### Criteria Grid

**Best Practices and Interventions for the Prevention and Awareness of Hepatitis C**

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Date of Review:</td>
<td>June 14, 2015</td>
</tr>
<tr>
<td>Reviewer(s):</td>
<td>Christine Hu</td>
</tr>
</tbody>
</table>

#### Part A

**Category:**
- Basic Science □
- Clinical Science □
- Public Health/Epidemiology □
- Social Science □
- Programmatic Review ⌂

**Best Practice/Intervention:**
- **Focus:** Hepatitis C ☑  Hepatitis C/HIV ☑  Other: __________________________
- **Level:** Group ☑  Individual □  Other: __________________________
- **Target Population:** people who inject drugs (PWID)
- **Setting:** Health care setting/Clinic ☑  Home □  Other: __________________________
- **Country of Origin:** United Kingdom
- **Language:** English ☑  French □  Other: __________________________

#### Part B

**Is the best practice/intervention a meta-analysis or primary research? Please go to Comments section.**

<table>
<thead>
<tr>
<th>YES</th>
<th>NO</th>
<th>N/A</th>
<th>COMMENTS</th>
</tr>
</thead>
</table>
| ☐   | ☐  | ☑   | Systematic review of reviews to assess the effectiveness of harm reduction interventions in relation to HIV, HCV transmission and injecting risk behavior.  
- Synthesize latest review-level evidence regarding the effectiveness of: needle and syringe programs, provision of injection paraphernalia, opiate substitution treatment, information, education and counseling, and supervised injecting facilities |
The best practice/intervention shows evidence of “scale up” ability

<table>
<thead>
<tr>
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<th>NO</th>
<th>N/A</th>
<th>COMMENTS</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>This article is an update and extension of previous published review of review on evidence for effectiveness of needle/syringe program in the prevention of HIV and HCV among PWID</td>
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The best practice/intervention shows evidence of transferability

<table>
<thead>
<tr>
<th>YES</th>
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The best practice/intervention shows evidence of adaptation

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Do the methodology/results described allow the reviewer(s) to assess the generalizability of the results?

<table>
<thead>
<tr>
<th>YES</th>
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<th>N/A</th>
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Are the best practices/methodology/results described applicable in developed countries?

<table>
<thead>
<tr>
<th>YES</th>
<th>NO</th>
<th>N/A</th>
<th>COMMENTS</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Results of this review of review are applicable to people who inject drugs worldwide.</td>
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</tbody>
</table>

Are the best practices/methodology/results described applicable in developing countries?

<table>
<thead>
<tr>
<th>YES</th>
<th>NO</th>
<th>N/A</th>
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The best practice/intervention has utilized a program evaluation process

<table>
<thead>
<tr>
<th>YES</th>
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Consultation and feedback with community has taken place

<table>
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The best practice/intervention is sensitive to gender issues

<table>
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<tr>
<th>YES</th>
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Review articles included in this review may have done analysis of gender difference and various population difference in HCV and HIV transmission among PWID

The best practice/intervention is sensitive to multicultural and marginalized populations

<table>
<thead>
<tr>
<th>YES</th>
<th>NO</th>
<th>N/A</th>
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The best practice/intervention is easily accessed/available electronically

<table>
<thead>
<tr>
<th>YES</th>
<th>NO</th>
<th>N/A</th>
<th>COMMENTS</th>
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<tbody>
<tr>
<td></td>
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<td>Purchase/journal subscription required for access from</td>
</tr>
<tr>
<td>Question</td>
<td>Yes</td>
<td>No</td>
<td>Comments</td>
</tr>
<tr>
<td>------------------------------------------------------------------------</td>
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<tr>
<td>Is there evidence of a cost effective analysis?</td>
<td>☑️</td>
<td>☐️</td>
<td>☐️</td>
</tr>
<tr>
<td>If so, what does the evidence say?</td>
<td></td>
<td></td>
<td>Please go to Comments section</td>
</tr>
<tr>
<td>How is the best practice/intervention funded?</td>
<td>☑️</td>
<td>☐️</td>
<td>☐️</td>
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<tr>
<td>Please go to Comments section</td>
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<tr>
<td>Is the best practice/intervention dependent on external funds?</td>
<td>☑️</td>
<td>☐️</td>
<td>☐️</td>
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<tr>
<td>Other relevant criteria:</td>
<td>☐️</td>
<td>☐️</td>
<td>☐️</td>
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The study was funded by the European Centre of Disease Prevention and Control (ECDC) and the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA).
Review

Interventions to prevent HIV and Hepatitis C in people who inject drugs: A review of reviews to assess evidence of effectiveness

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g Health Protection Services, Health Protection Agency, London, UK
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i Department of Mathematics and Statistics, University of Strathclyde, Glasgow, UK
j European Monitoring Centre for Drugs and Drug Addiction, Lisbon, Portugal

A R T I C L E   I N F O

Article history:
Received 27 June 2012
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Keywords:
Hepatitis C
HIV
Harm reduction
People who inject drugs
Review

A B S T R A C T

Background: Injecting drug use is a major risk factor for the acquisition and transmission of HIV and Hepatitis C virus (HCV). Prevention of these infections among people who inject drugs (PWID) is critical to reduce ongoing transmission, morbidity and mortality.

Methods: A review of reviews was undertaken involving systematic literature searches of Medline, Embase, CINAHL, PsycINFO, IBSS and the Cochrane Library (2000–2011) to identify English language reviews regarding the effectiveness of harm reduction interventions in relation to HIV transmission, HCV transmission and injecting risk behaviour (IRB). Interventions included needle and syringe programmes (NSP); the provision of injection paraphernalia; opiate substitution treatment (OST); information, education and counselling (IEC); and supervised injecting facilities (SIFs). Reviews were classified into ‘core’ or ‘supplementary’ using critical appraisal criteria. The strength of review-level evidence was assessed.

Results: Twelve core and thirteen supplementary reviews were included. From these reviews we identified: (i) for NSP: tentative review-level evidence to support effectiveness in reducing HIV transmission, insufficient review-level evidence relating to HCV transmission, but sufficient review-level evidence in relation to IRB; (ii) for OST: sufficient review-level evidence of effectiveness in relation to HIV transmission and IRB, but tentative review-level evidence in relation to HCV transmission; (iii) for IEC, the provision of injection paraphernalia and SIFs: tentative review-level evidence of effectiveness in reducing IRB; and either insufficient or no review-level evidence for these interventions in relation to HIV or HCV transmission.

Conclusion: Review-level evidence indicates that harm reduction interventions can reduce IRB, with evidence strongest for OST and NSP. However, there is comparatively little review-level evidence regarding the effectiveness of these interventions in preventing HCV transmission among PWID. Further studies are needed to assess the effectiveness and impact of scaling up comprehensive packages of harm reduction interventions to minimise HIV and HCV transmission among PWID.

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Introduction

Recent estimates suggest that there may be between 11 and 21 million people who inject drugs (PWID) worldwide (Mathers et al., 2008). Through the sharing of drug injection equipment, these individuals are at increased risk of acquiring blood-borne viruses such as HIV and Hepatitis C virus (HCV), and thus substantial morbidity...
and mortality. It is estimated that approximately 3 million (range 0.8–6.6 million) PWID might be living with HIV (Mathers et al., 2008), whilst 10 million (range 6.0–15.2 million) might have HCV (Nelson et al., 2011). Country-specific estimates of HIV prevalence amongst PWID are generally below 20%, but estimated prevalence is at least 40% in Spain, parts of Eastern Europe, Asia, Latin America and Sub-Saharan Africa (Mathers et al., 2008; Wiessing et al., 2008). Estimates of HCV prevalence among PWID are generally greater than 40%, and many countries have reported prevalence estimates greater than 60% (Nelson et al., 2011; Wiessing et al., 2011).

Prevention of primary infection with HIV and HCV is critical to reduce long-term morbidity in PWID. There is evidence to support the effectiveness of harm reduction interventions such as needle and syringe programmes (NSP) and opiate substitution treatment (OST) in reducing HIV transmission (Degenhardt et al., 2010; Kimber et al., 2010; Palmateer et al., 2008; Tilson et al., 2007), and recent studies indicate that the combination of OST and NSP can significantly reduce HIV and HCV incidence (Hagan, Pouget, & Des Jarlais, 2011; Turner et al., 2011; Van Den Berg, Smit, Van Brussel, Coutinho, & Prins, 2007). However, evidence relating to the effectiveness of NSP alone in relation to HCV transmission is less clear (Hagan et al., 2011; Palmateer et al., 2010) and there is comparatively little evidence regarding the effectiveness of other harm reduction interventions such as supervised injecting facilities (SIFs) and behavioural interventions in relation to HIV and HCV transmission (Hedrich, 2004; Kerr, Kimber, Debeck, & Wood, 2007; Sacks-Davis, Horyniak, Grebely, & Hellard, 2011). To date, few reviews have systematically examined evidence on the impact of the full range of harm reduction interventions in relation to both HIV and HCV transmission among PWID.

We previously published a review of reviews (RoR) (including reviews published up to March 2007) on evidence for the effectiveness of NSP in the prevention of HIV and HCV among PWID (Palmateer et al., 2010). In this paper, we update and extend the previously published RoR to collate and synthesise the latest review-level evidence regarding the effectiveness of the following harm reduction interventions: NSP, OST, information, education and counselling (IEC) and SIFs in preventing injecting risk behaviour (IRB), HIV and HCV transmission among PWID. Related reviews have informed European guidance for the prevention of infectious diseases among PWID, published jointly by the European Centre for Disease Prevention and Control (ECDC) and the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) (European Centre for Disease Prevention, 2011).

Methods

We used a review of reviews (RoR) approach: given the increasing number of reviews of effectiveness of public health interventions in the literature, the RoR aims to bring together evidence from reviews of the effectiveness of public health interventions, rather than undertaking a systematic review of the primary literature itself.

The methodology has been described elsewhere (Kelly et al., 2002; Palmateer et al., 2010). Briefly, the RoR entails: a systematic search of the literature for published reviews; selection and critical appraisal of the reviews; and synthesis of the findings into an evidence briefing, including summary evidence statements (Ellis et al., 2003) (Table 1).

Studies were included if they were a systematic review, synthesis, meta-analysis, or literature review that considered the effectiveness of interventions in relation to the prevention of HIV, HCV or IRB. The interventions considered were: NSP and models of its delivery (e.g. vending machines, pharmacies); the provision of sterile drug preparation equipment (including the provision of foil, in terms of stimulating the transition from injecting to smoking); IEC; OST; and SIFs. The outcomes considered were: HIV prevalence or incidence; HCV prevalence or incidence; and self-reported IRB (which included the borrowing, lending or re-use of needles/syringes or other drug preparation equipment; and injecting frequency). For OST, drug-related risk – assessed using tools such as the risk assessment battery and HIV risk-taking behaviour scale (Navaline, Snider, & Petro, 1994; Ward, Darke, & Hall, 1990) – was also included as an IRB-related outcome.

Studies were included if they were published in the English language between January 2000 and March 2011. Studies relating to the distribution of foil were included if they were published between 2007 and March 2011, owing to the fact that this intervention has been implemented more recently. Reviews were excluded if they had considered only the sexual transmission of HIV or HCV, or had considered interventions delivered exclusively in the prison setting.

Systematic searches were carried out using the Cochrane Library, EMBASE, Medline, CINAHL and PsychINFO. IBSS was searched to identify reviews relating to all topics covered in the study except drug treatment; searches for studies relating to drug treatment were carried out at a different site. We also searched for grey literature published by key international agencies, such as the ECDC, the EMCDDA, the National Institute on Drug Abuse, the US Institute of Medicine, the United Nations Office on Drug Control and Prevention, and the World Health Organization. Search strategies combined text words and MESH terms to maximise the retrieval of relevant studies.

Abstracts of identified papers were first screened by one reviewer for relevance. Thereafter, the full-text articles were screened by two reviewers for relevance and the selected papers were critically appraised by two reviewers using a tool developed by the Health Development Agency (Kelly et al., 2002). This tool considers the strength of the methods used in the reviews including the identification of relevant literature, the quality of the appraisal process and the appropriateness of the review’s conclusions. Using this tool, reviews were categorised into either high-quality ‘core’ reviews, which formed the basis of evidence used to assess effectiveness of interventions, or ‘supplementary’ reviews, which were not considered to be of sufficient quality to rely on the authors’ conclusions but potentially provided information on primary papers to complement the core reviews. This approach to appraisal and classification of reviews has been described in detail elsewhere (Palmateer et al., 2010).

From each review, we extracted information on the authors’ assessment of the evidence and the design and findings of relevant primary studies. The level of evidence in support of, or discounting, the effectiveness of an intervention was classified as ‘sufficient’, ‘tentative’, ‘insufficient’ or ‘no’ review-level evidence, using a framework (previously developed and adopted) based on the design and findings of the primary studies included in reviews, and concluding statements made by core review authors (Table 1) (Ellis et al., 2003; Palmateer et al., 2010). Using this approach, studies with longitudinal and case-control designs are considered more robust, whilst those with cross-sectional or ecological designs are considered to be weaker (Palmateer et al., 2010).

Results

A total of 1827 papers were identified in relation to NSP, the provision of sterile drug preparation equipment, IEC, SIFs, and the provision of foil; and 787 titles were identified in relation to OST. After removal of duplicates, screening of abstracts and full texts, and critical appraisal of relevant papers, twelve core reviews and
Table 1
Types of evidence statements and the level of evidence required to support each statement.

<table>
<thead>
<tr>
<th>Evidence statement</th>
<th>Level of evidence</th>
</tr>
</thead>
</table>
| Sufficient review-level evidence to either support or discount the effectiveness of an intervention | • Clear and consistent statement from one or more core reviews based on multiple robust studies, or  
• Consistent evidence across multiple robust studies within one or more core reviews, in the absence of a clear and consistent statement in the review(s) |
| Tentative review-level evidence to either support or discount the effectiveness of an intervention | • A tentative statement from one or more core reviews based on consistent evidence from a small number of robust studies or multiple weaker studies, or  
• Consistent evidence from a small number of robust studies or multiple weaker studies within one or more core reviews, in the absence of a clear and consistent statement in the review(s), or  
• Conflicting evidence from one or more core reviews, with the stronger evidence weighted towards one side (either supporting or discounting effectiveness) and a plausible reason for the conflict, or  
• Consistent evidence from multiple robust studies within one or more supplementary reviews, in the absence of a core review |
| Insufficient review-level evidence to either support or discount the effectiveness of an intervention | • A statement of insufficient evidence from a core review, or  
• Insufficient evidence to either support or discount the effectiveness of an intervention (either because there is too little evidence or the evidence is too weak), in the absence of a clear and consistent statement of evidence from a core review(s), or  
• Anything less than consistent evidence from multiple robust studies within one or more supplementary reviews |
| No review-level evidence                                                                 | • No core or supplementary reviews of the topic identified, possibly due to a lack of primary studies |

Modified from Ellis et al. (2003). Here, longitudinal cohort and case-control designs were considered to be robust studies, while ecological, serial cross-sectional and cross-sectional designs were considered to be weaker studies.

thirteen supplementary reviews were identified in relation to all of the harm reduction interventions (Fig. 1).

**Needle and syringe provision (NSP)**

Three core reviews (Gibson, Flynn, & Perales, 2001; Tilson et al., 2007; Wodak & Cooney, 2004) and three supplementary reviews (Hong & Li, 2009; Nacopoulos, Lewtas, & Ousterhout, 2010; Wright & Tompkins, 2006) were identified in relation to NSP (Table 2).

**Effects on injecting risk behaviour**

The three core reviews included 43 primary studies between them, 26 of which appeared in at least two of the reviews (Avants & Cooney, 2004; Cooney, 2007; Cooney et al., 2008).

**Fig. 1.** Studies identified in the review of reviews. (A) Selection of papers relating to needle and syringe programmes, the provision of sterile drug preparation equipment (including foil); information, education and counselling; and supervised injection facilities (2000-2011). (B) Selection of papers relating to opiate substitution treatment (2000–2011). (*) One core and one supplementary review identified here in relation to OST were also identified in the search for NSP, the provision of sterile drug preparation equipment, IEC and SIFs.
Table 2
Summary of core and supplementary reviews of the effectiveness of NSP, alternative access to needles and syringes, and the provision of sterile drug preparation equipment.

<table>
<thead>
<tr>
<th>Author and date</th>
<th>Title</th>
<th>Dates covered</th>
<th>Intervention covered in review</th>
<th>Type of review</th>
<th>Number of relevant primary studies included in the review, by outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gibson et al. (2001)</td>
<td>Effectiveness of syringe exchange programs in reducing HIV risk behaviour and HIV seroconversion among PWID</td>
<td>Up to 1999</td>
<td>NSP</td>
<td>Core</td>
<td>3 HCV 6 HIV 23 IRB</td>
</tr>
<tr>
<td>Gillies et al. (2010)</td>
<td>The provision of non-needle/syringe drug injecting paraphernalia in the primary prevention of HCV among PWID: a systematic review</td>
<td>Up to Feb 2010</td>
<td>Injection drug use equipment (specified as drug cookers, filters and/or water)</td>
<td>Core</td>
<td>1 HCV 0 HIV 13 IRB</td>
</tr>
<tr>
<td>Hong and Li (2009)</td>
<td>HIV/AIDS behavioural interventions in China: a literature review and recommendation for future research</td>
<td>Up to April 2008</td>
<td>NSP (among other harm reduction interventions)</td>
<td>Supplementary</td>
<td>2 HIV/HCV 1 HCV</td>
</tr>
<tr>
<td>Islam, Wodak et al. (2008)</td>
<td>The effectiveness and safety of syringe vending machines as a component of needle syringe programmes in community settings</td>
<td>Up to 2008</td>
<td>Alternative access to NSP: community vending machines</td>
<td>Supplementary</td>
<td>1 IRB</td>
</tr>
<tr>
<td>Jones et al. (2010)</td>
<td>Optimal provision of needle and syringe programmes for injecting drug users: A systematic review</td>
<td>Up to January 2008</td>
<td>Alternative access to NSP: pharmacy NSP, fixed NSP, outreach NSP, vending machines; not prison based</td>
<td>Core</td>
<td>2 HCV/HIV 9 IRB</td>
</tr>
<tr>
<td>Tilson et al. (2007)</td>
<td>Preventing HIV infection among injecting drug users in high-risk countries: an assessment of the evidence</td>
<td>Up to Jan 2006</td>
<td>NSP; alternative access to NSP (pharmacy NSP and vending machines); and injection drug use equipment (among other harm reduction interventions)</td>
<td>Core</td>
<td>6 HCV 12 HIV 24 IRB</td>
</tr>
<tr>
<td>Wodak and Cooney (2004)</td>
<td>Effectiveness of sterile needle and syringe programming in reducing HIV/AIDS among injecting drug users</td>
<td>Up to 2002</td>
<td>NSP (among other harm reduction interventions); prison NSP; alternative access to NSP (pharmacy NSP and vending machines)</td>
<td>Core</td>
<td>1 HCV 10 HIV 28 IRB</td>
</tr>
<tr>
<td>Wright and Tompkins (2006)</td>
<td>A review of the evidence for the effectiveness of primary prevention interventions for Hepatitis C among injecting drug users</td>
<td>Up to end 2002</td>
<td>NSP (among other harm reduction interventions)</td>
<td>Supplementary</td>
<td>9 HCV</td>
</tr>
</tbody>
</table>

et al., 1999; Avants et al., 2004; Baker et al., 1993; Ball et al., 1998; Batki et al., 1989; Bluthenthal et al., 1998; Bluthenthal et al., 2000; Brooner et al., 1998; Calsyn et al., 1992; Colon et al., 2009; Cox et al., 2000; Deren et al., 1995; Des Jarlais et al., 2000, 1994; Donohoe et al., 1992; Donohoe et al., 1989; Frischer and Elliott, 1993; Gibson et al., 2002; Gleghorn et al., 1998; Guydish et al., 1998, 1995; Hagan et al., 1993; Hart et al., 1989; Hartgers et al., 1989, 1992; Heimer et al., 2002; Heimer et al., 1998; Supplementary Table 1). Supplementary reviews are not described in relation to IRB since the evidence included in these reviews did not alter the evidence statement derived based on studies identified in core reviews (see Table 1). The majority of studies (i.e. thirty nine out of forty three studies) included in the core reviews reported a positive finding, i.e. a reduction in IRB associated with NSP (Table 3; Hsu and Ouellet, 2007; Iguchi, 1998; Keene et al., 1993; Kipke et al., 1997; Klee and Morris, 1995; Kwiatkowski and Booth, 2001; Lamden et al., 1998; Latkin et al., 2003; Lott et al., 2006; Magura et al., 1991; Mandell et al., 1994; Meandzija et al., 1994; Monterroso et al., 2000; Oliver et al., 1994; Paone et al., 1994; Peak et al., 1995; Power and Nozhkina, 2002; Robles et al., 1993; Sarkar et al., 2003; Schoenbaum et al., 1996; Sears et al., 2001a; Sears et al., 2001b; Shore et al., 1996; Simpson et al., 1995; Stein et al., 2002; Sterk et al., 2003; Strang et al., 2000; van Ameijden and Coutinho, 1998; van Ameijden et al., 1994; van den Hoek et al., 1989; Vazirian et al., 2005; Vertefeuille et al., 2000; Vlahov et al., 1997; Watters et al., 1994; Supplementary Table 1).

Tilson et al. (2007) included fourteen prospective studies that found that participation in multi-component harm reduction programs, including NSP, resulted in reductions in self-reported needle sharing (Supplementary Table 1). However, the authors acknowledged limitations of reliance of self-reported measures in such studies. Wodak and Cooney (2004) included twenty eight studies, twenty four of which reported positive findings. One additional study in this review reported negative findings and three reported
Table 3
Summary of evidence used to generate evidence statements for each intervention and outcome measure.

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Outcome</th>
<th>Statements from core reviews</th>
<th>Summary of findings from primary studies</th>
<th>Evidence Statement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Provision of needles/syringes and other injecting equipment&lt;sup&gt;a&lt;/sup&gt;</td>
<td>HIV</td>
<td>Tilson et al. (2007) provides a clear statement of evidence in support of NSP</td>
<td>43 studies identified in core reviews: 39 positive (20 COH, 1 EC, 18 CS) 1 negative (1 CS) 3 no association (1 COH, 2 CS)</td>
<td>Sufficient evidence to support the effectiveness of NSP in reducing IRB</td>
</tr>
<tr>
<td>(1) Needle and syringe programmes (NSP)</td>
<td>HCV</td>
<td>Tilson et al. (2007) provides a tentative statement of evidence in support of NSP</td>
<td>16 studies identified in core reviews: 10 positive (2 COH, 4 EC, 4 CS) 2 negative (2 COH) 4 no association (2 COH, 2 CC)</td>
<td>Tentative evidence to support the effectiveness of NSP in preventing HIV</td>
</tr>
<tr>
<td></td>
<td>IRB</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>HIV</td>
<td>Tilson et al. (2007) provides a tentative statement of evidence in support of NSP</td>
<td>17 studies identified in core and supplementary reviews: 9 positive (1 CC, 6 CS, 2 EC) 2 negative (2 COH) 6 no association (3 COH, 3 CS)</td>
<td>Insufficient evidence to either support or discount the effectiveness of NSP in preventing HCV</td>
</tr>
<tr>
<td></td>
<td>HCV</td>
<td>Tilson et al. (2007) provides a tentative statement of evidence in support of pharmacy NSP based on a small number of studies</td>
<td>4 studies identified in core reviews: 4 positive (4 CS)</td>
<td>Insufficient evidence to either support or discount the effectiveness of pharmacy access to needles/syringes in reducing IRB</td>
</tr>
<tr>
<td>(2) Alternative access to needles and syringes:</td>
<td>HIV</td>
<td>Jones et al. (2010) did not provide a clear statement of evidence relating to effectiveness</td>
<td>13 studies identified in core reviews: 8 positive (8 CS) 2 negative (2 CS) 3 no association (1 RCT, 2 CS)</td>
<td>Tentative evidence to support the effectiveness of pharmacy access to needles/syringes in reducing IRB</td>
</tr>
<tr>
<td>a) Pharmacy</td>
<td>HCV</td>
<td>No reviews identified</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>IRB</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>HIV</td>
<td>Jones et al. (2010) provides a statement of insufficient or incoherent evidence</td>
<td>1 study identified in core reviews: 1 no association (1 CS)</td>
<td>Insufficient evidence to either support or discount the effectiveness of vending machines in preventing HCV</td>
</tr>
<tr>
<td></td>
<td>HCV</td>
<td>No core reviews identified</td>
<td>No studies identified in either core or supplementary reviews</td>
<td>No review-level evidence</td>
</tr>
<tr>
<td></td>
<td>IRB</td>
<td>No core reviews identified</td>
<td>No studies identified in either core or supplementary reviews</td>
<td>No review-level evidence</td>
</tr>
<tr>
<td></td>
<td>HIV</td>
<td>Jones et al. (2010) does not provide an evidence statement</td>
<td>1 study identified in core review: 1 negative (1 CS)</td>
<td>Insufficient evidence to either support or discount the effectiveness of vending machine access to needles/syringes in preventing HIV</td>
</tr>
<tr>
<td></td>
<td>HCV</td>
<td>No core reviews identified</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(c) Mobile vans</td>
<td>IRB</td>
<td>No core reviews identified</td>
<td>No studies identified in either core or supplementary reviews</td>
<td>No review-level evidence</td>
</tr>
<tr>
<td></td>
<td>HIV</td>
<td>Jones et al. (2010) does not provide a statement of evidence</td>
<td>1 study identified in core review: 1 negative (1 CS)</td>
<td>Insufficient evidence to either support or discount the effectiveness of mobile van access to needles/syringes in preventing HIV</td>
</tr>
<tr>
<td></td>
<td>HCV</td>
<td>No core reviews identified</td>
<td>No studies identified in either core or supplementary reviews</td>
<td>No review-level evidence</td>
</tr>
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</table>
Table 3 (Continued)

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Outcome</th>
<th>Statements from core reviews</th>
<th>Summary of findings from primary studies*</th>
<th>Evidence Statement</th>
</tr>
</thead>
<tbody>
<tr>
<td>(3) Provision of drug preparation equipment</td>
<td>IRB</td>
<td>Gilles et al. (2010) provides a tentative statement of evidence in support of the provision of sterile injecting paraphernalia</td>
<td>15 studies identified in core reviews: 10 positive (6 COH, 4 CS) 5 no association (2 COH, 3 CS)</td>
<td>Tentative evidence to support the effectiveness of drug preparation equipment provision in reducing IRB</td>
</tr>
<tr>
<td></td>
<td>HIV</td>
<td>No core reviews identified</td>
<td>No studies identified in either core or supplementary reviews</td>
<td>No review-level evidence</td>
</tr>
<tr>
<td></td>
<td>HCV</td>
<td>Gilles et al. (2010) do not provide a statement of evidence</td>
<td>1 study identified in core review: 1 positive (1 CS)</td>
<td>Insufficient evidence to either support or discount the effectiveness of drug preparation equipment provision in preventing HCV</td>
</tr>
<tr>
<td>Drug dependence treatment</td>
<td>IRB</td>
<td>Gowling et al. (2008) provides a statement of evidence in support of OST</td>
<td>35 studies identified in core reviews in relation to: (a) injecting frequency: 22 positive (3 RCT, 16 COH, 3 CS) (b) sharing of injecting equipment: 16 positive (4 RCT, 8 COH, 4 CS) 3 no association (1 COH, 2 CS) (c) drug-related risk: 6 positive (1 RCT, 3 COH, 2CS) 1 no association (1 RCT)*</td>
<td>Sufficient evidence to support the effectiveness of OST in reducing IRB</td>
</tr>
<tr>
<td>Agonist pharmacological treatment (i.e. OST)</td>
<td>HIV</td>
<td>Gowling et al. (2008) provides a statement of evidence in support of effectiveness of OST</td>
<td>8 studies identified in core reviews: 5 positive (4 COH, 1 CC) 3 no seroconversions observed (2 RCT, 1 CS)</td>
<td>Sufficient evidence to support the effectiveness of OST in preventing HIV</td>
</tr>
<tr>
<td></td>
<td>HCV</td>
<td>No core reviews identified</td>
<td>12 studies identified in supplementary reviews: 4 positive (1 MA, 2 COH, 1 CC) 8 no association (8 COH)</td>
<td>Tentative evidence to support the effectiveness of OST in preventing HCV</td>
</tr>
<tr>
<td>Information, education and counselling (IEC)</td>
<td>IRB</td>
<td>Medley et al. (2009) provides a tentative statement of evidence in support of peer education interventions. Herbst et al. (2007) do not provide a statement of evidence</td>
<td>28 studies identified in core reviews: 18 positive (7 RCT, 10 COH, 1CS) 10 no association (8 RCT, 2 CS)</td>
<td>Tentative evidence to support the effectiveness of outreach which includes IEC in reducing IRB.</td>
</tr>
<tr>
<td></td>
<td>HIV</td>
<td>Tilson et al. (2007) does not provide a statement of evidence Needle et al. (2005) provides a tentative statement of evidence in support of community-based outreach</td>
<td>3 studies identified in core and supplementary reviews: 3 positive (1 COH, 1 CS, 1 EC)</td>
<td>Insufficient evidence to either support or discount the effectiveness of IEC in preventing HIV</td>
</tr>
<tr>
<td></td>
<td>HCV</td>
<td>No core reviews identified</td>
<td>1 study identified in a supplementary review: 1 positive (1 CS)</td>
<td>Insufficient evidence to either support or discount the effectiveness of IEC in preventing HCV</td>
</tr>
</tbody>
</table>
indeterminate findings. Gibson et al. (2001) identified a further two studies (Broadhead, van Hulst, & Heckathorn, 1999; Hagan, Des Jarlais, & Friedman, 1994) that were suggestive of a protective effect of NSP (Supplementary Table 1). Overall, the majority of studies reported positive associations. Thus, given consistent evidence across multiple robust studies, and strong statements of evidence supporting NSP from two core reviews, we conclude that there is sufficient review-level evidence of effectiveness in relation to IRB (Table 3).

**HIV transmission**

Although IRB can be viewed as a proxy for risk of HCV and HIV transmission, the primary studies included in the core reviews (Gibson et al., 2001; Tilson et al., 2007; Wodak & Cooney, 2004) report mixed findings regarding the impact of NSP on HIV incidence. Among the sixteen studies included in core reviews (Supplementary Table 1), ten reported reduced HIV incidence associated with NSP participation whilst four studies of robust design reported null findings (Table 3). Two prospective studies reported an increased risk of HIV transmission associated with NSP (Bruneau, Franco, & Lamothe, 1997; Bruneau et al., 1997; Strathdee, Patrick, Currie et al., 1997). However, Tilson et al. (2007) acknowledged that these findings might relate to: individuals that use NSPs being at higher risk of HIV infection or having higher baseline HIV prevalence; the extent of provision of needles/syringes not being sufficient to reduce risky injecting practices; and the possibility that those classified as ‘non-users’ of NSPs might be able to access clean needles/syringes from other sources, such as pharmacies. Tilson et al. (2007) also acknowledged that HIV prevalence has decreased since those studies were published whilst NSP access has increased.

Overall, the primary studies with the most rigorous designs reported mixed findings with an equal number of cohort studies reporting positive, null and negative associations (Table 3). There was greater consistency in findings among ecological studies, but these were regarded as having a weaker design. Thus, based on consistent evidence from less robust primary studies and a tentative statement from one core review (Tilson et al., 2007), we concluded that there is tentative review-level evidence to support the effectiveness of NSP in reducing HIV transmission among PWID.

**HCV transmission**

In relation to HCV incidence, the three core reviews (Gibson et al., 2001; Tilson et al., 2007; Wodak & Cooney, 2004) identified seven studies between them, whilst supplementary reviews (Hong & Li, 2009; Nacopoulos et al., 2010; Wright & Tompkins, 2006) identified an additional ten studies, three of which were identified in the two more recent supplementary reviews (Supplementary Table 2). Primary studies with stronger study designs (cohort and case-control studies) included in the core and supplementary reviews showed mixed findings: three found no association between NSP and HCV seroconversion (Hagan et al., 1999; Holtzman et al., 2009; van Ameijden, van den Hoek, Mientjes, & Coutinho, 1993), two found a negative association (Mansson, Moestrup, Nordenfelt, & Widell, 2000; Patrick et al., 2001), and one found a positive association (Hagan, Jarlais, Friedman, Purchase, & Alter, 1995). Positive associations (i.e. a reduction in HCV seroconversions associated with NSP) were mainly reported by weaker primary studies using ecological or cross-sectional design (Des Jarlais et al., 2005; Goldberg, Cameron, & McMenamin, 1998; Goldberg et al., 2001; Hutchinson et al., 2002; MacDonald et al., 2000; Neagu et al., 2008; Smyth, Keenan, & O’Connor, 1999; Somani et al., 2000; Taylor et al., 2000; Wu et al., 2007). As such, based on an absence of clear statements from core reviews, and inconsistent evidence from studies identified in both core and supplementary reviews, we found that there is insufficient review-level evidence to support or discount the effectiveness of NSP in reducing HCV transmission (Table 3).

**Delivery of NSP**

We identified three core reviews (Jones, Pickering, Sumnall, McVeigh, & Bellis, 2010; Tilson et al., 2007; Wodak & Cooney, 2004) and two supplementary reviews (Islam & Conigrave, 2007; Islam, Stern, Conigrave, & Wodak, 2008a; Islam, Wodak, & Conigrave, 2008b) that included evidence relating to NSP delivery (Table 2).

**Pharmacy-based access**

**Injecting risk behaviour**

Three core reviews (Jones et al., 2010; Tilson et al., 2007; Wodak & Cooney, 2004) included thirteen studies, eight of which reported positive findings in relation to pharmacy-delivered NSP and IRB (Supplementary Table 3). However, twelve of these studies had weaker study designs (Table 3; Supplementary Table 4).

Wodak and Cooney (2004) included six studies that reported reductions in IRB associated with access to needles/syringes via pharmacies (Calsyn, Saxon, Freeman, & Whittaker, 1991; Gleghorn, Jones, Doherty, Celentano, & Vlahov, 1995; Groseclose et al., 1995;
In attendance to cross-sectional data, one additional cross-sectional study identified by Tilson et al. (2007) reported reduced syringe sharing following liberalisation of laws allowing syringe sale from pharmacies in New York (Pouget et al., 2005).

The most recent review (Jones et al., 2010) included six additional studies: one RCT (Fisher, Fenaughty, Cagle, & Wells, 2003) examined differences in injecting frequency between one group of PWID that attended a pharmacy where needles/syringes were sold and another group that attended an NSP (or that used NSP and pharmacy). All participants reduced injection frequency over time with no difference between the groups. Five cross-sectional studies were also included, two of which found a negative association (Bluthenthal et al., 2004; Rhodes et al., 2004); two of which reported no difference in IRB associated with pharmacy distribution or other forms of distribution (Khoshnood, Blankenship, Pollack, Roan, & Altice, 2000; Obadia, Feroni, Perrin, Vlahov, & Moatti, 1999), and one of which reported significant reductions in IRB as NSP provision increased, with greater likelihood of sharing among those not accessing needles/syringes via a pharmacy (Singer, Himmelgreen, Weeks, Radda, & Martinez, 1997). Given tentative statements from two core reviews, and the large amount of evidence from studies of weaker design, we concluded that there is tentative review-level evidence that pharmacy access to NSP is at least as effective as dedicated NSP in reducing self-reported injecting risk behaviour (Table 3).

HIV transmission

In relation to HIV transmission, two of the core reviews (Jones et al., 2010; Wodak & Cooney, 2004) included four studies relating to HIV incidence (Table 3; Supplementary Table 4): one serial cross-sectional (Hunter, Donoghoe, Stimson, Rhodes, & Chalmers, 1995) and three cross-sectional studies (Miller, Tyndall, Spittal, Li, & Palepu, 2002; Nelson et al., 1991; Singer et al., 1997) which reported lower HIV prevalence among those with ready access to sterile syringes via pharmacies; among PWID who used pharmacies rather than other types of NSP; or associated with time periods of increased access to needles/syringes via NSP and pharmacies. Two additional studies were referred to by Wodak and Cooney (2004) in light of their contribution to the evidence base, which highlighted low HIV prevalence rates associated with availability of pharmacy distribution of needles/syringes (De Jong, Tsagareli, & Schouten, 1999; Des Jarlais et al., 1995). However, in light of a statement of insufficient evidence from one core review, and a tentative statement from a second core review; as well as the small number of studies using weaker designs, we concluded that there is insufficient review-level evidence to draw conclusions around the impact of access to NSP via pharmacies in relation to HIV incidence (Table 3).

HCV transmission

We did not identify any reviews which assessed the impact of pharmacy NSPs in relation to HCV incidence.

Vending machines

Injecting risk behaviour

The most recent core review (Jones et al., 2010) included a cross-sectional study which reported no difference in the reported sharing of needles among PWID who were primary users of vending machines compared to PWID who were primary users of NSP or pharmacy NSPs, although those who primarily used vending machines were less likely to report sharing of injection paraphernalia compared to those who used other sources (Obadia et al., 1999). Two core reviews (Tilson et al., 2007; Wodak & Cooney, 2004) included a cross-sectional pilot study of vending machines in a German prison (Heinemann & Gross, 2001); although the review authors' conclusions were slightly different, both inferred a positive finding. Lastly, a supplementary review which specifically assessed the effectiveness of vending machines (Islam, Stern et al., 2008; Islam, Wodak et al., 2008) included an additional study which reported that needle sharing did not differ between individuals who used vending machines compared to those who used NSP or pharmacy NSP (Islam, Stern et al., 2008; Islam, Wodak et al., 2008). Given the lack of primary evidence included in both the core and supplementary reviews, we concluded that there is insufficient review-level evidence to support or discount the effectiveness of needle/syringe vending machines in reducing IRB (Table 3).

HIV transmission

Two core reviews (Jones et al., 2010; Wodak & Cooney, 2004) identified one cross-sectional study (Obadia et al., 1999), which reported a reduced likelihood of HIV seropositivity among those who primarily used vending machines, although this was not statistically significant after adjustment. Thus there was insufficient review-level evidence to support or discount effectiveness of vending machines in relation to HIV transmission (Table 3).

HCV transmission

No reviews were identified that assessed the effects of vending machines on HCV incidence.

Outreach NSP (mobile vans)

Injecting risk behaviour

No reviews were identified that examined the impact of outreach NSP in relation to IRB.

HIV transmission

One core review (Jones et al., 2010) included one cross-sectional study (Miller et al., 2002b), which indicated that PWID who obtained needles/syringes via fixed site NSP and mobile vans had higher HIV prevalence compared to those using pharmacies. However, overall, there is currently insufficient evidence to support or discount the effectiveness of the provision of NSP via outreach in relation to HIV incidence.

HCV transmission

No reviews were identified that examined the impact of outreach NSP in relation to IRB or HCV incidence.

The provision of sterile drug preparation equipment

For the purposes of this review, drug preparation equipment or paraphernalia is defined as equipment for injecting or preparing drugs other than needles or syringes. Two core reviews (Gillies et al., 2010; Tilson et al., 2007) assessed evidence regarding the effectiveness of the provision of injecting paraphernalia.

Injecting risk behaviour

In relation to IRB, ten out of fifteen primary studies identified in the core reviews, including six cohort studies and four cross-sectional studies, reported positive findings, whilst five studies reported no association (Supplementary Tables 5 and 6). The most recent core review (Gillies et al., 2010) included thirteen studies: nine of these studies reported positive findings and four reported null findings. The authors tentatively concluded that 'current evidence suggests that attendance at NSP providing sterile injecting paraphernalia may be associated with reduced sharing of non-needle/syringe injecting paraphernalia'.

Tilson et al. (2007) identified two studies included by Gillies et al. (2010) (Hagan & Thiede, 2000; Longshore, Bluthenthal, &
Stein, 2001) and a further two cohort studies, one of which reported positive findings (Ouellet, 2004), whilst the other (Huo, Bailey, Garfein, & Ouellet, 2005) reported no association between use of NSP (assumed to provide drug preparation equipment although this was not explicitly stated) and the sharing of such equipment. Given consistent evidence from a small number of robust studies and a tentative statement of evidence from a core review, we concluded that there is tentative review-level evidence to support the effectiveness of the provision of injecting paraphernalia in reducing IRB (Table 3).

HIV transmission

No reviews examined the impact of provision of sterile drug preparation equipment in relation to HIV transmission.

HCV transmission

One core review (Gillies et al., 2010) assessed the impact of providing sterile drug preparation equipment in relation to HCV incidence. This review included only a single cross-sectional study (Morissette et al., 2007) that reported positive findings; thus, we concluded that there is insufficient evidence regarding the impact of sterile drug preparation equipment provision in relation to HCV transmission (Table 3).

Provision of foil to stimulate route transition

We did not find any reviews relating to the provision of foil to stimulate route transition, i.e. from injecting to smoking drugs. This is unsurprising given that the provision of foil is a relatively recent intervention thus primary studies might not yet be published or included in reviews.

Opiate substitution treatment (OST)

Injecting risk behaviour

Three core reviews (Gowing, Farrell, Bornemann, Sullivan, & Ali, 2008; Sorensen & Copeland, 2000; Tilson et al., 2007) were identified in relation to IRB (Table 4). Supplementary reviews are not described in relation to IRB, since evidence from these reviews did not alter the evidence statement based on the studies identified in core reviews.

As for NSP, many more studies of OST focused on IRB outcomes compared to HIV or HCV incidence. A total of thirty-five studies were identified in the three core reviews that related to sharing needles/syringes or injection frequency (Supplementary Table 7). As shown in Table 3, twenty-two studies related to injecting frequency, nineteen to sharing of needles/syringes, and seven to drug-related risk.

The majority of studies reported positive findings and used robust study designs (Table 3). Tilson et al. (2007) and Gowing et al. (2008) together identified thirteen studies that assessed: the prevalence of injecting drug use before and after OST; frequency of injecting at baseline and follow up; or the proportion and frequency of injecting. All of the studies reported a significant decrease in IRB between baseline and follow-up, although studies varied with respect to the duration of follow-up (3–12 months) and measurement of frequency of injecting drug use. Nine additional studies reported by Sorensen and Copeland (2000) reported positive effects of OST in relation to prevalence and frequency of injecting (Supplementary Table 7).

In relation to needle/syringe sharing, eight of nine studies identified by Gowing et al. (2008) and Tilson et al. (2007) reported reductions in the sharing of needles and syringes between baseline and follow up (Camacho, Bartholomew, Joe, Cloud, & Simpson, 1996; Chatham, Miller, Rowan-Salzl, Joe, & Simpson, 1999; Dolan et al., 2003; Gossop, Marsden, Stewart, & Rolfe, 2000; Grella, Anglin, Rawson, Crowley, & Hasson, 1996; Margolin, Avants, Warburton, Hawkins, & Shi, 2003; Schroeder, Epstein, Umbricht, & Preston, 2006; Teesson et al., 2006) whilst one cohort study reported no association (King, Kidorf, Stoller, & Brooner, 2000). Eight of an additional ten studies identified by Sorensen and Copeland (2000) reported positive findings (Capplehorn & Ross, 1995; Greenfield, Bigelow, & Brooner, 1995; Klee, Faugier, Hayes, & Morris, 1991; Longshore, Hsieh, Danila, & Anglin, 1993; Magura, Kang, NwaKeze, & Densky, 1998; Rhodes, Creson, Elk, Schmitz, & Grabowski, 1998; Saxon, Calsyn, & Jackson, 1994; Stark, Muller, Bienzle, & Guggenmoos-Holzmann, 1996) and two cross-sectional studies reported no association (Baker, Kochan, Dixon, Wodak, & Heath, 1995; Calsyn et al., 1991).

Lastly, seven studies included in two core reviews (Gowing et al., 2008; Tilson et al., 2007) reported impacts of OST on risk scores, for which a higher score indicates a higher level of risk behaviour. Four studies (Abbott, Moore, Weller, & Delaney, 1998; Avants, Margolin, Kosten, Rounsaville, & Schottenfeld, 1998; Chatham et al., 1999; Marsch, Bickel, Badger, & Jacobs, 2005) reported significant decreases in HIV risk behaviour scores before and after MMT; one study reported no significant difference in mean risk scores between baseline and 6-month follow up (Sees et al., 2000); and two studies reported significantly lower mean scores in those currently receiving MMT compared to those not in treatment (Baker et al., 1995; Mark et al., 2006).

In light of primary evidence and statements of evidence from core reviews in support of OST, we concluded that there is sufficient evidence to support effectiveness of OST in reducing IRB.

HIV transmission

The three core reviews (Gowing et al., 2008; Sorensen & Copeland, 2000; Tilson et al., 2007) included evidence relating to HIV from eight studies, seven of which had more robust study designs. Three cohort studies demonstrated reduced odds of HIV seroconversion among PWID in continuous OST (Metzger et al., 1993; Moss et al., 1994; Williams, McNelly, Williams, & D’Aquila, 1992). Lower dose of methadone and more time spent out of OST was reported to be associated with higher risk of HIV transmission in a cohort study and case-control study (Hartel & Schoenbaum, 1998; Serpelloni et al., 1994), and a cross-sectional study reported that no PWID receiving OST over the long-term had seroconverted (Novick et al., 1990). In two further studies, there were no seroconversions among participants of an RCT comparing methadone dosage of 50 mg vs. 80 mg over a six month period (Rhoades et al., 1998) and no seroconversions among participants of an RCT of prison-based MMT versus waitlist controls; although this was in the context of low HIV prevalence and a four-month follow up period (Dolan et al., 2003). Given supportive statements of evidence in core reviews and evidence from multiple robust studies, we concluded that there is sufficient review-level evidence to conclude that OST is effective in reducing HIV seroconversion (Table 3).

HCV transmission

Fewer robust reviews were identified regarding effectiveness of OST in relation to HCV transmission. No core reviews assessed the impact of OST in relation to HCV incidence, but two supplementary reviews were identified (MacArthur & Hickman, 2011; Wright & Tompkins, 2006) which included relevant studies. Although MacArthur and Hickman (2011) was principally a RoR, it also included a review of more recent primary studies relevant to OST and HCV transmission.

Together the two supplementary reviews included twelve studies: one meta-analysis, ten cohort studies and a case-control study. Wright and Tompkins (2006) identified six studies: a case-control study (Rezza et al., 1996) which reported lower HCV incidence associated with methadone treatment; a cohort study (Thiede, Hagan,
Table 4
Summary of reviews of the effectiveness of opiate substitution treatment (OST).

<table>
<thead>
<tr>
<th>Author and date</th>
<th>Title</th>
<th>Dates covered</th>
<th>Intervention covered in review</th>
<th>Type of review</th>
<th>Number of relevant primary studies included in the review, by outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Degenhardt et al. (2010)</td>
<td>Prevention of HIV infection for people who inject drugs: why individual, structural, and combination approaches are needed</td>
<td>Up to 2009</td>
<td>OST (among other harm reduction interventions including antagonist pharmacotherapy)</td>
<td>Supplementary</td>
<td>2 HIV</td>
</tr>
</tbody>
</table>

Murrill, 2000) which reported a non-significant reduction in HCV incidence among those in treatment compared to those who are out of treatment or who have left treatment; one cohort study that reported no decrease in annual HCV incidence associated with MMT (in combination with NSP) over a four year period (van Ameijden et al., 1993); and three cohort studies which reported no difference in HCV incidence among those in or out of MMT (Chamot, de Saussure, Hirschl, Deglon, & Perrin, 1992; Crofts, Nigro, Oman, Stevenson, & Sherman, 1997; Selvey, Denton, & Plant, 1997). However, the authors highlighted that the dose of OST used in studies was unclear, with only one study reporting mean dose, raising the possibility that under-dosing of OST might have influenced effectiveness. Moreover, the authors highlighted that PWID may present to treatment services in later years, after HCV has been contracted.

MacArthur and Hickman (2011) included a further five community-based primary studies and a meta-analysis of six UK studies. One cohort study reported lower HCV incidence among PWID in treatment for seven to twelve months but not among those in treatment for up to six months (Graine et al., 2009); one cohort study reported that MMT in the past 6 months was protective against HCV infection (Miller et al., 2004); and a third cohort study reported lower incidence among PWID in continuous compared to interrupted OST although the difference was not statistically significant (Hallinan, Byrne, & Dore, 2004). One cohort study reported no difference in risk of HCV infection among PWID recruited from NSP or OST programmes (Maher et al., 2006) and lastly a cohort study demonstrated reduced risk of HCV seroconversion among PWID with full participation in harm reduction, i.e. OST and NSP, although this was not the case when MMT was provided alone (Van Den Berg et al., 2007). Critically, however, a pooling of data from UK studies demonstrated that OST alone was associated with reduced risk of HCV seroconversion in unadjusted and adjusted analyses (Turner et al., 2011).

Overall, therefore, whilst a number of studies reported no association between OST and NSP, four robust studies reported positive findings, one of which is a pooled analysis that provides strong evidence of effectiveness using a robust study design. In light of other statements of insufficient review-level evidence in our review being based on one or fewer robust studies, but tentative statements being based on a small number of robust studies (or a larger number of weaker studies), we considered that the evidence is more consistent with the latter. We thus conclude that there is tentative review-level evidence to support the effectiveness of OST in reducing HCV transmission (Table 3).

Information, education and counselling (IEC) and outreach

Six core reviews (Copenhaver, Johnson, Lee, Harman, & Carey, 2006; Herbst et al., 2007; Needle et al., 2005; Prendergast, Urama, & Podus, 2001; Tilson et al., 2007) and two supplementary reviews (Coyle, Needle, & Normand, 1998; Hong & Li, 2009) were identified that were relevant to effectiveness of IEC in relation to IRB, HIV or HCV transmission (Table 5). We describe studies included only in these reviews since evidence from supplementary reviews did not alter the evidence statement.

Injecting risk behaviour

All six core reviews considered the impact of IEC on IRB, five of which provided tentative or conclusive evidence statements in support of effectiveness of IEC in reducing IRB (Table 3). The core reviews included twenty-eight studies. Eighteen studies were positive (seventeen of which had robust study designs), and ten showed no association (eight of which had robust study designs) (Table 3; Supplementary Table 8).

One core review (Copenhaver et al., 2006) reported findings of a meta-analysis of randomised studies relating to education, condom use and self-management skills, and drug and sex-related risk reduction. The study included twelve studies relating to IRB (Supplementary Table 8) and demonstrated that the inclusion of IEC alongside other interventions was associated with significant reductions in drug use, although no significant reductions were evident in the sharing of needles or equipment. The authors highlighted that the latter finding might be related to comparison with control conditions that were similar to the interventions being evaluated; a statement of evidence in support of behavioural interventions was nevertheless provided (Table 3).
Table 5
Summary of reviews of the effectiveness of information, education, and counselling (IEC).

<table>
<thead>
<tr>
<th>Author and date</th>
<th>Title</th>
<th>Dates covered</th>
<th>Intervention covered in review</th>
<th>Type of review</th>
<th>Number of relevant primary studies included in the review, by outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coyle et al. (1998)</td>
<td>Outreach-based HIV prevention for injecting drug users: a review of published outcome data</td>
<td>Not specified</td>
<td>IEC, Outreach</td>
<td>Supplementary</td>
<td>20 IRB</td>
</tr>
<tr>
<td>Herbst et al. (2007)</td>
<td>A systematic review and meta-analysis of behavioural interventions to reduce HIV risk behaviours of Hispanics in the United States and Puerto Rico</td>
<td>1988 to Dec 2005</td>
<td>IEC, Outreach (Latino populations only)</td>
<td>Core</td>
<td>3 IRB</td>
</tr>
<tr>
<td>Hong and Li (2009)</td>
<td>HIV/AIDS behavioural interventions in China: a literature review and recommendation for future research</td>
<td>Up to April 2008</td>
<td>HIV behavioural interventions (among other interventions like NSP and MMT)</td>
<td>Supplementary</td>
<td>1 HIV/HCV 2 IRB</td>
</tr>
<tr>
<td>Medley et al. (2009)</td>
<td>Effectiveness of peer education interventions for HIV prevention in developing countries: a systematic review and meta-analysis</td>
<td>Up to November 2006</td>
<td>Peer education in developing countries (inc ‘upper-middle income countries’)</td>
<td>Core</td>
<td>4 IRB</td>
</tr>
<tr>
<td>Needle et al. (2005)</td>
<td>Effectiveness of community-based outreach in preventing HIV/AIDS among injecting drug users</td>
<td>Not specified</td>
<td>IEC, Outreach</td>
<td>Core</td>
<td>2 HIV 4 IRB</td>
</tr>
<tr>
<td>Tilson et al. (2007)</td>
<td>Preventing HIV infection among injecting drug users in high-risk countries: an assessment of the evidence</td>
<td>Up to Jan 2006</td>
<td>IEC, Outreach</td>
<td>Core</td>
<td>1 HIV 4 IRB</td>
</tr>
</tbody>
</table>

Herbst et al. (2007) conducted a systematic review and meta-analysis of studies in Latino populations in the United States. Four studies assessed the impact of IEC on IRB (Castro & Tafoya-Barazza, 1997; Colon, Robles, Freeman, & Matos, 1993; Robles et al., 2004; Schilling, Fernando, Fontdevila, & El-Bassel, 2000). The meta-analysis reported no significant effect of interventions including IEC and/or outreach in relation to needle sharing (OR 0.92, 95% CI 0.81–1.04), but a significant effect on odds of sharing cotton or cookers (OR 0.73, 95% CI 0.63–0.85). However, the impact of confounders was not explored owing to the small number of studies included and the authors did not include a statement of evidence.

Prendergast et al. (2001) included two randomised controlled trials that examined the impact of counselling, discussion, skills building, and demonstration of condom use and syringe disinfection which demonstrated no association with IRB (Gibson, Lovelle-Drache, Young, Hudes, & Sorensen, 1999; Sorensen et al., 1994). Prendergast et al. (2001) also conducted a meta-analysis of HIV risk reduction interventions within drug treatment programmes, all of which included IEC. The study pooled data from nine studies and demonstrated a beneficial effect on ‘risk reduction skills’ (mean difference 0.62, 95% CI 0.45–0.79) but not ‘injection practices’ (mean difference 0.04, 95% CI −0.14–0.22), although these outcomes were not precisely defined (Prendergast et al., 2001). The authors concluded that IEC ‘targeted specifically at HIV risk behaviours delivered within a drug treatment program can have an impact over and above that produced by drug treatment alone’.

Tilson et al. (2007) included four studies (Colon, Sahai, Robles, & Matos, 1995; Chen & Liao, 2005; Kumar, Mudaliar, & Daniels, 1998; Neaigus et al., 1990) and cited two reviews (Coyle et al., 1998; Needle et al., 2005) and gave a tentative statement of evidence in support of IEC. However, the authors highlighted that secular trends could account for the changes observed in IRB and noted the difficulty in assessing the impact of individual interventions when several are implemented simultaneously.

One additional core review (Needle et al., 2005) was an update of an earlier review (Coyle et al., 1998) and thus only included studies published after 1998. Three additional cohort studies were included (Broadhead et al., 1998; Latkin, 1998; Wiebel et al., 1996), all of which reported a reduction in HIV-related risk behaviour associated with outreach, and the authors concluded that community-based outreach enables PWID to reduce the sharing of syringes or other drug preparation equipment.

Lastly, a recent systematic review and meta-analysis regarding the effectiveness of peer education interventions (Medley, Kennedy, O’Reilly, & Sweat, 2009) included four studies (two cohort studies and two cross-sectional studies), three of which reported a statistically significant reduction in the sharing of drug injection equipment (including needles/syringes, rinse water and/or cookers) (Broadhead et al., 2006; Hammett et al., 2006; Sergeyev et al., 1999) and one of which reported a non-significant reduction in needle sharing (Li, Luo, & Yang, 2001). The meta-analysis identified a significant reduction in equipment sharing after the implementation of the interventions (OR 0.37, 95% CI 0.20–0.67) and the authors concluded that ‘peer education interventions were associated with . . . and reduced equipment sharing among PWID’ (Medley et al., 2009).

Based on clear and tentative statements supporting the effectiveness of IEC in five core reviews, which base their conclusions
on multiple weaker studies, we concluded that there is tentative review-level evidence to support the effectiveness of IEC, particularly in outreach settings, in reducing IRB in PWID (Table 3).

**HIV transmission**

Two core reviews considered evidence relating to HIV transmission (Needle et al., 2005; Tilson et al., 2007), which identified two relevant studies (Des Jarlais et al., 1998; Wiebel et al., 1996), whilst a supplementary review (Hong & Li, 2009) identified a further cross-sectional study (Wu et al., 2007) (Tables 3 and 5). One prospective study of a street-based outreach intervention targeting social networks among HIV-negative PWID demonstrated a decline in HIV incidence over the four year follow up period (Wiebel et al., 1996), whilst the other demonstrated that outreach was associated with maintained low HIV prevalence in several cities, although it was acknowledged that the impacts of outreach could not be separated from the other interventions (Des Jarlais et al., 1998). Wu et al. (2007) reported that rates of HIV infection were lower in communities receiving outreach whilst HIV rates either remained the same or increased in control communities, and HIV incidence was significantly lower among PWID in one province of two where the intervention was implemented. Needle et al. (2005) concluded that 'community-based outreach...provides credible risk reduction information and the means for behaviour change to enable PWID populations to reduce drug use, to reduce reuse of syringes and other drug injecting equipment...' and that 'reducing risk behaviours greatly reduces HIV transmission.' Overall, however, in light of a lack of clear statements from core reviews and the small number of relevant primary studies, we concluded that there is insufficient review-level evidence to either support or discount the effectiveness of IEC and/or outreach in preventing HIV transmission.

**HCV transmission**

We did not identify any core reviews that examined the effects of IEC in relation to HCV transmission (Table 3). One supplementary review (Hong & Li, 2009) identified a single serial cross-sectional study that reported a reduction in HCV transmission associated with the introduction of a social marketing campaign in China (Wu et al., 2007). However, insufficient review-level evidence was identified to support or discount the effectiveness of IEC in relation to HCV transmission.

**Supervised injecting facilities (SIFs)**

**Injecting risk behaviour**

One core review (Tilson et al., 2007) and six supplementary reviews (Dolan et al., 2000; Hedrich, 2004; Kerr et al., 2007; Kimber, Dolan, Van Beek, Hedrich, & Zurhold, 2003; Wood, 2006; Wright & Tompkins, 2006) assessed effectiveness of SIFs (also known as drug consumption rooms) in relation to IRB (Table 6).

Tilson et al. (2007) included two cross-sectional studies relating to IRB (MSCIC Evaluation Committee, 2003; Kerr, Tyndall, Li, Montaner, & Wood, 2005). One cross-sectional study (Kerr et al., 2005) in Vancouver demonstrated a statistically significant association between attendance at the SIF and a reduction in the sharing of syringes (OR 0.30, 95% CI 0.11–0.82; p = 0.02), whilst a cross-sectional evaluation of a SIF in Australia (MSCIC Evaluation Committee, 2003) reported a non-significant difference in the use of sterile syringes and sharing of syringes or equipment among SIF clients compared to non-SIF clients. Among the additional primary studies identified in supplementary reviews, two prospective cohort studies in Vancouver (Stoltz et al., 2007; Wood, Tyndall, & Stolz, 2005) and a series of cross-sectional studies relating to a SIF in Berne, Switzerland (Nejedly & burki, 1996; Reyes Fuentes, 2003; Ronco, Spuhler, & Kaiser, 1996) reported a positive association; and

### Table 6

<table>
<thead>
<tr>
<th>Author and date</th>
<th>Title</th>
<th>Dates covered</th>
<th>Intervention covered in review</th>
<th>Type of review</th>
<th>Number of relevant primary studies included in the review, by outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dolan et al. (2000)</td>
<td>Drug consumption facilities in Europe and the establishment of supervised injecting centres in Australia</td>
<td>Up to 2000 (no dates specified in paper)</td>
<td>Drug consumption facilities</td>
<td>Supplementary</td>
<td>4 IRB</td>
</tr>
<tr>
<td>Hedrich (2004)</td>
<td>European report on drug consumption rooms</td>
<td>Up to end 2003</td>
<td>Supervised drug consumption rooms</td>
<td>Supplementary</td>
<td>1 HCV/HIV&lt;sup&gt;a&lt;/sup&gt; 1 HCV 12 IRB</td>
</tr>
<tr>
<td>Kerr et al. (2007)</td>
<td>The role of safer injection facilities in the response to HIV/AIDS among injection drug users</td>
<td>Up to 2007 (no dates specified in paper)</td>
<td>Supervised safer injection facilities</td>
<td>Supplementary</td>
<td>10 IRB</td>
</tr>
<tr>
<td>Tilson et al. (2007)</td>
<td>Preventing HIV infection among injecting drug users in high-risk countries: an assessment of the evidence</td>
<td>Up to Jan 2006</td>
<td>Supervised injection facilities</td>
<td>Core</td>
<td>1 HCV/HIV&lt;sup&gt;a&lt;/sup&gt; 2 IRB</td>
</tr>
<tr>
<td>Wright and Tompkins (2006)</td>
<td>A review of the evidence for the effectiveness of primary prevention interventions for Hepatitis C among injecting drug users</td>
<td>Up to end 2002</td>
<td>Drug consumption rooms</td>
<td>Supplementary</td>
<td>1 HCV&lt;sup&gt;a&lt;/sup&gt; 5 IRB</td>
</tr>
</tbody>
</table>

<sup>a</sup> Notifications of newly diagnosed infection.
two cross-sectional studies (Benninghoff & Dubois-Arber, 2002; Benninghoff, Solai, Hussouf, & Dubois-Arber, 2003) reported no association in reported sharing among SIF clients compared to PWID (Table 6; Table 3; Supplementary Table 9). Additional studies that were included in core and supplementary reviews that reported impacts of SIFs on injecting practices outside the remit of our study are listed in Supplementary Table 9.

Tilson concluded that ‘the evidence regarding SIFs whilst encouraging – is insufficient for drawing conclusions on the effectiveness of this intervention in reducing drug-related HIV risks among IDUs’, whilst Hedrich concluded that ‘consumption rooms, provide a hygienic environment for drug use and, for regular attendees at least, decrease exposure to risks of infectious diseases. They contribute to a reduction in levels of risk-taking among their clients.’ Kerr et al. (2007) concluded that ‘a growing body of quantitative data point to the impact of SIF use on syringe sharing’. Based on a statement of insufficient evidence from a core review, tentative statements of evidence from two supplementary reviews, and evidence from a number of robust studies, we concluded that there is tentative review-level evidence to support the effectiveness of SIFs in reducing IRB and improving injecting hygiene (Table 3).

HIV transmission

Tilson et al. (2007) included one serial cross-sectional study (also identified by Hedrich, 2004) which reported no evidence of an increase or decrease in the number of HIV infections associated with introduction of the SIF, although the authors note low prevalence of HIV among PWID over the time period of evaluation (MSIC Evaluation Committee, 2003). The authors of one of the supplementary reviews (Kerr et al., 2007) concluded that SIFs can complement HIV prevention strategies and that they can attract individuals at heightened risk of HIV infection, but no primary studies were included in the review that directly assessed HIV transmission. As such, we concluded that there is insufficient review-level evidence to support or discount the effectiveness of SIFs in relation to HIV transmission (Table 3).

HCV transmission

Tilson et al. (2007) and Hedrich (2004) reported findings of the MSIC evaluation (2003) outlined above, which reported no evidence of an increase or decrease in HCV incidence which could be attributed to the SIF. Overall, therefore, in light of the lack of robust studies relating to this outcome, we concluded that there is insufficient review-level evidence to either support or discount the effectiveness of SIFs in relation to HCV transmission (Table 3).

Discussion

In this study, we have undertaken a RoR to update and expand on a previous study by our group (Palmateer et al., 2010) relating to the effectiveness of harm reduction interventions for PWID. The RoR includes only the most robust reviews and takes into account the quality of the reviews, the conclusions of the review authors, and the design and findings of primary studies included. The updated RoR identified sufficient or tentative review-level evidence to support the effectiveness of NSP, the provision of sterile drug preparation equipment, OST, IEC and SIFs in relation to IRB or HIV or HCV transmission among PWID. However, we found a lack of tentative or sufficient review-level evidence to support effectiveness of any single intervention in relation to all three outcomes.

Evidence was strongest for effectiveness of NSP and OST; for both of these interventions we identified sufficient or tentative review-level evidence of effectiveness in relation to IRB and HIV. However, despite identifying a number of reviews and primary studies that demonstrated effectiveness of interventions in relation to IRB, we found little review-level evidence relating to the impact on HCV transmission. Whilst we cannot discount the possibility that this finding may reflect the lack of recent reviews which prevented inclusion of more recent studies relating to HCV transmission, the lack of review-level evidence is of concern given the high incidence and prevalence of HCV in PWID (Miller, Tyndall, Spittal, Li, & Laliberte, 2002; Nelson et al., 2011; Roy et al., 2006; Ruan et al., 2007; Turner et al., 2011) and the substantial morbidity and mortality associated with HCV infection (Wong, McQuillan, McHutchison, & Poynard, 2000).

However, it is possible that reductions in IRB observed in the primary studies identified are not sufficient to reduce risk of incident HCV infection. HCV has greater transmissibility via syringe sharing or needle-stick injury compared to HIV (Bell, 1997; Gerberding, 1995) and very low levels of sharing (e.g. a few times per month) may be required to have a substantial impact on the extent of HCV transmission between PWID, particularly among those that have been injecting for a number of years (Kretzschmar & Wiessing, 1998; Vickerman, Hickman, & Judd, 2007). Moreover, evidence suggests that interventions need to target recent initiators of injecting drug use as well as longer-term injectors to impact on HCV incidence (Vickerman et al., 2007).

Recent studies also report that combined provision of several harm reduction services at sufficient coverage have a greater impact on BVV transmission compared to single interventions (Degenhardt et al., 2010; Hagan et al., 2011; Turner et al., 2011; Van Den Berg et al., 2007) and it is possible that the provision of NSP or OST alone is not sufficient to impact on HCV transmission between PWID. A recent meta-analysis of UK studies demonstrated a synergistic impact of NSP and OST in relation to HCV incidence such that those receiving OST and at least one sterile needle from NSP per injection had a 79% reduction in risk of HCV seroconversion compared to those not receiving OST and with less than one sterile needle per injection (Turner et al., 2011), whilst a cohort study reported greater benefit of participation in NSP and OST compared to NSP or OST alone in relation to both HCV and HIV transmission (Van Den Berg et al., 2007). Modelling studies also suggest that NSP and OST have a greater impact on HIV incidence at higher coverage (Degenhardt et al., 2010).

Despite these findings, global provision of key interventions remains low with just 6–12% of PWID estimated to be in receipt of OST and 1–4 needles and syringes estimated to be distributed per PWID per month (Mathers, 2010; Sharma, Burrows, and Bluthenthal, 2007). Critically, provision is minimal in many of the countries where the incidence and prevalence of both HIV and HCV is highest (Mathers, 2010; Mathers et al., 2008; Nelson et al., 2011; Sharma et al., 2007). Taken together, the above studies suggest that scale up of combinations of harm reduction interventions provided with sufficient coverage is needed to impact on HCV and HIV incidence.

Where services are provided, the mode of their delivery may need to be tailored to account for different characteristics and patterns of drug use among attendees (Craine et al., 2010) to facilitate maximum attendance and thus high coverage. For instance, in relation to NSP, low prices, access to NSP, convenience of location and time, supportive attitudes, and the option to receive additional services all facilitate attendance, whilst inconvenient opening hours, a lack of privacy and a fear of being caught by police can act as barriers to attendance (Green et al., 2010; Trubnikov, Khodakevich, Barkov, & Blagov, 2003) (Cooper et al., 2011; Sarang, Rhodes, & Platt, 2008; Voytek, Sherman, & Junge (2003); Williams and Metzger, 2010). A greater awareness of preferred models of delivery of services among PWID and the impact of setting may enhance their potential effectiveness in preventing HIV and HCV infection.
Whilst much of the evidence focused on effectiveness of NSP and OST, the lack of primary and review-level evidence relating to the effectiveness of additional harm reduction interventions is of concern and must not be overlooked. Although we identified additional evidence and/or updated evidence statements following our previous study (Palmateer et al., 2010), either no reviews or insufficient review-level evidence were identified in relation to SIFs, IEC, the provision of drug preparation equipment and alternative access to NSP in relation to HCV and HIV incidence. We acknowledge, however, that SIFs are not a common intervention which may account for the lack of evidence on the effectiveness of this intervention.

Our finding is supported by recent systematic reviews that identified a small number of robust studies and a lack of effectiveness of behavioural interventions, non-OST drug treatment, and syringe disinfection in relation to HCV and HIV incidence (Hagan et al., 2011; Sacks-Davis et al., 2011; Tilson et al., 2007). Further studies are needed to examine the impact of the full range of available interventions and the effectiveness of combinations of interventions in relation to HIV/HCV incidence in PWID.

We have used a rigorous process to identify and appraise the available evidence, and have derived evidence statements in this paper based on the quality of the reviews, the conclusions of review authors, and designs and findings of primary studies included in the reviews. However, it must be noted that the ‘review of reviews’ method has limitations. It is possible that relevant primary studies might not have been included in the reviews identified; we included core reviews covering papers on the key interventions published up to 2006, and supplementary reviews covering papers published up to 2010 (up to 2007 for SIFs). The studies identified in different reviews, the extent to which authors considered bias and limitations of individual studies, and the conclusions drawn by authors were variable between reviews. The inclusion only of reviews published in the English language may also have excluded important studies.

Identification of insufficient review-level evidence relating to particular interventions does not necessarily highlight a lack of effectiveness, but rather a gap in the evidence base, a lack of adequate power to detect an effect in primary studies, inappropriate design of studies, or findings that may not yet have been published. Furthermore, variation in contextual factors between harm reduction programmes, variability in prevalence and incidence of HIV or HCV and the inclusion of PWID at highest risk, may limit the conclusions that can be drawn (Bastos and Strathdee, 2000; Bruneau, Franco et al., 1997; Bruneau et al., 1997; Strathdee, Patrick, Archibald et al., 1997).

Although we have considered the ‘weight’ of evidence primarily in relation to study design, primary studies in this field may also be at risk of bias, due to weaker study design and the inclusion of a self-selecting group of people who inject drugs that access services which may over or underestimate the effects reported (Bruneau, Franco et al., 1997; Bruneau et al., 1997; Sorensen and Copeland, 2000; Strathdee, Patrick, Archibald et al., 1997; Tilson et al., 2007). Notably, the authors of reviews identified in our study emphasized the difficulties of examining the impact of single interventions in isolation, given that other interventions may be available concurrently or may even be part of the intervention under study. Nevertheless, evidence relating to the impact of combinations of interventions is increasing.

Overall, our findings demonstrate that whilst individual harm reduction interventions such as OST, NSP or IEC can be effective in reducing HIV or HCV transmission and/or IRB, the evidence base regarding the impact of the range of harm reduction interventions on HIV and HCV transmission remains limited. Emerging evidence indicates that interventions need to be provided at high coverage and in combination to minimise the risk of HCV and HIV infection in PWID. As such, there remains a clear need to strengthen the evidence base pertaining to the effectiveness, and the impact of scaling up, of a range and combination of harm reduction interventions in different settings to prevent HIV and HCV infection across populations of people who inject drugs.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at http://dx.doi.org/10.1016/j.djuglo.2013.07.001.

Conflict of interest

Conflict of Interest to be provided at a later date.

References


