rates in vulnerable populations (75). Most commercial preparations of HBV vaccine offer similar rates of seroprotection in healthy adults (76-78). Higher-dose HBV vaccines boost response in groups with impaired immune response to the vaccine (79, 80).

At a population level HBV vaccination has been demonstrated to be cost-effective, especially as the cost of the vaccine itself has declined in recent years (81). Cost-effectiveness is particularly apparent in countries with intermediate and high endemicity (82, 83). The most cost-effective delivery of HBV vaccination is vaccinating without performing HBV antibody testing (84).

Most countries have both targeted and population-wide HBV vaccination programmes, including infant, catch-up and risk-group vaccination. Risk groups include PWID, men who have sex with men, sexual partners of persons living with HIV, prisoners and others such as recipients of blood product and health-care workers. By 2008, 177 countries had incorporated HBV vaccination into their national schedule. An estimated 69% of the 2008 birth cohort received three doses of the vaccine (8). The implication of national HBV vaccination programmes is that HBV vaccination for PWID and other high-risk groups will become less challenging over time as increasing cohorts of young adults are immunized in infancy and thus protected.

### **Rapid HBV vaccination schedules for PWID**

Completing the hepatitis B vaccine schedule is important. It results in the strongest immune response, as indicated by higher HBsAg titres, and therefore provides longer immune protection from disease. Although there has been debate about the immunogenicity of HBV vaccine for PWID, there appears to be little difference between the rates of protection among PWID and those in the general population (85); the vaccine works as effectively when administered to PWID as when administered to others. However, HIV and HCV infection, common among PWID, may attenuate the immune response (86-89). Administering a higher dose of the vaccine boosts effectiveness in HIV-infected individuals (90).

Due to social instability and poor access to health care, PWID may be less likely than many other people to complete a six-month schedule. Shorter vaccine schedules for PWID should promote adherence and may also encourage health services to take advantage of opportunities for vaccination (91). Services that could provide vaccination on a rapid schedule include drug treatment sites, needle and syringe programmes and other harm-reduction services that engage regularly with PWID (92, 93).

The systematic review examined the case for a rapid schedule and/or high-dose HBV vaccination in PWID to increase adherence rates and effectiveness.

### ***Evidence***

Of the 2700 citations screened, two randomized controlled trials (RCTs) fulfilled eligibility criteria (94,95). One study was conducted with PWID in a community setting (94), while the other was conducted in both a community setting and a prison setting (95).

### ***Summary of findings***

Meta-analysis of the two RCTs found a 60% greater rate of vaccination completion with rapid vaccination than with the standard vaccination schedule. The risk ratio (RR) was 1.6 (95% CI: 1.42–1.81). The other study analysed the benefit of higher-dose HBV vaccine given on a rapid schedule. The results were in favour of programmes combining a short schedule and a high dose. No study was identified that assessed individuals' satisfaction or quality of life. The overall quality of evidence for rapid vaccination compared with standard HBV vaccination for PWID is very low and was rated down for risk of bias and for indirectness of both the outcome and the population.

### ***Benefits and risks***

The panel judged that the risk–benefit profile was in favour of a rapid schedule compared with the standard schedule, given the higher completion rates and immune response rates. The effect on quality of life is unknown.

### ***Acceptability***

The values and preferences study found that the most common reported barrier to complete HBV vaccination is the length of time between injections. Approximately half of all participants found returning three times over the course of six months to be a barrier to vaccine completion. Most participants were not aware of the rapid regimen for HBV vaccination. Given the choice, most participants preferred to have the regimen delivered over a shorter period.

### ***Resource use***

The panel judged that vaccination using a rapid regimen might increase workload and require more vaccine stocks. Higher-dose regimens would require more vaccine stock. Cold chain storage and other vaccine equipment are necessary for the administration of HBV vaccination in locations convenient to PWID, such as NSPs. Staff training is necessary for the administration of vaccinations in non-medical settings.

### ***Feasibility***

A rapid regimen for HBV vaccination and a higher dose for each vaccination are feasible in most settings.

**Recommendation 1:**

It is suggested to offer people who inject drugs the rapid hepatitis B vaccination regimen.  
*Conditional recommendation, very low-quality evidence*

**Complementary remarks**

- A higher-dose HBV vaccine should be used with the rapid regimen.
- HBV vaccine is already strongly recommended for PWID, per WHO guidelines (96).
- The priority for any regimen is delivery of the first dose of vaccine.
- Completion of three doses is more important than following a specific schedule. A missed dose should be given at the earliest opportunity without re-initiating the regimen.
- Individuals with inadequately treated HIV or with chronic HCV may have suppressed immunogenicity and may benefit more from the standard regimen.
- Both rapid and standard HBV vaccine regimens should be offered to PWID.

**Research questions**

Although a significant amount of research has been conducted on HBV vaccination, high-quality studies focusing on PWID and other drug-using populations are generally lacking. The following list of research needs was formulated by consensus at the Guidelines Consensus Meeting:

1. randomized controlled trials comparing the effect of the high-dose HBV vaccine with that of the standard HBV vaccine on HBV incidence among PWID;
  - Question: Is high-dose vaccine of greater benefit to PWID than the standard dose, regardless of delivery schedule?
2. randomized controlled trials comparing the effectiveness of new adjuvant vaccines with the standard HBV vaccine on HBV incidence among PWID;
3. randomized controlled trials comparing intramuscular with intradermal administration of the HBV vaccine among PWID;
4. immunogenicity studies of rapid and standard HBV vaccination regimens among PWID co-infected with HIV and HCV.

**Incentives to increase HBV uptake and completion rates among PWID**

Opportunities to vaccinate PWID often may be lost because of poor access or reluctance to be vaccinated (97). Providing PWID with incentives to be vaccinated and offering convenient access may increase HBV vaccination uptake and adherence (98,99). It is important to note that even partial immunization confers some immunoprotection (100), supporting the case for maximizing the proportion of individuals receiving a second dose.

Provision of financial, voucher and other incentives can enhance behavioural change, resulting in improved health outcomes among the general population, including improved vaccination rates, in both high-income countries and low- and middle-income countries (101-108). To date, there has been only limited investigation into the effectiveness of financial, voucher and other incentives to encourage HBV vaccination among PWID. Providing incentives to increase vaccination rates in PWID may be problematic where resources are constrained.

Immediate availability of HBV vaccine—for example at NSPs, prisons, or drug treatment programmes—can increase awareness of HBV vaccine and assist delivery of vaccination to PWID (92,109,110). Other strategies, such as testing for HBcAb (that is, for previous exposure) on first vaccination, can also encourage engagement (111).

The systematic review examined the case for financial, voucher and other incentives to enhance HBV vaccine uptake, the proportion receiving a second dose and vaccination completion rates.

### **Evidence**

Of the 2700 citations screened, four studies fulfilled eligibility criteria (98,112-114). All four were community-based studies in high-income countries. Two studies were RCTs (113,114), while the other two were prospective cohort studies (37,44).

### **Summary of findings**

Meta-analysis of the two RCTs found that vaccination completion rates were more than twice as high among PWID receiving monetary incentives as among those who received no monetary incentives. The RR was 2.53 (95% CI: 1.64–3.90). We identified no studies assessing the impact of incentives on vaccine efficacy or protection from HBV infection. One RCT found that a greater proportion of those receiving monetary incentives received the second vaccine dose. The RR was 1.53 (95% CI: 1.22–1.92). The overall quality of the studies was judged to be low due to serious risk of bias and serious imprecision. Pool analysis of the cohort studies was not possible due to differences in the outcome variables. Outcomes for vaccine completion, receiving a second dose and receiving at least one dose were all in favour of incentives and convenience of location. Modest financial incentives combined with a convenient location for vaccine administration for PWID (e.g. through an NSP) was more effective in increasing vaccination uptake and completion than higher monetary incentives alone.

### **Benefits and risks**

The panel judged the risk–benefit profile to be in favour of incentives to increase vaccination rates in PWID. The panel was strongly in favour of vaccination being administered at a location convenient for PWID.

### ***Acceptability***

The values and preference survey found that the majority of participants favoured incentives for increasing vaccination rates, although some were strongly opposed. The incentive of vouchers (for food or transport) was raised as an alternative to money. The majority stated that it is preferable that people choose to be vaccinated because they want to take care of their health.

### ***Resource use***

The panel judged that providing incentives might be problematic in resource-limited settings. Incentives should be appropriate to the local environment. In fact, some settings may preclude the use of incentives.

### ***Feasibility***

The panel judged that the incentives would be feasible in most settings, although possibly not in resource-limited settings.

#### **Recommendation 2:**

It is suggested to offer people who inject drugs incentives to increase uptake and completion of the hepatitis B vaccine schedule.

*Conditional recommendation, very low- to low-quality evidence*

### ***Complementary remarks***

- Vaccinations should be provided at a location and time convenient for PWID.
- This recommendation applies to settings with lower vaccination uptake rates among PWID and where other efforts to increase vaccination uptake are already in place.
- This recommendation is conditioned on local acceptability and resource availability.
- An inability to provide incentives should not discourage countries or settings from offering HBV vaccination to PWID.

### ***Research questions***

The Guidelines Consensus Meeting identified a number of gaps in the literature from which to generate research questions. The most apparent gap was the lack of studies examining HBV vaccination among PWID in low- and middle-income countries. The panel recommended the following further research:

1. randomized controlled trials on the effect of providing incentives versus not providing incentives on the initiation and completion of the HBV vaccination regimen among PWID;
2. acceptability studies examining the preferences of PWID and service providers as to type of incentive, e.g. cash, voucher, other;

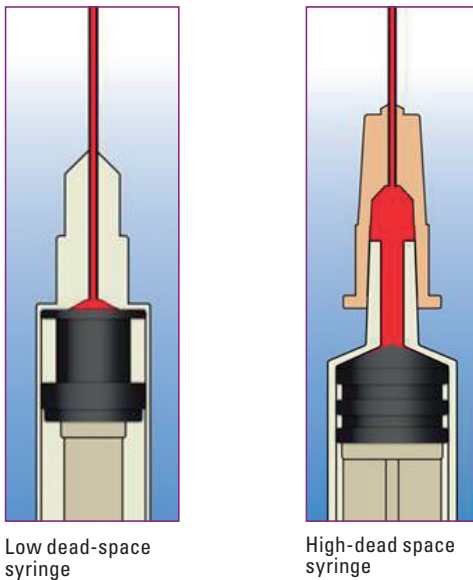
3. cost-effectiveness studies of incentives in local settings, especially resource-limited settings, in increasing rates of completion of the HBV vaccine regimen;
4. investigation into whether there is any evidence that providing cash incentives for public health interventions leads to decreased rates of participation in subsequent interventions that do not offer incentives.

## 6.2 Type of syringes

### Low dead-space syringes

Low dead-space syringes (LDSS) commonly have a non-detachable needle, which directly connects with the syringe barrel itself. This design is most commonly seen in a 1 ml syringe type and is less common in 3 ml, 5 ml and 10 ml or larger syringes. In contrast, high dead-space syringes (HDSS) consist of a detachable needle connected to a syringe. These are either packaged already connected together or can be connected by the user. The needle in a HDSS is not directly connected to the syringe barrel, but instead it is separated by a volume of “dead space”. When the plunger is completely depressed, the volume of dead space is substantially higher in HDSS than in LDSS (Figure 3).

Figure 3. Examples of low and high dead-space syringes



In a standard high dead-space syringe, the amount of dead space ranges from 51 to 158  $\mu\text{L}$ ; whereas in a low dead-space syringe, the dead space ranges from 1 to 9  $\mu\text{L}$  (115). Following the rinsing of syringes twice with phosphate-buffered normal saline solution, the mean volume of retained blood remaining was  $<0.001 \mu\text{L}$  in LDSSs ( $n = 10$ ) compared with 0.86–1.01  $\mu\text{L}$  in HDSS ( $n = 10$ ). Furthermore, the survival of HCV depends on the volume of residual blood in the syringe (116). In a laboratory experiment, Painsil (116) found that HCV was not detectable in LDSS (2  $\mu\text{L}$  dead space), while HCV was detectable for up to seven days in HDSS. Also, HCV survived longer at lower storage temperatures in HDSS. HIV survival in syringes follows a similar pattern (117). No information is currently available on the survival of HBV in syringes.

Field-based trials comparing HDSS with LDSS in preventing bloodborne virus transmission among PWID are difficult to conduct, as continued access to HDSS or LDSS (and consistent use of the same type of syringe by the two groups) would be necessary over a period of time in order to establish the incidence of bloodborne infections. Consequently, only cross-sectional and ecological studies have been published. A recent rapid assessment on needle and syringe types in Eastern Europe and Central Asia found both HDSS and LDSS available in most countries (118). Only in Azerbaijan were LDSS the more common syringe type, used by an estimated 70% of PWID. In most countries LDSS were used by a small minority of PWID. The major problems with LDSS were that they were available only in the 1 ml syringe size, while many PWID preferred larger syringes; that the needle was not detachable; and that the needle became blocked more easily during drug preparation, discouraging their use. Nonetheless, many PWID preferred the thin needle. The authors concluded that the success of any roll-out of LDSS would depend on the availability of a wider variety of syringe sizes and of detachable needles (118).

The systematic review examined the evidence for the effectiveness of LDSS in reducing HCV transmission among PWID. Given the limited literature available, HIV transmission was interpreted as a proxy for HCV transmission.

### **Evidence**

Of the 1260 citations screened, two studies (three articles) met the eligibility criteria (119–121). No RCTs or prospective cohort studies were identified. Both of the included studies were cross-sectional studies conducted in the community. One compared PWID in two different countries (119,120), while the other was conducted in a single state of one country (121).

### **Summary of findings**

The quality of the studies was considered very low, as both were cross-sectional. HIV was used as a surrogate outcome for HCV infection in PWID. Pooled analysis of the likelihood of being HIV-infected having used LDSS was 71% less than after having used HDSS (RR 0.29; 95%

CI: 0.18–0.46). The likelihood of HCV infection was 51% less (RR 0.49; 95% CI: 0.44–0.55) in those who used LDSS. The panel judged the effect estimate to be large, although the observational designs of the studies were a major limitation.

### ***Benefits and risks***

Further literature supporting the biological plausibility of the intervention in reducing transmission of bloodborne viruses was discussed in the Guidelines Consensus Meeting. Despite the limited evidence, the panel judged provision of LDSS to be a potentially important intervention. The panel judged the risks associated with providing LDSS to be low, although, given the lack of variety in syringe size currently available, there might have been drawbacks to a recommendation to use LDSS in preference to HDSS. The panel judged this potential drawback could be overcome by adding LDSS to the inventory of NSPs rather than replacing HDSS.

### ***Acceptability***

Participants in the values and preferences study did not express strong feelings for or against LDSS. They were most interested to know if LDSS syringes could come in different sizes and with removable needles. According to participants, one type of syringe will not fit all needs. Different drugs require different-sized syringes, and not all PWID prefer the same type of syringe. When sharing drugs, many consider it important to be able to remove the syringe from the needle.

### ***Resource use***

The panel judged the resources required to stock LDSS in existing NSPs to be low, given the relatively similar costs associated with LDSS and HDSS. The panel noted, nevertheless, the current limitations on the supply of LDSS, given that HDSS dominate the supply market and LDSS are manufactured in only a limited number of syringe sizes.

### ***Feasibility***

Taking into account the current limited availability of LDSS in many countries, the panel judged the use of LDSS in addition to other syringe types in needle syringe programmes to be feasible in many settings. The panel noted that currently available LDSS are not acceptable to PWID in all places. This may impede their uptake. However, the panel cited examples of PWID communities that, over time, adopted the use of LDSS.

### **Recommendation 3:**

It is suggested that needle and syringe programmes also provide low dead-space syringes for distribution to people who inject drugs.

*Conditional recommendation, very low-quality evidence*



### ***Complementary remarks***

- Needle and syringe programmes should offer all types of syringes appropriate for local needs.
- LDSS are currently produced in a limited number of sizes. Larger syringes should also be offered if appropriate to local needs, regardless of dead-space volume.
- Education should be provided to PWID and programme planners on the advantages of LDSS.
- NSPs should also provide other injecting paraphernalia, such as cotton, spoons, etc.
- LDSS syringes should also be available at other sites for syringe distribution i.e. pharmacies.

### ***Research questions***

The Guidelines Consensus Meeting noted the potential of this intervention but also the lack of high-quality and longitudinal studies. Nevertheless, the existing literature indicates the potential for LDSS to reduce HCV and HIV transmission among PWID. Although not studied, there are implications for HBV transmission as well. Further ethnographic exploration is needed of drug preparation techniques using the different types of syringes, as are prospective studies examining HCV and HIV incidence in populations in which the type of injecting equipment differs, to establish a causal relationship between LDSS use and reduced HCV transmission from sharing injecting equipment. Areas of further investigation include:

1. randomized controlled trials comparing the effectiveness of LDSS and HDSS in decreasing the incidence of HIV, HBV and HCV infection among PWID;
2. operational research on the acceptability of and preferences for different syringe sizes with detachable needles among PWID;
3. studies modelling potential harms if preferred equipment is not available (e.g. potential increases in re-use of (own) syringes, receptive syringe sharing, injecting-related injuries and bloodborne infections);
4. observational studies assessing:
  - a. the impact of changes in types of syringes distributed in different settings
  - b. within-country variations in types of equipment distributed
  - c. types of equipment distributed in locations with high and low HCV incidence.

## **6.3 Psychosocial and peer interventions**

### **Psychosocial interventions for viral hepatitis prevention**

Psychosocial interventions, also known as behavioural interventions, aim to change behaviour through the exchange of information, typically delivered by a clinician or educator. They include, but are not limited to, brief interventions, motivational interviewing, cognitive behavioural therapy, contingency management and self-help groups.

Psychosocial interventions are part of the recommended options for substance use disorders (122), although they may not always be of added benefit compared with more effective pharmacotherapy options (123). There is limited evidence supporting psychosocial interventions in reducing injecting and sexual risk behaviour associated with HIV transmission among PWID (124). A recent independent meta-analysis found no evidence to support psychosocial interventions as stand-alone initiatives to prevent HCV transmission among PWID (125). Notably, the provision of psychosocial interventions was not associated with adverse outcomes.

This systematic review examined the impact of psychosocial interventions to reduce HCV seroconversion as well as the injecting and sexual risk behaviour of PWID. A wide range of psychosocial interventions was considered.

### ***Evidence***

There were 1258 citations screened in the systematic review process. Of these, eight studies fulfilled eligibility criteria (126-133). A psychosocial intervention was defined as any intervention resulting in knowledge transfer from the health worker to the recipient. The psychosocial interventions studied were grouped together in the analysis. The definition excluded interventions in which equipment (e.g. injecting equipment) or medication (e.g. OST) was the primary intervention. All studies were conducted in the community. PWID may or may not have participated in other interventions during these studies.

### ***Summary of findings***

The quality of the studies was considered low for evidence on psychosocial interventions to prevent HCV transmission and to reduce injecting risk behaviour. The quality was considered very low also for evidence on psychosocial interventions to reduce sexual risk behaviour. Two RCTs examined psychosocial interventions for the prevention of HCV infection. No relationship was identified. The combined RR was 0.75 (95% CI: 0.33–1.71). Two RCTs examined the effect of psychosocial interventions in reducing injecting risk behaviour. There was no relationship in the dichotomous analysis. The RR was 0.70 (95% CI: 0.49–1.02). Continuous analysis of three studies found no relationship with injecting drug behaviour, either. One RCT examined psychosocial interventions to reduce sexual risk behaviour in PWID (dichotomous analysis). There was no relationship. The RR was 1.11 (95% CI: 0.89–1.38). Similarly, continuous analysis of three studies showed no relationship with sexual risk-taking. Quality of life was not measured. Psychosocial interventions cannot be suggested as a core intervention because no evidence was found of effectiveness for the reduction of viral hepatitis transmission.

### ***Benefits and risks***

The panel judged there to be no additional benefit to the use of psychosocial interventions to reduce HBV and HCV transmission. Still, the risks associated with psychosocial interventions are low. The panel noted that, while there was little evidence of a significant effect of

psychosocial interventions when compared with controls, most studies reported reductions in the outcome variables relating to viral hepatitis transmission from baseline to completion, regardless of study arm. This result was interpreted as suggesting that simply engagement with PWID may itself be an effective intervention.

The panel noted that psychosocial interventions are recommended for the management of other conditions such as a substance use disorders (68). The panel also noted that most studies were conducted in high-income settings, which may limit the applicability of their findings in low- and middle-income countries.

### ***Acceptability***

Respondents in the values and preferences survey were generally in favour of psychosocial interventions, if they were done well. Participants indicated that it is extremely important that information is accurate and appropriately shared. They did not specify a setting that would be best suited for receiving psychosocial interventions.

Other respondents were reluctant to support psychosocial interventions. Reasons given focused on time management issues, such as the need to obtain injecting equipment quickly from NSPs rather than engage in a psychosocial intervention.

### ***Resource use***

The panel judged psychosocial interventions to depend on human resources. Apart from brief interventions, the psychosocial interventions described in the analysed studies were relatively resource-intensive, requiring substantial and specific training, as well time to deliver. Although no harms are associated with psychosocial interventions, the panel stated that resources (human and other) should not be distracted from interventions that are proven to be effective in preventing viral hepatitis transmission.

### ***Feasibility***

Feasibility depends on human resource capacity and availability, especially in resource-limited settings and other settings where specifically trained health workers may not be available.

#### **Recommendation 4:**

Psychosocial interventions are not suggested for people who inject drugs to reduce the incidence of viral hepatitis.

*Conditional recommendation, very low- to low-quality evidence*

### ***Complementary remarks***

- Psychosocial interventions should not be suggested as a stand-alone intervention for the prevention of viral hepatitis.
- Psychosocial interventions should not be excluded as part of comprehensive intervention for drug dependence treatment or other outcomes (68).
- This recommendation does not include peer-delivered interventions.
- PWID should always be offered access to needle and syringe programmes.
- PWID should always be offered access to effective substance use treatment programmes, in particular OST for those dependent on opioids.

### ***Research questions***

The Guidelines Consensus Meeting noted the lack of evidence to support psychosocial interventions for the prevention of viral hepatitis transmission among PWID. It also noted that there were few studies addressing this issue. The following was proposed:

- Randomized controlled trials comparing the effects of psychosocial interventions with no psychosocial interventions on HCV, HBV, and HIV incidence and on quality of life among PWID.

### **Peer interventions**

Peer interventions, also known as peer-driven interventions or peer education, are a well-established component of services that work with PWID (134). Peer-based interventions include initiatives that involve peers (current or former PWID) in service delivery. Services working with PWID may include peer workers in order to improve communication, uptake and adherence to prevention and treatment, including NSPs, OST and HCV treatment. First developed in the 1980s, peer interventions are now present in many countries throughout the world where people inject drugs (4,6,135-137).

This systematic review examined the effectiveness of peer interventions to reduce HBV and HCV transmission as well as to change injecting and sexual risk behaviour.

### ***Evidence***

There were 1258 citations screened in the systematic review process. Two studies fulfilled eligibility criteria (138,139). Both studies were RCTs conducted in high-income settings.

### ***Summary of findings***

The quality of the studies was low for injecting risk behaviour and very low for sexual risk behaviour. Meta-analysis was limited because the studies did not report absolute numbers in outcome analysis; therefore, only pooled odds ratios could be calculated. The two RCTs were

included in the analysis of peer interventions for reducing injecting risk behaviour. Results were in favour of peer interventions. The OR was 0.61 (95% CI: 0.44–0.85). One RCT was included in the analysis of peer interventions to reduce sexual risk behaviour. It found no relationship. The OR was 0.90 (95% CI: 0.67–1.21). Quality of life was not measured.

### ***Benefits and risks***

The panel noted the limited number of studies and the limitations of the analysis, given the studies' reporting and design. The panel acknowledged the importance of programmes and services utilizing peer workers when working with PWID in order to enhance engagement and improve the acceptability of services. The panel noted the absence of harm associated with peer interventions for PWID.

### ***Acceptability***

The overwhelming majority of participants in the values and preferences survey stated strongly that peer interventions are key in providing services, especially to PWID. Respondents said that having peers deliver services improves the atmosphere of service delivery because peers generally do not discriminate against peers, and this contributes greatly to their acceptance by and success with PWID. As one participant stated, peers have “a connection with the community and are accepted by drug users”.

### ***Resource use***

The panel judged the value of peer interventions to depend on human resources. Peer-based interventions require the training of peers, particularly in settings where there are no trained peer workers. Nevertheless, the cost associated with training and employing peers is generally much less than the cost of training and employing health professionals. Given the limited data on effectiveness, however, the panel agreed that significant human resources should not be invested in this area.

### ***Feasibility***

Feasibility depends on human resource capacity and availability, especially in resource-limited settings. The use of peer workers is widespread in many, but not in all, countries reporting drug use. Peer workers in some countries are hampered by conflict with law enforcement, which may affect their ability to deliver interventions to PWID.

#### **Recommendation 5:**

It is suggested to offer peer interventions to people who inject drugs to reduce the incidence of viral hepatitis.

*Conditional recommendation, low- to moderate-quality evidence*

### ***Complementary remarks***

- Involving peers is an important modality of service delivery to PWID, as described in the WHO Evidence for Action Series: Technical papers and policy briefs on HIV/AIDS and injecting drug users (140).

### ***Research questions***

The Guideline Consensus Meeting noted that the broad definition of the term “peer intervention” might be an impediment to examination of the effect of peer interventions on viral hepatitis transmission. There was consensus on the importance of involving peers in any intervention or service working with PWID in order to improve the acceptability of the intervention or service for PWID. The group recommended the following further research:

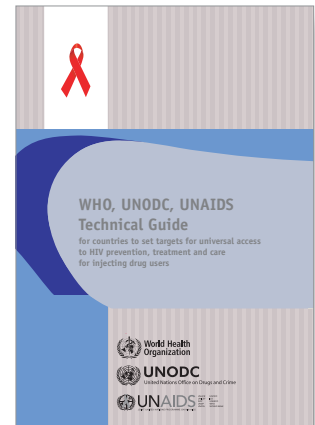
1. randomized controlled trials and other high-quality studies, using biological and behavioural endpoints, comparing peer interventions with other prevention interventions, e.g. high coverage levels of opioid substitution therapy and needle and syringe programmes, on HBV, HCV and HIV incidence among PWID;
2. randomized controlled trials of peer-driven interventions in multiple settings;
3. operational research in resource-limited settings.

## 7. EXISTING RECOMMENDATIONS

### Technical guide for countries to set targets for universal access to HIV prevention, treatment and care for injecting drug users

Preventing HIV transmission through injecting drug use is one of the key challenges to universal access in the health sector (3). The following comprehensive package of nine interventions for the prevention, treatment and care of HIV among PWID is recommended:

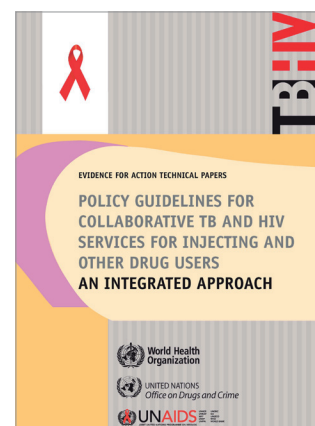
1. needle and syringe programmes
2. opioid substitution therapy and other drug dependence treatment
3. HIV testing and counselling
4. antiretroviral therapy
5. prevention and treatment of sexually transmitted infections
6. condom programmes for PWID and their sexual partners
7. targeted information, education and communication for PWID and their sexual partners
8. vaccination, diagnosis and treatment of viral hepatitis
9. prevention, diagnosis and treatment of tuberculosis.



### Evidence for Action Series: Technical papers and policy briefs on HIV/AIDS and injecting drug users

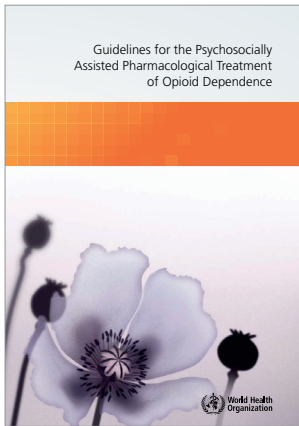
WHO has synthesized the scientific evidence for the effectiveness of the key components of the comprehensive package of interventions in the Evidence for Action Series (58). This series consists of the following documents, which focus on preventing HIV among PWID:

- integrated TB and HIV services
- antiretroviral therapy
- community-based outreach
- sterile needle and syringe programming
- drug dependence treatment
- interventions to address HIV in prisons.



## WHO position paper on HBV vaccine

Hepatitis B vaccine, available since 1982, is 95% effective in preventing HBV infection and its chronic consequences, and it is the first vaccine against a major human cancer. The WHO position paper on HBV vaccination recommends HBV vaccination in childhood immunization programmes and catch-up programmes targeted for at-risk populations (8).



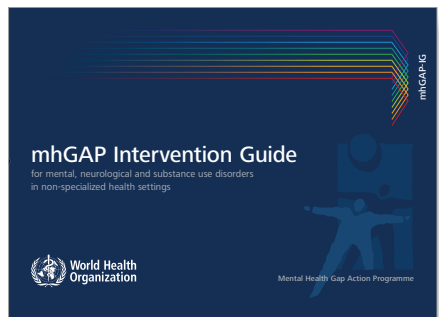
## WHO guidelines for the psychosocially assisted pharmacological treatment of opioid dependence

WHO recommendations for the pharmacological treatment of opioid dependence, including maintenance with methadone or buprenorphine, and the management of detoxification where necessary (68).

## Mental Health Gap Action Programme intervention guide for mental, neurological and substance abuse disorders in non-specialized health settings

The Mental Health Gap Action Programme (mhGAP) intervention guide was developed for use in non-specialized health-care settings (141). It is aimed at health-care providers working at first- and second-level facilities, e.g. district-level hospitals or clinics. Of specific relevance to this viral hepatitis guidance document are the following recommendations:

- assessment and management of hazardous drug use and drug dependence
- psychosocial interventions for drug use disorders
- pharmacotherapy for drug use disorders.





## 8. ADAPTING THESE GUIDELINES

These guidelines have been developed for a global audience. It is expected that regions and countries will adapt the recommendations to suit their own circumstances. These circumstances include the epidemiology of viral hepatitis in the country, social and cultural norms and economic factors. In order to achieve the desired impact of this guidance, these recommendations should be implemented at the national level. A national alliance composed of government, civil society, non-governmental organizations and donors is crucial to attain this objective.

This guidance is intended to be adapted to regional and local needs in line with national and sub-national strategies and inclusive of all partners. Regional and local requirements should be informed by epidemiological and needs assessments and take into account the existing programmatic response. Policy-makers should consider how the recommendations in this set of guidelines align with recommendations in other WHO guidelines. This guidance is not intended as a stand-alone document but rather one in the context of previous and future WHO guidance.

WHO and ministries of health, along with key stakeholders, should participate in country-level programme reviews to support adaptation and implementation of the guidelines\*. Feedback from communities and other stakeholders will help to guide revision of the next edition of these guidelines.

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\* For a guide to adapting WHO HIV guidelines, see: *Adapting WHO normative HIV guidelines for national programmes: essential principles and processes*. Geneva, World Health Organization, July 2011. [http://whqlibdoc.who.int/publications/2011/9789241501828\\_eng.pdf](http://whqlibdoc.who.int/publications/2011/9789241501828_eng.pdf)

## 9. OPERATIONAL AND IMPLEMENTATION ISSUES

It is recommended that this guidance be implemented in phases, consistent with the level of resources available. Consideration should be given to building awareness of this guidance among health-care workers and PWID. Specific issues regarding viral hepatitis among PWID that should be considered in the implementation of these guidelines in the local context include health systems, prevention services and community involvement.

### 9.1 Health systems

Health systems should work to increase awareness of viral hepatitis among health-care workers. The approach should include, but not be limited to, decreasing stigma towards most-at-risk populations and increasing the willingness of health-care workers to provide services to them. Efforts to decrease stigma involve addressing service providers' beliefs about and attitudes towards these populations. Also, health systems should build the capacity of health-care providers working with PWID to offer viral hepatitis and HIV prevention, testing, and diagnosis and treatment services.

### 9.2 Prevention services

Prevention services should promote health and treatment literacy about viral hepatitis transmission and prevention and should offer HBV vaccination for PWID. In addition, prevention services should advocate and implement a comprehensive package of harm reduction interventions.

### 9.3 Community involvement

PWID community groups should be involved in implementing the response to this guidance to ensure that it meets community needs. It is important to consider the context in which injecting drug use occurs and in which services for PWID are delivered.

## 10. NEXT STEPS

This guidance will be updated in future in accordance with WHO policy. In addition and as a companion to this document, guidance on surveillance and case definitions for population-level surveillance is currently being prepared. Likewise, the forthcoming WHO consolidated HIV treatment guidelines will include specific recommendations on HIV management in patients co-infected with HBV and/or HCV. Finally, the WHO Global Hepatitis Programme is developing guidelines for the treatment of HCV.

Multisectoral engagement is needed to increase the uptake by PWID of viral hepatitis prevention and treatment initiatives. There is a high prevalence of disease co-morbidity among PWID. The need for coordination between HBV and HCV intervention programmes and HIV, TB, mental health and drug dependence treatment services as well as harm reduction services for PWID cannot be overemphasized (142).

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