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Commentary

# WHO guidance on the prevention of viral hepatitis B and C among people who inject drugs

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ABSTRACT

Viral hepatitis B and C (HBV, HCV) disproportionately affect people who inject drugs (PWID) across the world. To date there has been little global action focusing on prevention, care and treatment of HBV and HCV among PWID. Here we report on the development process and discuss the implications of evidence informed WHO Guidelines for the Prevention of HBV and HCV in PWID. The World Health Organization (WHO) convened a Guideline Development Panel to develop recommendations on the prevention of HBV and HCV among PWID. The process followed the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology. It included the development of PICO (Population, Interventions, Comparator, Outcomes) questions and conducting systematic reviews. Quality of evidence was classified into 4 levels: high, moderate, low, and very low. In the process of moving from evidence to recommendations, the following were considered: quality of evidence, balance of benefits and harms, community values and preferences and resource use. The WHO recommendations include the following for working with PWID: offer the rapid HBV vaccination regimen; offer incentives to increase uptake and completion of the HBV vaccine schedule; needle and syringe programs should also provide low dead-space syringes for distribution; and offer peer interventions to reduce the incidence of viral hepatitis. This guideline complements other WHO documents regarding PWID, including HIV prevention initiatives such as needle and syringe programs and opioid substitution therapy. This guidance offers a first step in the prevention of HBV and HCV among PWID. However, the lack of high quality evidence in this area necessitates further research and resources for implementation.



## Introduction

The silent epidemic of viral hepatitis affects a large part of the world's population. It is estimated that around 240 million people are chronically infected with hepatitis B virus (HBV) and 184 million are chronic carriers of hepatitis C (HCV) antibody (Hanafiah, Groeger, Flaxman, & Wiersma, 2012; Ott, Stevens, Groeger, & Wiersma, 2012; WHO, 2009a, 2011b). These numbers far exceed the number of people living with human immunodeficiency virus (HIV), estimated at 34 million (WHO, UNAIDS, & UNICEF, 2011). HBV, HCV and related diseases are endemic among people who inject drugs (PWID) (Nelson et al., 2011). Globally there are an estimated 16 million PWID, and injecting drug use is reported in at least 148 countries (Mathers et al., 2008). To date, however, the urgency of preventing HIV among PWID has overshadowed the epidemic of viral hepatitis.

In 2011, it was estimated that approximately 1.2 million (range 0.3–2.7 million) PWID were living with chronic hepatitis B, as indicated by hepatitis B surface antigen (HBsAg), while nearly 6.4 million (range 2.3–9.7 million) were positive for hepatitis B core antibody (HBcAb), indicating previous exposure to the virus (Nelson et al., 2011). In the same study, it was estimated that 10 million (range 6–15.2 million) PWID are infected with HCV worldwide, as indicated by the presence of the HCV antibody (HCVAb) (Nelson et al., 2011). In addition, HCV HIV co-infection is common among HIV-infected PWID – close to universal in a number of countries – with the epidemiology similar to that of HIV infection (Amin et al., 2004; Cook & Kanaef, 2008; Kirby Institute, 2011; Walsh, Higgs, & Crofts, 2007). Like HIV and TB, the prevalence of HBV and HCV in prisons and other closed settings are higher than in the community.

The major modes of HBV transmission for PWID are the sharing of injecting equipment and sexual transmission. For HCV, sharing contaminated needles and syringes is also the most common mode of transmission, although sexual transmission is possible in the context of HCV HIV coinfection particularly for male-to-male sex (Danta et al., 2007; MMWR, 2011). Sharing injecting paraphernalia

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such as spoons and filters is also associated with HCV transmission (Hagan et al., 2001; Pouget, Hagan, & Des Jarlais, 2012). Similar studies have not been performed for HBV in PWID.

Both HBV and HCV cause acute inflammatory hepatitis that may result in fulminant liver failure. Chronic infection can result in liver fibrosis and ultimately cirrhosis and hepatocellular carcinoma—conditions resulting in increased mortality (Dienstag, 2008; Poynard, Yuen, Ratziu, & Lai, 2003). Furthermore, both HBV and HCV can complicate HIV treatment, and HIV accelerates the progression of HCV liver related disease (Chen, Ding, Seage Iii, & Kim, 2009; Dieterich, Robinson, Love, & Stern, 2004; Greub et al., 2000; Macias et al., 2004; Mohsen et al., 2003; Montessori, Harris, & Montaner, 2003; Sulkowski, 2004; Tedaldi et al., 2003).

To date the global response to the need for the prevention and management of viral hepatitis B and C has been poor. In 2010 the World Health Organization (WHO) Executive Board recommended to the Sixty-third World Health Assembly, the adoption of resolution EB126.R16, which resulted in the establishment of the WHO Global Hepatitis Programme (WHA, 2007). This Programme aims to reduce the transmission of the various agents that cause viral hepatitis; to reduce morbidity and mortality due to viral hepatitis, to improve the care of patients with viral hepatitis and to reduce the socioeconomic impact of viral hepatitis at individual, community and population levels.

WHO seeks to translate evidence into practice by providing normative guidance to inform policy and programming at the regional and country level (WHO, 2010b). This WHO guidance originates from the need for action given the disproportionate burden of viral hepatitis B and C among PWID, and was commenced prior to the establishment of the Global Hepatitis Programme.

The objective of this paper is to describe the development of the WHO guidance recommendations, report and discuss the recommendations. This paper provides additional data, such as GRADE decision tables, not contained in the published guidelines. The full guidance document is available online (http://www.who.int/hiv/pub/guidelines/hepatitis/en/index.html).

## Methods

### *WHO guideline development process*

The WHO guideline development process is standardised to develop evidence informed policy recommendations (WHO, 2012b). First, a core guideline group is formed to manage guidelines development. Next, a representative (of gender and geography) Guideline Development Group is formed. In addition, scoping exercises are conducted to define the content of the guidelines. WHO uses GRADE (Grading of Recommendations Assessment, Development and Evaluation) methodology (Guyatt et al., 2011) which includes: developing the PICO (Population, Interventions, Comparator, Outcomes) questions of interest; conducting systematic reviews to identify evidence relevant for each PICO question; rating the quality of evidence for each PICO question by outcome (Balshem et al., 2011); and finally moving from evidence to recommendation. The process is overseen by the Guideline Review Committee to ensure high methodological quality and a transparent, evidence-based decision-making process. This process is revisited every few years, or when appropriate in the case of new evidence emerging.

### *Viral hepatitis guidance development methodology*

The WHO Department of HIV/AIDS led the development of this guidance 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 (Walsh et al., 2010). A subsequent expert consultation with civil society representatives and the Cochrane Collaboration Drug and Alcohol Review Group was held in September 2010 to select the research questions. This expert consultation, including representatives of the affected community, took account of the findings of the scoping document, existing WHO guidance and reached consensus through a deliberative process focusing on priority areas by consensus(Fretheim, Schunemann, & Oxman, 2006a; Oxman, Schunemann, & Fretheim, 2006). Table 1 lists the PICO selected questions.

**Table 1**
PICO questions.

| | |
|---|---|
| PICO question 1 | Should a rapid HBV vaccination regimen versus a standard HBV vaccination regimen be used among PWID? |
| PICO question 2 | Should incentives for HBV vaccination completion versus no incentives be used among PWID? |
| PICO question 3 | Should low dead space syringes versus high dead space syringes be provided to PWID? |
| PICO question 4 | Should psychosocial interventions versus no psychosocial interventions be used among PWID? |
| PICO question 5 | Should peer based interventions versus no peer based interventions be used among PWID? |

One of the original PICO questions 'Should motivational interviewing versus no motivational interviewing be used in people who inject drugs?" was dropped by the GDG by consensus noting redundancy given the recommendation for psychosocial interventions.

Systematic reviews were conducted to address these PICO questions; their detailed methodology is published elsewhere (WHO, 2012a). Briefly, the reviews focused on PWID and viral hepatitis and addressed: (1) Rapid compared with standard schedule HBV vaccination; incentive (financial or non-financial) compared with no incentives for increasing HBV vaccination uptake and adherence; (2) psychosocial interventions for HCV prevention; and (3) peer interventions for HCV prevention. Databases searched included Pubmed, EMBASE, CINAHL, WHO regional databases and the Cochrane library. Search strategies included both controlled and free text terms specific to each PICO question. Titles and abstracts were screened in duplicate and independently, and full texts were obtained for potentially relevant studies. Full texts were screened in duplicate and independently. Discrepancies on inclusion or exclusion were resolved by consensus. Data abstraction and risk of bias assessment were done in duplicate. Treatment effects were assessed through meta-analysis of included studies. Quality of the evidence was assessed following the GRADE methodology by considering: study design, risk of bias, inconsistency, indirectness, imprecision and other limitations. The quality of evidence was classified in 4 levels: high, moderate, low, and very low.

In addition to conducting systematic reviews, 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 final recommendations on prevention, surveillance and HIV management in patients with viral hepatitis-HIV co-infection (to be published at later date). The multidisciplinary expert panel included public health professionals, clinicians, academics, programme managers, implementers, civil society representatives and a GRADE methodologist.

In moving from evidence to recommendations, the panel considered: the quality of evidence, the balance of benefits and harms, values and preferences of the affected community, and resource use. Decision tables are used to summarize these factors. The panel

used a consensus process to determine the direction (for or against) and strength (strong or conditional) of each recommendation. Complementary remarks, agreed by GDG consensus, were appended to each recommendation for added clarity on specific issues relevant to the recommendation. A draft version of the guidance was circulated among the expert panel members and external peer reviewers for feedback. In addition, the guidelines were developed with a framework based on human rights principles reflected in a number of international agreements (UN, 1948; UNHCR & UNAIDS, 2006).

## Findings

The resultant guidance includes existing recommendations for the prevention of HIV that are, possibly, even more important for the prevention of HCV, as well as four new ones. These existing (HIV based) recommendations are outlined elsewhere (WHO, UNODC, & UNAIDS, 2012). For each new recommendation, we provide a brief background, a 'decision table' summarizing the factors considered, and the recommendation statement. That statement is followed by the rating of the quality of supporting evidence, the strength of recommendation, and complementary remarks.

Detailed results data are published elsewhere (WHO, 2012a). We used sharing needles and syringes and sexual risk behaviour as proxies for potential episodes of HBV and HCV transmission, given these are key modes of viral transmission, noting sexual transmission occurs more commonly in HBV than for HCV.

### *Rapid HBV vaccination*

Most countries have both targeted and population-wide HBV vaccination programmes, including infant, catch-up and risk-group vaccination. By 2008, 177 countries had incorporated HBV vaccination into their national schedule (WHO, 2009a). There appears to be little difference between effectiveness of the vaccine among PWID compared with the general population (Baral, Sherman, Millson, & Beyrer, 2007). Nevertheless, rates of HBV vaccination among PWID are often low (Day et al., 2010; Gerlich, Gschwend, Uchtenhagen, Kramer, & Rehm, 2006; Hagan et al., 1999; Kuo, Sherman, Thomas, & Strathdee, 2004; Quaglio, Lugoboni, Mezzelani, Des Jarlais, & Lechi, 2006). The standard schedule for HBV immunization is 0, 1 and 6 months (WHO, 2009b). Accelerated schedules are shorter (e.g. 0, 1, 2 months) while the rapid schedule is 0, 1, and 21 days. A booster at 1 year may enhance immune response for the rapid schedule.

The systematic review examined rapid schedule and/or high-dose HBV vaccination compared to standard schedule/dose in PWID (Table 2).

**Table 2**
Grade decision table—Rapid regimens for HBV vaccination.

| Factor | Explanation/evidence | Judgment |
|---|---|---|
| Quality of Evidence | 2 included studies. One RCT, one partially randomized (Brissette, Gomez, Lambert, & Willems, 2002; Christensen et al., 2004) | Very low to low |
| Balance of Benefits vs. Harms | Results for completing vaccination are in favour of accelerated regimen<br>Response rate to the vaccine were in favour of programmes combining short schedule and high dose. | Benefits outweigh harms |
| Values and Preferences | The most common reported barrier to HBV vaccination was the number of injections (i.e. 3 was viewed as too many by some). Many (not all) of the participants did not know that there is an accelerated regimen for HBV vaccination. Given the choice, participants prefer a shorter regimen. | In favour of an accelerated regimen |
| Resource Use | High dose regimens require increased vaccine stock<br>More intensive regimens may increase workload and required increased vaccine stocks | Increases vaccine stock requirement, workload |
| Feasibility | Interventions are feasible in most settings | Feasible |

***Recommendation 1:***
It is suggested to offer PWID 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 (WHO, 2009b).
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. The implication is that 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.

### *Incentives for HBV vaccination*

Opportunities to vaccinate PWID may be lost because of poor access or reluctance to be vaccinated (Kuo et al., 2004). Providing PWID with incentives and offering convenient access may increase HBV vaccination uptake and adherence (Des Jarlais et al., 2001; Lum et al., 2003). It is important to note that even partial immunization confers some immunoprotection (Hall, 1993), supporting the case for maximizing the proportion of individuals receiving a second dose. Immediate availability of HBV vaccine—for example at needle and syringe programmes (NSPs), prisons, or drug treatment programmes—can increase awareness of HBV vaccine and assist delivery of vaccination to PWID (Altice, Bruce, Walton, & Buitrago, 2005; Baars, Boon, Garretsen, & van de Mheen, 2010; Ramasamy et al., 2010). Other strategies, such as testing for HBcAb (that is, for previous exposure) on first vaccination, can also encourage engagement (van Steenbergen, 2002).

The systematic review studied financial, voucher and other incentives to enhance HBV vaccine uptake (Table 3).

***Recommendation 2:***
It is suggested to offer PWID 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.

**Table 3**
Grade decision table—incentives for HBV vaccination.

| Factor | Explanation/evidence | Judgment |
|---|---|---|
| Quality of Evidence | 2 RCTs (Seal et al., 2003; Stitzer, Polk, Bowles, & Kosten, 2010) and 2 prospective cohort studies (Macalino et al., 2004; Vandelli et al., 2004). | Low |
| Balance of Benefits vs. Harms | *Monetary incentives* vs. *no monetary incentives:* Results for completing vaccination, receiving a second vaccine dose, injections received on time and longest number of consecutive sessions attended without a miss were in favour of receiving monetary incentives. *Monetary incentives* vs. *no monetary incentives or different incentives:* Results for vaccine completion were in favour of receiving HAV/HBV results 6–8 weeks after enrolment Results for receiving a second vaccine dose was in favour of modest monetary incentives plus vaccination delivered in a convenient location. Vaccine uptake (receiving at least one dose of vaccine) were in favour of vaccine available immediately on site. | Benefits outweigh harms |
| Values and Preferences | The majority of participants stated it is preferable that people choose to be vaccinated because they want to take care of their health. If incentives are to be used, vouchers (for groceries or transport) were preferred over money | Undetermined |
| Resource Use | Financial resources required for provision of monetary incentives; Vaccine delivery resources required for delivery in convenient locations e.g. trained staff and cold chain. | Monetary incentives appropriate in some settings, convenient location may require resources in some locations |
| Feasibility | Interventions are feasible in most settings, apart from financial incentives which may be problematic in resource limited settings. | Feasible |

*Low dead-space syringes for needle and syringe programmes*

Low dead-space syringes (LDSS) usually have a non-detachable needle, which directly connects with the syringe barrel. 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 adjacent 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 1).

This reduction in dead space reduces the amount of residual blood during potential needle syringe sharing after rinsing which reduces the likelihood of intact HCV or HIV virus presence or survival in this residual volume (Abdala, Stephens, Griffith, & Heimer, 1999; Paintsil, He, Peters, Lindenbach, & Heimer, 2010; Zule, Pande, & Bobashev, 2010).

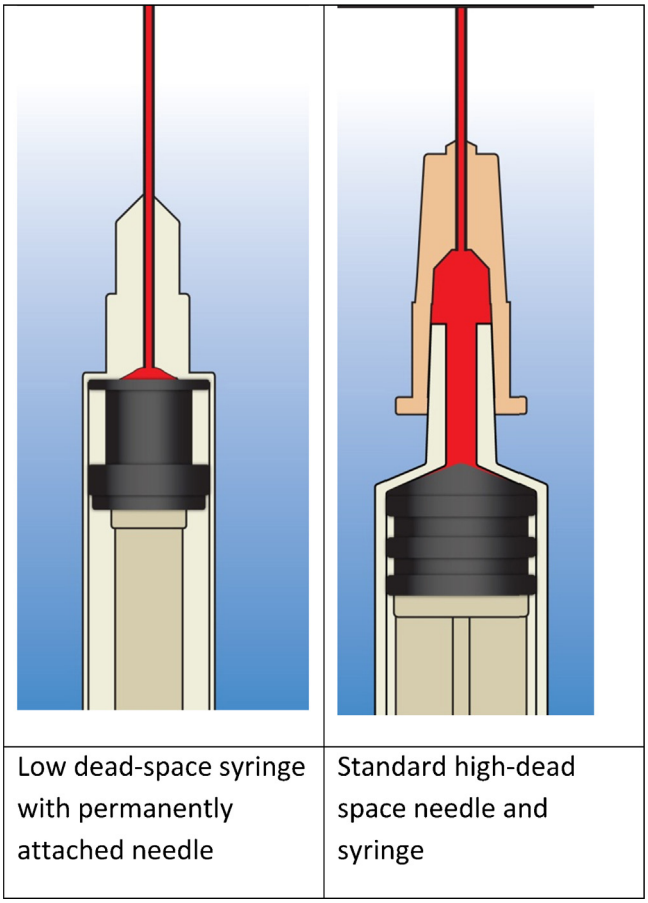


**Figure 1.** Low and high dead space syringe examples (Zule, 2012).

The systematic review examined the effectiveness of LDSS in reducing HCV transmission among PWID. For this review, HIV was included in addition to HCV, as the literature regarding LDSS was scant (Table 4).

***Recommendation 3:***
It is suggested that needle and syringe programmes also provide low dead-space syringes for distribution to PWID.
*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.

*Psychosocial interventions*

Psychosocial 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, graded exposure therapy and self-help groups.

**Table 4**
Grade decision table—low dead space syringes.

| Factor | Explanation/evidence | Judgment |
|---|---|---|
| Quality of Evidence | 2 studies (3 articles) included (Gyarmathy et al., 2010; Gyarmathy, Neaigus, Mitchell, & Ujhelyi, 2009; Zule, 2009). No RCTs or prospective cohort studies were identified. Cross sectional studies only. | Very low quality |
| Balance of Benefits vs. Harms | For HIV, results were in favour of LDSS compared with HDSS<br>For HCV, results were in favour of LDSS compared with HDSS | Benefits outweigh harms |
| Values and Preferences | Participants' did not express strong feelings for or against LDSS.<br>Most interested to know if LDSS syringes could come in different sizes and with removable needles as 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. | Potentially in favour |
| Resource Use | Switching from HDSSs to LDSSs may incur cost differences. | Possible resource implications |
| Feasibility | LDSSs are usually only available as 1 ml syringes and may not be appropriate for all PWID, nor all drug types. | Feasible only as a component of broader NSP |

Psychosocial interventions are part of the recommended options for substance use disorders (National Institute for Health and Clinical Excellence (NICE, 2008), although they may not always be of added benefit compared with more effective pharmacotherapy options (Amato, Minozzi, Davoli, & Vecchi, 2011). There is limited evidence supporting psychosocial interventions in reducing injecting and sexual risk behaviour associated with HIV transmission among PWID (Meader, Li, Des Jarlais, & Pilling, 2010). A recent independent meta-analysis found no evidence to support psychosocial interventions as stand-alone initiatives to prevent HCV transmission among PWID (Hagan, Pouget, & Des Jarlais, 2011). Notably, the provision of psychosocial interventions was not associated with adverse outcomes.

The systematic review examined the impact of psychosocial interventions to reduce HCV seroconversion as well as injecting and sexual risk behaviour of PWID. A wide range of psychosocial interventions was considered, including motivational interviewing, brief interventions and contingency management (Table 5).

***Recommendation 4:***
Psychosocial interventions are not suggested for PWID 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.
This recommendation does not include peer-delivered interventions.
PWID should always be offered access to NSP.
PWID should always be offered access to effective substance use treatment programmes, in particular opioid substitution therapy (OST) for those dependent on opioids.

**Table 5**
Grade decision table—psychosocial interventions.

| Factor | Explanation/evidence | Judgment |
|---|---|---|
| Quality of Evidence | 8 studies included (Abou-Saleh et al., 2008; Gagnon, Godin, Alary, Bruneau, & Otis, 2010; Gilbert et al., 2010; Nyamathi, Sinha, Greengold, Cohen, & Marfisee, 2009; Stein, Herman, & Anderson, 2009; Tucker et al., 2004; Wu et al., 2007; Zule, Costenbader, Coomes, & Wechsberg, 2009). | Low |
| Balance of Benefits vs. Harms | *Seroconversion for hepatitis C at the longest follow up:* no significant differences<br>*Sharing needles/equipment* no significant differences<br>*Risk behaviour/unprotected sex* No significant differences | No benefits, no harms |
| Values and Preferences | Most participants expressed that there is too much misinformation about viral hepatitis among both health care workers and PWID. Participants view psychosocial interventions as a means of accessing information, which they feel is important to both PWID and health care workers. | In favour |
| Resource Use | Given that there is no evidence for effectiveness, but no harms associated with psychosocial interventions, major resources (human and other) should not be invested in this area | Significant resource use |
| Feasibility | Feasibility depends on capacity and availability or human resources per setting, inclusive of low and middle income countries. | Feasibility might vary by setting, country |

### *Peer interventions*

Peer interventions, also known as peer-driven interventions or peer education, are a well-established component of services that work with PWID (Needle et al., 2004). Peer-based interventions include initiatives that involve peers (a 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 HIV treatment. First developed in the 1980s, peer interventions with PWID are now operating in many countries throughout the world (Broadhead et al., 1998; Latkin, 1998; Mathers et al., 2010; Wiebel, 1988, 1993).

This systematic review examined the effectiveness of peer interventions compared to no peer interventions in the prevention of HCV (Table 6).

***Recommendation 5:***
It is suggested to offer peer interventions to PWID 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 (WHO, 2004).

**Table 6**
Grade decision table - Peer based interventions.

| Factor | Explanation/Evidence | Judgment |
|---|---|---|
| Quality of Evidence | 2 RCTs (Garfein et al., 2007; Latka et al., 2008). | Low to moderate |
| Balance of Benefits vs. Harms | *Sharing needles/equipment* Results in favour of peer interventions (pooled odds ratios) *Sexual risk behaviour/unprotected sex* No significant difference | Benefits may outweigh harms |
| Values and Preferences | The overwhelming majority of participants stated strongly that peer-based interventions are key in providing services, especially to PWID. Respondents said that having other peers deliver services improves the atmosphere of service delivery because peers, generally, do not discriminate towards other peers, which contributes greatly to their acceptance by and success with PWID. | In favour |
| Resource Use | Training and employment of peers requires human resources limited financial resources (less than trained health professionals) | Limited resource requirements |
| Feasibility | Feasibility depends on availability of potential peer workers. Law enforcement issues in some countries for peer workers. | might vary by setting, country |

## Discussion

This guidance was developed to raise awareness of how to prevent HBV and HCV infection among PWID and to provide normative guidance as a tool for policy-making and advocacy as well as clinical recommendations for front-line health professionals. Additional audiences for the guidance include, but are not limited to, community and civil society organizations, nongovernmental organizations, national programme managers, researchers, international funding agencies, and the scientific media.

Policy makers and program developers should adapt these recommendations to suit the local context of viral hepatitis among PWID. This includes aligning these with other WHO guidelines to from an integrated response at both policy and program levels. WHO and ministries of health, along with key stakeholders, should participate in country-level programme reviews to support adaptation and implementation of the guidelines (WHO, 2011a). Feedback from communities and other stakeholders will help to guide revision of the next edition of these guidelines. In accordance with WHO policy, these recommendations will be updated in the future to reflect new developments.

Implementation of this guidance should be in phases, consistent with the level of resources available. Implementation issues should be considered at all levels of the health system, including the health system as a whole, at the community and individual level. Because stigma and discrimination remain significant problems for people living with HIV and for PWID, it is essential that any implementation of the guidance adheres to basic tenets related to self-determination, privacy, informed decision-making and protection. Guiding principles during implementation should include the protection of human rights for PWID, access to health care (WHO, UNODC, & UNAIDS, 2007a), access to justice (UNGA, 1966), acceptability of services as a key component of effectiveness, a focus on increasing health literacy by health services and where possible, integrated service provision for the multiple co-morbidities and poor social situations that PWID often face (WHO, UNAIDS, & UNODC, 2008).

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 programs, on one hand, and, on the other, HIV, TB, mental health and drug dependence treatment services as well as harm reduction services for PWID cannot be overemphasized (Getahun, Gunneberg, Sculier, Verster, & Raviglione, 2012).

A key limitation was that the evidence base for HCV prevention is not as strong as that for prevention of HIV and HBV. This meant relying on the best available evidence, which in many cases consisted of low or very low quality evidence. This should not be viewed as a limitation of the process itself. In fact, the process was developed in response to reports that systematic reviews and concise summaries of findings were rarely used in WHO guideline development. Another finding was that the previous WHO process relied mostly on experts, and did not involve patient representatives and other stakeholders (Oxman, Lavis, & Fretheim, 2007).

There may be barriers to guidance implementation. National or sub-national levels are better able than WHO to tailor implementation strategies to their specific circumstances, though capacity and resources may be limited, particularly in low and middle income countries (Fretheim, Schunemann, & Oxman, 2006b). Financial incentives for HBV vaccination may not be appropriate in all locales, especially in resource limited settings. This emphasizes the importance of appropriate application of this guidance, taking into consideration local needs and resource availability. Currently, LDSSs are available in a limited number of sizes and these may not be preferred over existing needles and syringes. Nevertheless, others have demonstrated that changes in type of needle and syringes used by PWID is possible over time (Zule, Cross, Stover, & Pretorius, 2013; Zule, Desmond, & Neff, 2002), in addition to a demand driven increase in the types of injecting equipment available in the current marketplace. Finally, the evidence for effective HCV prevention interventions for PWID is substantially more limited than that of HIV or HBV, restricting the scope of these recommendations and the potential for eliminating, or markedly reducing, HCV transmission among PWID at the community level through these interventions alone.

Since release of these guidelines in mid-2012, further evidence has become available supporting the recommendations. An Australian RCT of rapid schedule HBV vaccination for PWID found financial incentives associated with increased schedule completion (Topp et al., 2013). A recent mathematical model based on increased uptake of LDSS by PWID suggests that substantial reduction in HIV prevalence (>33% assuming 50% uptake) is possible, dependant on syringe rinsing behaviour and preferential use of LDSS over HDSS (Vickerman, Martin, & Hickman, 2013). While the latter study modelled HIV transmission rather than HCV, the findings of both studies support the recommendations.

In 2009 global consensus was reached on a public health driven comprehensive package of nine interventions (see below Table) that best address HIV in countries facing epidemics of injecting drug use (WHO, UNODC, & UNAIDS, 2009). This document was subsequently endorsed at the highest political level, including by the United Nations Economic and Social Council (UNESC, 2009). A revision of this document was completed in 2012 (WHO et al., 2012).

The nine interventions defined for HIV in the comprehensive package are also relevant for the prevention of other bloodborne viruses such as HBV and HCV, in particular the provision of sterile injecting equipment through NSPs and OST (Vickerman,

Martin, Turner, & Hickman, 2012). Despite global endorsement, implementation and coverage of these specific and crucial interventions related to injecting drug use remain substantially under resourced and insufficiently effective in many countries. Dramatically increasing the delivery and coverage of these interventions has become paramount if we want to have any chance of curbing the twin epidemics of HIV and viral hepatitis.

To date, the global response to HBV and HCV among PWID has been poor, with continuing epidemics in many countries as a result. The field of hepatitis C research is rapidly changing. Here we outline initial guidance for HBV and HCV prevention among PWID. Nevertheless, substantial work from researchers to policy makers is still required in the viral hepatitis arena, together with sufficient funding and effective implementation at all levels to attenuate transmission and avert liver disease and increased mortality from these two insidious hepatitis viruses.

Integration with existing recommendations

This guidance complements existing recommendations including the ones from the WHO/UNODC/UNAIDS Technical guide for countries to set targets for universal access to HIV prevention, treatment and care for injecting drug users (WHO et al., 2009, 2012), Evidence for Action Series: Technical papers and policy briefs on HIV/AIDS and injecting drug users (WHO, UNODC, & UNAIDS, 2007a), the WHO position paper on HBV vaccine (WHO, 2009a), the Mental Health Gap Action Programme (mhGAP) intervention guide for mental, neurological and substance abuse disorders in non-specialized health settings (WHO, 2010a) and the. WHO guidelines for the psychosocially assisted pharmacological treatment of opioid dependence (WHO, 2008)

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## Conflicts of interest statement

There is no conflicts of interest statement.

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