



# A literature review of the effectiveness of primary prevention measures to reduce transmission of hepatitis C infection in injecting drug users

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## Abstract

The hepatitis C virus (HCV) is an important public health problem because the majority of infections do not resolve but lead to serious long-term consequences. A high proportion of these infections are attributable to injecting drug use, making the high rates of HCV transmission in this group a serious cause for concern. There are major challenges in the development of an effective vaccine; available treatments are only partly effective and not always offered to injecting drug users (IDUs). The challenge of reducing the rate of spread of HCV infection among IDUs is considerable and must at present mainly rely on primary initiatives. A literature review of the published literature on the effectiveness of primary prevention interventions to reduce either prevalence or incidence of HCV infections was undertaken. A synthesis of main observational studies was used to determine the most effective interventions, and if there were any significant gaps in the research. The review resulted in the inclusion of 26 relevant, but not methodologically strong studies. Thus the research evidence base has been dominated by 'lower' levels of evidence, which will in turn receive lower grades of recommendation. Decreasing transmission of HCV amongst IDUs will be dependent on the commissioning of a range of prevention activities together with increased testing, diagnosis and treatment for IDUs. Needle exchange will have a key role to play in prevention strategies. Public health interventions must comprise all IDUs, including newly initiated IDUs, and must be sustained for many years to reduce HCV infection

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## Introduction

Hepatitis C is a blood-borne virus that is a major cause of chronic liver infection, which can lead to severe liver damage and even death. In recent years hepatitis C infection has emerged as a major threat to public health and World Health Organization (WHO) has declared it as a public health problem worldwide (1). It is estimated that about 3% of the world's population is infected with hepatitis C virus (HCV) with about 170 million carriers (2). Many patients, even those who are chronically infected are unaware about their illness (3). Hepatitis C infection may lead to chronic hepatitis in 50%-80% of individuals. According to WHO in 2004 the annual number of deaths due to HCV related liver cancer and cirrhosis were 308 000 and 785 000 respectively (4). The main driver of hepatitis C epidemic is injecting drug use in many developed countries,

## Key Point

Hepatitis C is a blood-borne virus that is a major cause of chronic liver infection, which can lead to severe liver damage and even death. In recent years hepatitis C infection has emerged as a major threat to public health and World Health Organization (WHO) has declared it as a public health problem worldwide. It is estimated that about 3% of the world's population is infected with hepatitis C virus (HCV) with about 170 million carriers. Many patients, even those who are chronically infected are unaware about their illness. Hepatitis C infection may lead to chronic hepatitis in 50%-80% of individuals. According to WHO in 2004 the annual number of deaths due to HCV related liver cancer and cirrhosis were 308 000 and 785 000 respectively. The main driver of hepatitis C epidemic is injecting drug use in many developed countries, although other routes of infection contribute to the overall burden of disease.



although other routes of infection contribute to the overall burden of disease. Injecting drug users (IDUs) are now the group at greatest risk of infection, accounting for up to 60% to 90% of new infections (5). The substantial morbidity and mortality attributable to HCV related chronic liver disease has become a major consequence of injecting drug use. This represents a major public health challenge for policy makers, health care professionals and the public.

## Materials and Methods

To evaluate the effectiveness of primary prevention measures in reducing the transmission of HCV infection in IDUs and to meet the objectives, a comprehensive literature review was carried out. A number of keywords regarding the subject were taken into account to identify relevant literature and the selected studies were critically appraised.

### Research question

What interventions are effective in reducing the HCV infection transmission in IDUs?

### Search strategy

Search strategy was designed to be sensitive (identification of relevant information) and specific (exclusion of irrelevant documents). Both the elements were influenced by the search terms used, and by the time period covered in the dissertation. Hence, there should be a trade-off between conducting a modest research (that may miss some information but would not affect the overall strength of findings/evidence) and an exhaustive search (additional resources of findings) (6).

### Time period

The time period that the literature search covered depended on the information available on the work done for prevention of HCV in IDUs. Some information was taken from 1985 to 2011 for the discussion and background evidence. However, in literature review only studies from 1990 to 2011 were included because they showed the detailed information.

### Replication of search results

The search strategy of literature was aimed to be transparent and clear with provision of search terms and keywords used in various databases. It was done so that the similar results could be replicable by somebody else to carry out further research and also to improve the results. All the information retrieved has been stacked and represented in the bibliography.

### Objective of search strategy

The main objective was to search, identify and critically appraise the available relevant literature in the English language to answer the defined review question, in order to assess the effectiveness of harm reduction interventions with an outcome to modify prevalence or incidence of HCV in IDUs. Also to provide summary of evidence in

order to assist with development of best practice framework to reduce HCV related disease burden among IDUs in Pakistan.

*Key search terms used:* Hepatitis C, HCV, injecting drug users, IDUs, needle exchange, needle sharing, Pakistan, transmission, prevention, prevention strategy, prevention frame work, prevention model, intervention, harm reduction, needle exchange program, primary prevention and epidemiology.

*Databases:* Keywords which are mentioned above were used in EMBASE and Ovid Medline databases. The studies were searched from period 1990 to 2011. Science Direct, Web of science by Web of knowledge and Google Scholar were also searched to find out the available relevant studies and articles by using the same search sentences and keywords. Bibliographies of every article were also carefully examined for search of any relevant studies. In order to search more relevant information Google search was also used for any additional references.

### Inclusion criteria

- Only studies published between 1990 and 2011 were reviewed.
- Only observational, interventional studies or systematic reviews were included.
- Studies explained a primary prevention intervention targeting the injecting drug with an outcome to modify either, the incidence or prevalence of HCV infection were included.
- Studies in English language
- Studies done only on human

### Exclusion criteria

- Studies which do not meet the above mentioned inclusion criteria.
- Descriptive, qualitative, editorials or opinion pieces (graded as level V, in Table 1).
- Which did not fulfil the require grade of evidence as assessed by applying critical appraisal programme assessment tool (Public Health Resource Unit 2006) and NICE/SIGN assessment tool (NICE 2006; SIGN 2001) (Section 2.9).
- Interventions targeted the general population e.g. prevention of vertical transmission or screening of the blood products.

### Data extraction

The papers included were categorised according to themes of opioid substitute treatment, needle and syringe exchange, bleach disinfectant, drug consumption rooms, and Multi-faceted harm reduction programmes.

### Validity of studies

The quality or validity of a study depends on its design, methodology and analysis (internal validity), also on populations, interventions and the outcome measures (external validity). Even within a specific design, there

is variability between different studies (7). Initially, quality assessment was used to determine a minimum quality threshold for the selection of studies to be included in the review, using inclusion/exclusion criteria and the initial screening questions from Critical Appraisal Skill Programme (CASP) assessment tool (8). Detailed quality assessment using National Institute of Clinical Excellence (NICE)/Scottish Interrogate Guidelines Network (SIGN) tool (9) followed to scrutinise the quality of included studies in order to explore quality differences as an explanation for heterogeneity in study results. This aids interpretation of the results and allows the generation of inferences to inform practice and research.

**Grade of evidence**

Papers were classified according to hierarchy of evidence used by the NHS Centre for the reviews and dissemination for epidemiological studies (7). The grading can be seen in Table 2. These studies were further evaluated by a coding system used by NICE and SIGN as shown in Table 2 (NICE, 2006; SIGN, 2001):

**Results**

This section gives an overview and the analysis of literature review. This chapter also includes evidence based key results acquired through the literature review (Table 3). By searching the key words in different above mentioned databases, the review process identified 682 abstracts and studies.

Out of 682 identified studies only 418 abstracts and studies left after excluding the duplicate studies. Two hundred seventy-three studies were excluded on basis of irrelevant titles. Out of remaining 145 studies 90 were removed on the basis of irrelevant abstract. Fifty-five abstracts and studies were further reviewed and evaluated against the above-mentioned inclusion and exclusion criteria and 29 more studies not relevant to review were excluded. In the end, only 26 studies met the inclusion criteria (Figure 1).

Out of selected 26 studies, Canadian, Asian, European, Australian and 5 Americans were 1, 1, 12, 6, and 5, respectively. In the studies there was variation in the number of IDUs taking part and the composition of IDUs population. The female to male IDUs ratio was approximately one to two. The review consisted of 1 systematic review, 2 RCTs, 3 case control studies, 8 cross-sectional studies and 12 cohort studies. On the whole, the literature review resulted in inclusion of 26 relevant but mostly not the methodologically strong studies. But the important point to note was that some studies had the clear aim to evaluate harm reduction interventions in regards of HCV infection.

**Discussion**

The evidence suggest that in spite of wide spread implementation of harm reduction strategies the incidence and prevalence of HCV still remained high in a number of studies (10). Moreover, the seroconversion of HCV among participants of different harm reduction programmes shows that the prevention which was focussed against transmission of HIV is only moderately effective in reducing HCV infection in the IDUs.

**Limitations of methodology**

The findings of the review need to be considered in context of certain limitations:

- There was limited robust literature to determine the impact of primary prevention interventions on reducing incidence and prevalence of HCV infections in IDUs. The evidence that was available had flaws in study design that compromised their ability to contribute to the evidence base.
- This review was mainly focussed on HCV infection and ideally, an effective primary intervention should reduce the risk of all blood borne viruses. Therefore, studies which were focussed on other blood borne viruses other than HCV infection might have been missed.

**Table 1.** Hierarchy of evidence for different epidemiological studies

Level	Study design
I	Interventional studies (e.g. RCTs with allocation concealment)
II	Quasi-experimental studies (e.g. interventional study without the randomisation)
III	Observational studies with control groups a. Cohort studies b. Case control studies
IV	Observational studies or cross-sectional without control groups
V	Opinion of experts based on bench research and consensus

Abbreviation: RCTs, randomised controlled trials.  
Source: NHS centre for reviews and dissemination

**Table 2.** Overall assessment of a study

Code	Criteria
++	Study fulfilled entire or most of the criteria. Where they have not been fulfilled the conclusions of a study are thought very unlikely to modify.
+	Study fulfilled some of the criteria. The criteria that have not been fulfilled or not sufficiently described are thought unlikely to modify the conclusions.
-	Study fulfilled only some or no criteria. The conclusions of a study are thought likely or very likely to modify.

Source: Methodology checklists (Nice 2006; SIGN 2001).

**Table 3.** Results of searching in Medline and EMBASE

Search keywords	No. of papers
Hepatitis C	82446
HCV	46362
Hepatitis C + HCV	84959
Injecting drug users	3370
IDU's	4304
Needle exchange	1700
Needle sharing	1445
Injecting Drug Users +IDU's+ Needle exchange +needle sharing	8042
(Injecting Drug Users +IDU's+ Needle exchange +needle sharing)+(HCV+ Hepatitis C)	1918
Pakistan	14671
(Pakistan)+(Injecting Drug Users +IDU's+ Needle exchange +needle sharing)+(HCV+ Hepatitis C)	17
Transmission	184314
(Transmission)+( Injecting Drug Users +IDU's+ Needle exchange +needle sharing)+(HCV+ Hepatitis C)	686
(Transmission)+ (Pakistan)+(Injecting Drug Users +IDU's+ Needle exchange +needle sharing)+(HCV+ Hepatitis C)	10
Prevention	348243
Prevention+(Injecting Drug Users +IDU's+ Needle exchange +needle sharing)+(HCV+ Hepatitis C)	385
Prevention+(Pakistan)+(Injecting Drug Users +IDU's+ Needle exchange +needle sharing)+(HCV+ Hepatitis C)	0
Prevention Strategy	1922
Prevention Strategy+ (Injecting Drug Users +IDU's+ Needle exchange +needle sharing)+(HCV+ Hepatitis C)	5
Prevention Strategy+ (Pakistan)+(Injecting Drug Users +IDU's+ Needle exchange +needle sharing)+(HCV+ Hepatitis C)	0
Prevention Framework	64
Prevention Framework+ (Injecting Drug Users +IDU's+ Needle exchange +needle sharing)+(HCV+ Hepatitis C)	0
Prevention Framework+ (Pakistan)+(Injecting Drug Users +IDU's+ Needle exchange +needle sharing)+(HCV+ Hepatitis C)	0
Prevention Model	201
Prevention Model+ (Injecting Drug Users +IDU's+ Needle exchange +needle sharing)+(HCV+ Hepatitis C)	0
Prevention Model+ (Pakistan)+(Injecting Drug Users +IDU's+ Needle exchange +needle sharing)+(HCV+ Hepatitis C)	0
Intervention	384674
Intervention+ (Injecting Drug Users +IDU's+ Needle exchange +needle sharing)+(HCV+ Hepatitis C)	134
Intervention+ (Pakistan)+(Injecting Drug Users +IDU's+ Needle exchange +needle sharing)+(HCV+ Hepatitis C)	3
Harm Reduction	4115
Harm Reduction + (Injecting Drug Users +IDU's+ Needle exchange +needle sharing)+(HCV+ Hepatitis C)	204
Harm Reduction + (Pakistan)+(Injecting Drug Users +IDU's+ Needle exchange +needle sharing)+(HCV+ Hepatitis C)	2
Needle exchange Program	270
Needle exchange Program+ (Injecting Drug Users +IDU's+ Needle exchange +needle sharing)+(HCV+ Hepatitis C)	27
Needle exchange Program+ (Pakistan)+(Injecting Drug Users +IDU's+ Needle exchange +needle sharing)+(HCV+ Hepatitis C)	0
Primary prevention	28933
Primary prevention + (Injecting Drug Users +IDU's+ Needle exchange +needle sharing)+(HCV+ Hepatitis C)	22
Primary prevention + (Pakistan)+(Injecting Drug Users +IDU's+ Needle exchange +needle sharing)+(HCV+ Hepatitis C)	0
Epidemiology	140957
Epidemiology+ (Injecting Drug Users +IDU's+ Needle exchange +needle sharing)+(HCV+ Hepatitis C)	179
Epidemiology+(Pakistan)+(Injecting Drug Users +IDU's+ Needle exchange +needle sharing)+(HCV+ Hepatitis C)	3

- The primary studies reviewed were almost exclusively observational. Few of the studies had the specific objective of directly evaluating harm reduction strategies in relation to HCV infection. The validity of observational studies is threatened, because of their vulnerability to selection bias, misclassification bias and residual confounding. In order to evaluate the effectiveness of such study strategies in modifying levels of HCV infection, a longitudinal design with a large number of IDUs randomly assigned to interventional group (receive the intervention) and others to control group (receive no intervention) together with a significantly high anti-HCV seroconversion rate over time would be necessary. Legal and ethical considerations preclude implementation of such an experimental study design in the face of evidence in relation to HIV transmission.
- The review considered effectiveness in terms of modifying end point measures of anti-HCV prevalence and incidence. Emphasis on these end point outcomes may well have masked the effectiveness of interventions reviewed in terms of modifying intermediate measures towards declines in anti-HCV prevalence and incidence. An example would be a lower level of engagement in HCV related risk behaviours, such as the sharing of injecting equipment. Whilst not studying the outcome of anti-HCV incidence, two observational studies conducted in America showed that the introduction of NSE led to a self-reported reduction in sharing when associated with an increase in injecting drug use, or a switch from non-injecting (10,11).
- Measuring the effects of interventions has been hampered by the fact that IDUs are a 'hidden population'.
- Time frame to review and analyse all the studies ma-

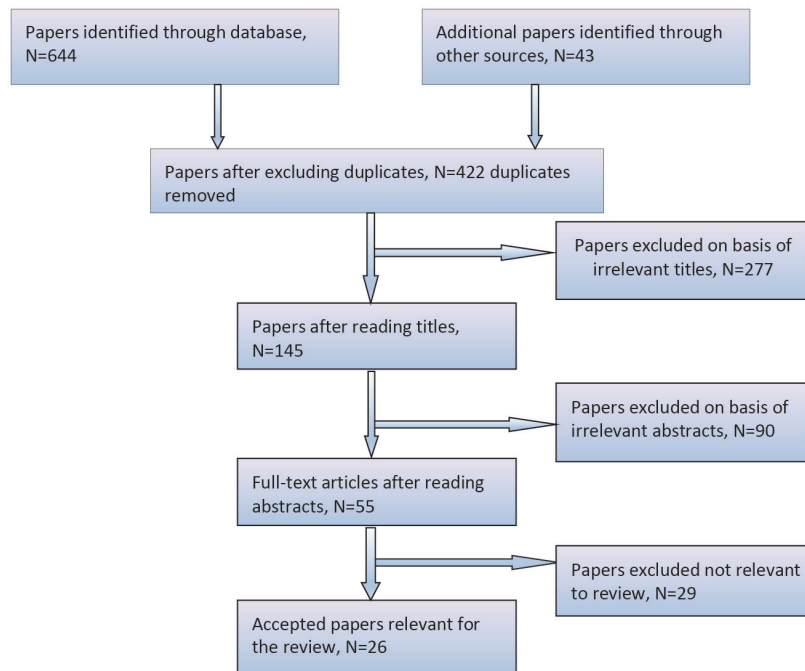


Figure 1. A flow chart of papers identified in the review.

terial was short.

- The introduction of concurrent interventions has made it difficult to attribute change to any one of them.
- The review was limited to studies in the English language only. The studies in other languages were not included, which could have been significant and relevant to answer the research question.

### Needle and syringe exchange

As already discussed in the 'Results' chapter NSE appeared to be the most effective intervention (12). In the past, evaluation of NSE effectiveness at reducing the transmission of blood borne viruses has been limited due to various reasons, such as;

- It is difficult to measure the direct effect of NSE, as mostly there is an interference with the other interventions of harm reduction causing reduction, or it may be due to effect of secondary exchange (13,14).
- MA bigger problem is that RCTs are often considered impractical.
- The political authority (which has been erratic among different countries)

Observational research came across marked difficulty in decreasing the selection bias of most high risk users into NSE which has started a controversial debate on whether the NSE leads to an increase in transmission of different blood borne viruses or not. An example of this can be seen in a study conducted in Vancouver, Canada in the year 1994, which was carried out to find out the causal association between HIV infections and NSE. In 1989 after introduction of NSE a rapid increase in the prevalence of HIV was seen. Earlier to this outbreak, the prevalence rate of HIV was very low in Vancouver and it was considered that this reduction was due to NSE effectiveness.

In the beginning a univariate analysis showed an insignificant association between the positive serostatus of HIV and recurrent NSE attendance. A lot of criticism was done against the NSE to promote the unsafe injecting drug use behaviour. In the United States, the interpretation of results was taken as an evidence of a causal association between the seroconversion of HCV and use of NSE, leading to a sustained ban on use of the federal funds to support NSE. Though, later on a multivariate analysis showed that despite the fact that cumulative incidence of HCV was markedly on higher side in the frequent NSE attendees, there was no causal association between the seroconversion of HIV and NSE attendance (15).

The NSE cost-effectiveness is an important concern for the policy makers. By using the ecological study methodology, health and ageing department of Commonwealth of Australia published a detailed report on the NSE cost-effectiveness. The results suggested that the NSE is an effective intervention in lowering the incidence of HCV and HIV infections and also represents an effectual return on the Government financial investment, calculated at lifetime saving to the treatment costs of 3653 million Australian dollars in the treatment costs. On the whole, total gain of 170279 QALYs (Quality adjusted life years) was estimated by avoiding the infections of both HIV and HCV (16).

Another research on cost-effectiveness of NSE which was carried out in the United States suggested that more broad harm reduction models along with the referral of active IDUs to the drug treatment centres, must harmonize NSE to successfully control the spread of HCV infection among IDUs (17).

### Opioid substitute treatment

Small sample size, short follow up period and usage of small doses of MMT made the results of studies equivo-

cal. The results of study suggest that MMT continuity and longer retention in the treatment plays an important role in decreasing the transmission of HCV infection. This was evident in the prisons where dropout rate is greatest during the sentences of short prison.

An important point to note is that a considerably small number of IDUs are in the drug treatment at any point in time, although centres for drug treatment have considerably expanded in the United Kingdom during the last few years. Along with that, treatment mainly drags the attention of old IDUs, in which largely have already been infected with the virus of hepatitis C; treatment through drugs may be expected to have a vague impact on the transmission of HCV (18). MMT intervention against IDUs alone is not essentially effective in preventing the spread of HCV infection. On the whole, the protective effect of opioid substitute treatment has great public health significance and it needs further research work and investigations.

### Multi-faceted harm reduction programmes

Anti-HCV prevalence in those who commenced injecting in the 1990s remained high against a background of expanded harm reduction strategies. It was hard to make a final conclusion from the evidence which was identified through the review. However, behavioural interventions which work on the principles of physiological theory (Nice 2007) along with other harm reduction interventions may provide help in reducing the incidence or prevalence of HCV infection.

### Bleach disinfection

The issue of whether to distribute bleach to IDUs has at sometimes been contentious. It has been squabbled that training the IDUs to clean syringe and needles gives bogus reassurances in regards to the danger of reusing injecting paraphernalia and also reduces health policy imperative to make sure that sufficient needles and syringes are distributed (19,20). On the other hand, studies show that the needle sharing is more likely due to lack of access of IDUs to the clean injecting paraphernalia but has acquired drugs and is in the withdrawal stage (21). Over all, further research work is required to estimate the effectiveness of bleach distribution.

### Drug consumption rooms

These are legally authorized and supervised places to control the public order and health problems related to illegal injecting of drugs. The main purpose of these places is to provide hygienic and low risk conditions to IDUs. The IDUs are allowed to inject drugs under the supervision of trained staff to avoid the risk of high drug injecting, to immediately respond to any emergency and also to make sure the hygienic ways. (18-24). In addition, no physical help is provided to IDUs for injecting drugs. There are almost 65 DCRs in 40 different cities in 8 countries around the globe. Not of all these facilities have been subjected to a thorough evaluation. One descriptive analysis in Australia suggested that no change in the notifications of incidence of HCV

infections is seen among local IDUs during an 18-month time period, in spite of getting an increase in notifications from the surrounding places. However, report shows that the due to low prevalence of infection in Australia and due to confounding factor in the study i.e. heroin drought it was hard to identify any statistically significant change (23).

A review concludes that the personalised and direct education on safer use in settings of the supervised consumption rooms plays an important role in reducing the transmission of infectious diseases even outside the room (24); Although, it is extremely difficult to show beyond doubt.

### Breaking the cycle

Reducing the prevalence and incidence of HCV infections continues to present a big public health challenge. This may be due to number of factors:

- HCV was already established in the IDUs population before the introduction of measures to reduce risks;
- Individuals with chronic HCV infection may be more infectious than those with HIV; and
- HCV may be more robust – it may be able to survive longer outside the body, and injecting paraphernalia as well as contaminated needles and syringes may also pose a risk of infection.

Parental transmission is estimated to be approximately 10 times more efficient than HIV (25) and HCV is often the first blood-borne virus (BBV) infection acquired by new initiates to injecting drug use (26). Primary prevention measures need to target IDUs very early in their injecting careers and include those at risk of starting to inject. Although not primary prevention, improved testing and diagnosis followed by treatment for patients who are infected has an important role in reducing the spread of HCV. Effective treatment, offered to IDUs can help clear the virus, thus reducing some of the reservoir of infective individuals.

### Conclusion

In order to bring the HCV epidemic under control and trim down the ongoing transmissions to the desirable sporadic level, more efficient interventions of prevention need to be identified and executed urgently. Until that time the incidence and prevalence of HCV infection will remain inevitably high. The delivery of the theoretical and ground breaking prevention interventions to IUDs have become a vital public health priority. The various HCV prevention intervention techniques do not hold strong evidence base foundation owing to the fact that the 'Gold standard' RCT cannot be performed in most of these interventions resulting in an observational study design only. Therefore the results of the research have to be categorized under the label of 'lower' levels of evidence base practice which in return makes it less applicable for being 'highly recommended'. Therefore, there is a dire need for the provision of substantial pragmatic guidance to policy makers and health officials in selecting the most appropriate prevention interventions for practice and/or future research.

### So what does work?

With no immediate prospect of a vaccine against HCV (27), over reliance should not be placed on any one harm reduction intervention to control this epidemic. The following interventions are identified as the basis of effective prevention strategy for HCV infection in IDUs:

#### Reducing the risks associated with injecting drug use

The greatest impact is likely to come from implementation of improved models of NSE. Much of the preventative work has focussed on encouraging IDUs to use sterile needles and syringes and to avoid sharing. Whilst this will continue to be a very important part of prevention, this is not sufficient to stop the spread of HCV infection. Much more attention needs to be paid to indirect sharing through distribution of injecting paraphernalia alongside needles and syringes with encouragement of IDUs never to share any paraphernalia. There is a need to ensure that all aspects of injecting process is sterile or at least clean and disinfected through the availability of high quality NSE throughout Pakistan. Supporting bleach distribution would appear to be appropriate at present. Drug consumption rooms as a hygienic place for those who engage in public injecting merit further evaluation.

Public health measures to reduce HIV risk related injecting behaviours have had an impact on HIV transmission. However, in views of the large reservoir of existing HCV infection in the IDU population and the high degree of infectivity and transmissibility of HCV per episode of blood contact compared with HIV, research should be conducted to examine the feasibility of modifying existing programmes or developing new ones that target the elimination rather than the reduction of HCV risk related injection behaviours. The degree of behaviour change necessary to control HCV is much greater than that necessary to keep HIV from spreading.

In the context of low prevalence of HIV among IDUs, it is likely that many young injectors will not know an HIV infected person. If HCV does not engender the same respect and fear among IDUs and HIV does, then it is unsurprising that the sharing of injecting equipment continues. It has been argued that a single needle/syringe sharing event is unlikely to lead to HIV infection where prevalence of HIV is low in a population. However, this may not be the case for HCV (28). If 'zero sharing' and the elimination of HCV transmission is the goal, then further efforts are needed to improve existing, and develop new measures to reduce harm in all settings. However, there is a need for further studies, powered to detect changes in prevalence or incidence, to evaluate the effect of such interventions.

#### Reducing the frequency of injecting drug use

The role of opioid substitution treatment in reducing injecting and sharing behaviour is well documented (13). High quality treatment programmes that provide optimal maintenance doses associated with complete cessation of injecting, rather than simply reducing HCV risk related injecting practices, may lower the risk of HCV infection

in current IDUs. Maximising retention in treatment is an important aspect of these programmes.

Behavioural interventions to reduce injecting risk behaviour amongst current injectors e.g. encouraging transitions to less risky non-parenteral forms of drug use such as smoking and swallowing. Intervention programmes to injecting should be developed and evaluated.

There is therefore, an urgent need for expansion of those public health interventions that are known to work, supported by pragmatic research activity to contribute to the emerging evidence base. The National Programme for Prevention and Control of Hepatitis for Pakistan provides an opportunity to focus political, research and clinical resources upon the common goals of reducing prevalence and incidence of HCV. In order to inform policy makers and public health action, good models are needed to estimate the impact of harm reduction interventions on HCV transmission. Improved surveillance to monitor trends in HCV infection is essential so that the effectiveness of prevention interventions can be measured.

#### Developing and commissioning prevention interventions

Decreasing transmission of HCV amongst IDUs will be dependent on the commissioning of a range of prevention activities together with increased testing, diagnosis and treatment for IDUs. Needle exchange will have a key role to play in prevention strategies. However, there must be political will to engage with this often polarised and still contentious intervention. Public health interventions must include all IDUs, including newly initiated IDUs, and must be sustained for many years to reduce HCV infection. In the absence of a vaccine to prevent HCV infection, effective programs must rely on changing behaviour. To date, the majority of interventions for IDUs have concentrated on HIV prevention with an ancillary focus on preventing HCV infection. The focus of public health interventions should shift to a combined focus on HIV and blood borne hepatitis. Given the over whelming burden of HCV infection among IDUs, the lack of an effective vaccine against HCV, and a treatment that is not completely effective and in many cases not offered to IDUs (29-32), the need for comprehensive and effective HCV prevention interventions is compelling.

#### Recommendations for optimum harm reduction in Pakistan

Although evidence suggests that harm reduction interventions can significantly reduce HCV transmission (33), however, in order to implement these programme more effectively in Pakistan political legitimacy and cost-effectiveness evaluation of such intervention programmes are required. The results and the conclusions of the above-mentioned studies on primary prevention interventions included in this review, have led to the following specific recommendations:

#### Recommendations for ministry of health

- The Ministry of Health should play leadership role on

bringing HCV in IDUs on the priority agenda and to obtain political commitment within the government and other relevant ministries;

- Pragmatic research activity on different harm reduction interventions to contribute to the emerging evidence base as there is limited evidence;
- Developing an effective surveillance system to monitor trends in HCV infection in order to measure the effectiveness of prevention measures;
- Reinforcing blood safety and infection control mechanisms;
- Efforts of raising awareness on HCV in IDUs as well as in general population are needed to be scaled up;
- Developing good models to estimate the impact of harm reduction interventions on HCV transmission;
- Decreasing the frequency of both direct and indirect sharing of injecting equipment and paraphernalia through high quality NSE;
- Counselling of infected persons including behavioural and psychological aspects, as an attempt to prevent transmission of HCV infection to healthy individuals;
- Improving accessibility and the effectiveness of NSE and other harm reduction services;
- Formalising referral systems with services without discriminating IDUs;
- Legislation should be done in order to respond the comprehensive service needs of IDUs in both public and private health sectors.

#### Recommendations for NGOs

- Increased capacity and mechanisms in governance, transparency accountability is essential.
- Capacity of implementation of programs and coordination need to be enhanced.
- Intensive advocacy with political leadership is required to make them realise the HCV among IUDs as public health problem and for support in response.
- Facilitating comprehensive policy dialogue, involving politicians, public departments, NGO sector and civil society.

#### Recommendations for donors

- Fill financing gaps for HCV prevention and other health care services, especially for neglected groups such as IUDs.
- Support national monitoring and evaluation and health systems strengthening for better implementations and impact assessments.

Moreover, further extensive research on harm reduction interventions as discussed earlier, is still needed to identify the most effective primary prevention intervention to reduce transmission of HCV infection among IDUs.

#### Authors' contribution

AMAA and CMJN conducted search of the papers. TK and JAA wrote the primary draft. CMJN edited the paper.

#### Conflicts of interest

The authors declared no competing interests.

#### Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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