A review of the effectiveness and cost-effectiveness of needle and syringe programmes for injecting drug users

Final full report (revised)

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GLOSSARY

Backloading	Backloading is done with insulin type syringes with fixed needles, where the plunger is removed from the recipient syringe and the drug solution squirted in through the back opening.
Bias	A systematic, rather than random, distortion of statistical results as a factor of recruitment, sampling and other procedures.
Case-Control	Comparison of exposure to interventions between participants with the outcome (cases) and those without the outcome (controls).
Cohort Study	Comparison of outcomes between participants who have received an intervention and a group that has not (i.e. not allocated by investigator) in a follow-up study.
Community Sample	Sample from general IDU population, rather than NSP using population.
Confidence Interval	A measure of precision of a statistical estimate.
Confounder	A variable that obscures or makes it impossible to interpret the relations among other variables.
Coverage	The area, groups or number of persons served or reached by a particular intervention. Also used to refer to the number of syringes distributed per injector per injection.
Crack Cocaine	Powder cocaine heated and mixed with bicarbonate of soda to form into 'rocks' for smoking or injecting.
Cross-Sectional Study	Examination of the relationship between disease and other variables of interest as they exist in a defined population at one particular time.
Distributive Sharing	Passing on used needles and/or syringes to another IDU.
Ecological Study	Study design in which the unit under study is a community or population.
Effect Size	The statistical measure of the size of the effect of an intervention.
External Validity	The accuracy of scientific results when generalized beyond the laboratory or survey situation to the real world.
Forest Plot	A common method of displaying the results from a meta-analysis. The results of each study are displayed graphically as squares centred on each study's point estimate of the intervention effect with horizontal lines representing confidence intervals (usually a 95% confidence interval) of the effect.
Frontloading	The practice of drawing up a drug solution into a 'donor' syringe and then measuring out appropriate amounts into one or more syringes.

Harm Reduction	Approach to drug use which seeks to reduce individual and social harm resulting from drug use, for example through providing sterile injecting equipment, without necessarily seeking to reduce an individual's drug consumption.
Iatrogenic	Effects induced unintentionally by a physician through his diagnosis, manner or treatment.
Injection Risk Behaviour	High risk behaviours related to injection drug use, such as receptive and distributive sharing, sharing paraphernalia and syringe re-use.
Intention to Treat Analysis	A method of data analysis in which all participants are analysed in the group they were assigned to at random regardless of treatment adherence.
Internal Validity	A standard or criteria against which research results are judged. To be internally valid the results of an experiment or of a survey are considered to be accurate indications of the manipulation of an independent variable in the case of an experiment, or of the attitudes or knowledge of respondents in the case of a survey.
Logit	The natural logarithm of the quotient of a probability and its complement.
Meta-Analysis	The combination of quantitative evidence from a number of studies.
Methadone Maintenance Treatment	Long term prescription of methadone.
Observational Study	A controlled or uncontrolled study of the effects of an intervention that did not involve randomisation.
Odds Ratio	The odds of an event occurring in one group (e.g. intervention) divided by the odds of the event occurring in the other group (e.g. control).
Opiate Substitution Therapy (OST)	Administration, sometimes under medical supervision, of a prescribed psychoactive substance, usually oral methadone, to reduce opioid dependence (e.g. heroin).
Randomised Controlled Trial (RCT)	Individuals, or defined groups of individuals (clusters), are randomised to either an intervention or a control group. If well implemented, randomisation should ensure that intervention and control groups differ only in their exposure to treatment.
Receptive Sharing	Using needles and/or syringes previously used by someone else.
Relative Risk	The risk of the event in one group (e.g. intervention) divided by the risk of the event in the other group (e.g. control).

Repeated Cross-Sectional Study	Cross-sectional studies taken at regular intervals; they differ from cohort studies in not necessarily including the same participants as at previous waves.
Seroconversion	Development of antibodies in blood serum as a result of infection.
Seroprevalence	The frequency of individuals in a population who have a particular element in their blood serum.
Shooting Gallery	Location where IDUs meet to inject; can be licit or illicit.
Speedball	The simultaneous injection of heroin and cocaine.
Sublingual	Under the tongue.
Uncontrolled Before and After Study	A study with no control group in which data is collected before and after the intervention has been administered.

ABBREVIATIONS

ACMD	Advisory Council on the Misuse of Drugs
AIDS	Acquired Immune Deficiency Syndrome
AOR	Adjusted Odds Ratio
BBV	Blood Borne Virus(es)
CBA	Cost-Benefit Analysis
CDC	Center for Disease Control
CEA	Cost-Effectiveness Analysis
CHCV	Community Health Care Van
CI	Confidence Interval
CIDUS	Collaborative Intravenous Drug Users Study
CS	Cross-Sectional Study
CT	Cohort Study
DH	Department of Health
ED	Emergency Department
EMCDDA	European Monitoring Centre for Drugs and Drug Addiction
GUM	Genitourinary Medicine
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
HPA	Health Protection Agency
ICER	Incremental Cost-Effectiveness Ratio
IDU	Injecting Drug User
IQR	Interquartile Range
IRR	Incidence Rate Ratio
JR	Job-Seeking Readiness
MI	Motivational Interviewing
MMT	Methadone Maintenance Treatment
MRSA	Metacillin Resistant *Staphylococcus aureus*
NGO	Non-Governmental Organisation
NICE	National Institute for Health and Clinical Excellence
NPV	Net Present Value
NSP	Needle and Syringe Programme
NTA	National Treatment Agency for Substance Misuse
OR	Odds Ratio
OST	Opiate Substitution Therapy
PPP	Prevention Point Philadelphia
PSE	Prison-Based Syringe Exchange
PY	Person Years
RCT	Randomised Controlled Trial
ROI	Return on Investment
SD	Standard Deviation
SR	Systematic Review
STI	Sexually Transmitted Infection
UAPMP	Unlinked Anonymous Prevalence Monitoring Programme

UBA	Uncontrolled Before and After Study
UK	United Kingdom
UN	United Nations
USA	United States of America
WHO	World Health Organisation

EXECUTIVE SUMMARY

Background

National estimates suggest that in 2005/06 there were approximately 129,977 injecting opiate and/or crack cocaine users in England. Injecting drug users (IDUs) experience high levels of morbidity and mortality and in 2006 there were 1,469 deaths relating to drug misuse in England including those who died as a result of accidental overdose, intentional self-poisoning and from drug use and drug dependence. Sharing needles and syringes is a key route by which blood borne viruses (BBV) may be transmitted among IDUs, and almost a quarter of IDUs report sharing in the previous four weeks. Sharing injecting equipment such as filters, mixing containers and water is also potentially an important route of infection, particularly in the case of hepatitis C (HCV) and almost half of IDUs have recently shared these types of injecting equipment. HCV is currently the most important infectious disease affecting IDUs, with approximately 40% of IDUs infected. In comparison, HIV prevalence rates are relatively low among IDU populations.

The first needle and syringe exchange programmes (NSPs) were established in the UK in 1985, and since then provision of these services has grown rapidly. Needle exchange services in England are based across a range of services including specialist services, pharmacies, outreach/mobile services, custody suites and A&E departments. However, over 70% of needle exchange services in England are provided by pharmacies. A recent joint report by the Healthcare Commission and the National Treatment Agency for Substance Misuse (NTA) of a three-year review of drug treatment and harm reduction services concluded that generally pharmacy and specialist needle exchanges provided a wide range of harm reduction information and advice. However, the report highlighted that there was a clear national shortfall in the provision of out-of-hours needle exchange, and that vaccination for hepatitis B (HBV), and testing and treatment for hepatitis C was not provided widely enough by local drug treatment partnerships.

Objectives

This review sought to determine the optimal provision of needle exchange schemes among IDUs. The following key research questions were addressed: (1) What level of coverage of needle and syringe programmes (NSPs) is the most effective and cost-effective?; (2) What types of NSPs are effective and cost effective?; (3) Which additional harm-reduction services offered by NSPs are effective and cost effective?;

and (4) Are NSPs delivered in parallel with, or alongside, opiate substitution therapy (OST) effective and cost-effective?

Methods

The methods for the review of effectiveness and cost-effectiveness followed NICE protocols for the development of NICE Public Health Guidance. Fifteen databases were searched for good quality systematic reviews of experimental and observational studies, randomised controlled trials, controlled non-randomised studies, controlled and uncontrolled before and after studies, cross-sectional studies, cohort studies, case-control studies, ecological studies and full economic evaluation studies published since 1990. Two reviewers independently screened all titles and abstracts. Data extraction and quality assessment of individual studies was undertaken independently by one reviewer and checked for accuracy by a second reviewer. Each study was graded (++, + or -) based on the extent to which the design and execution of the study minimised the potential sources of bias. Results of the data extraction and quality assessment are presented in structured tables and as a narrative summary. Evidence statements were developed based on the narrative summary of the evidence. These evidence statements are presented below and are numbered according to the Section that they refer to within the main body of the report.

Review of effectiveness

The review of effectiveness included a total of 10 systematic reviews and meta-analyses, and 24 primary studies[1]. Although a large number of studies were identified during the review process that had examined the effects of NSPs on risk behaviours and BBV incidence and prevalence among IDUs, few studies addressed the research questions of interest for this review.

Systematic reviews and meta-analyses

The majority of the systematic reviews and meta-analyses identified considered there to be good evidence that NSPs reduce injection risk behaviours among IDUs. However, the evidence was less clear in relation to HIV incidence; whilst two reviews considered there to be good evidence to support the effectiveness of NSPs in reducing HIV incidence, another review concluded that the evidence was less robust. Two reviews considered the impact of NSPs on the prevalence and incidence of HCV,

[1] References to the included studies can be found in the Main report

concluding that NSPs have less of an impact on HCV infection than HIV infection. None of the systematic reviews and meta-analyses identified for inclusion in the review directly addressed the research questions of interest.

Evidence statements

5.1a. There is evidence from one good quality (++) and five moderate quality (+) systematic reviews and meta-analyses that participation in NSPs reduces injection risk behaviours among IDUs, in particular self-reported sharing of needle and syringes, and frequency of injection. The evidence is not clear in relation to the impact of participation in NSPs on sharing of other injection equipment such as cookers, filters or water because few studies have examined these outcomes.

5.1b. There is evidence from two good quality (++) systematic reviews to support the effectiveness of NSPs in reducing HIV infection among IDUs. However, findings from two other systematic reviews, including one high-quality (++) review, suggest that the evidence may be less convincing. There is insufficient evidence from two systematic reviews to determine the impact of NSPs on HCV infection in IDUs.

5.1c. There is evidence from two good quality (++) systematic reviews to suggest that access to sterile needles and syringes via pharmacies provides specific benefits in addition to those available through specialist NSPs.

Primary studies

Twenty-four primary studies were identified that addressed one or more of the four key research questions. One study examined issues related to coverage, 14 studies examined different types of NSPs, seven studies examined additional harm reduction services offered by NSPs, and two studies examined NSPs delivered alongside OST. The findings of the primary research studies identified for inclusion in the reviews are discussed under the four key research questions below.

Review of cost-effectiveness

Thirteen full economic evaluations were identified for inclusion, including 12 cost-effectiveness analyses and one cost-benefit analysis. Eleven studies examined reduction in HIV incidence, one study examined HCV incidence and one study examined reductions in both HIV and HCV incidence. All 12 studies that examined the impact of NSPs on HIV infection concluded that NSPs were cost-effective, and

compared to the lifetime costs of HIV/AIDS treatment were cost-saving. Two studies examined the impact of NSPs on HCV infection but drew differing conclusions.

Evidence Statements

7.1a. There is evidence from 11 CEAs and one CBA to suggest that in terms of reducing HIV incidence and prevalence among IDUs NSPs are cost-effective.

7.1b. There is evidence from one CEA to suggest that in terms of HCV incidence and prevalence among IDUs NSPs are not cost-effective.

Applicability: Cost and benefit estimates were either based on locally derived data or from studies conducted in North America, and a range of assumptions were made limiting the applicability of the findings beyond individual studies.

Key research questions

Question 1: What level of coverage of needle and syringe programmes (NSPs) is the most effective and cost-effective?

One cross-sectional study was identified that examined individual syringe coverage among NSP participants in California. Individual syringe coverage was calculated by multiplying the number of monthly NSP visits by the participant by the number of syringes they had retained from the last visit. This was then divided by the number of illicit drug injections they reported in the last thirty days and multiplied by 100 to obtain a percentage. High levels of individual syringe coverage (150% coverage or more) were found to be associated with safer injection risk behaviours. NSP participants who were homeless, reported recent heroin injection or crack cocaine use, or were not in treatment had lower levels of syringe coverage. In a further analysis of this data, NSPs that had less restrictive dispensation policies were found to have more clients with adequate syringe coverage (100% or more); clients of unlimited needs-based distribution and unlimited one-for-one plus exchange had a higher prevalence of adequate syringe coverage compared to clients of more restrictive syringe dispensation models.

Two CEAs examined the cost-effectiveness of increasing the level of coverage of NSPs. One study that considered a hypothetical cohort of IDUs in the USA found that the programme was cost-effective across all levels of coverage and cost-saving compared to HIV treatment costs at levels of coverage up to 88.4%. A second study

examined the effects of scaling up harm reduction activities for IDU in a population with high HIV prevalence in the Ukraine. The results of the model suggested that increasing intervention coverage to the 60% target recommended by WHO/UNAIDS resulted in reductions in both HIV incidence and prevalence and that the additional resources required to achieve this level of coverage represented a 'worthwhile use of resources'. One CEA that sought to determine the optimal allocation of resources within a multi-site needle exchange programme found that cost-effective allocation within a multi-site NSP required that sites were located where the density of IDUs was highest and that the number of syringes exchanged per client was equal across sites. By way of an example, the author reported that a multi-site programme in Philadelphia, USA, could spend the same budget more effectively by equalising the number of syringes exchanged per client, which could be achieved by increasing operating hours across the sites, in particular at sites in areas of the city with a high density of IDUs.

Further modelling studies have suggested that there are critical coverage thresholds for syringe distribution that need to be reached to substantially reduce HIV prevalence among IDU populations. For example, to reduce the HIV prevalence in London to less than 1%, the coverage of syringe distribution would need to increase to 27%.

Evidence statements

6.1a. There is evidence from one poor quality (-) cross-sectional study to suggest that higher syringe coverage is associated with lower levels of injection risk behaviours among IDUs who participated in NSPs, including sharing needles and syringes, sharing cookers and syringe re-use.

6.1b. There is evidence from one poor quality (-) cross-sectional study to suggest that IDUs who were homeless, reported recent heroin injection or crack cocaine use, or were not in treatment had lower levels of syringe coverage.

Applicability: As this study was conducted in the USA, it is unclear whether the findings are applicable to the UK given the differences in the political acceptance of NSPs and wider harm reduction services for IDUs. However, the concept of coverage is applicable in terms of NSP provision in the UK.

7.1b. There is evidence from two CEAs to suggest that intervention coverage may be increased to higher levels at a low cost per HIV infection averted.

7.1c. There is evidence from one CEA to suggest that cost-effective allocation within

a multi-site NSP requires that sites are located where the density of IDUs is highest and that the number of syringes exchanged per client is equal across sites.

Applicability: Cost and benefit estimates were either based on locally derived data or from studies conducted in North America, and a range of assumptions were made limiting the applicability of the findings beyond the individual studies.

Question 2: What types of NSPs are effective and cost effective?

Few studies examined how different types of approaches to the distribution of injecting equipment impact on effectiveness and cost-effectiveness. However, based on the literature identified we were able to examine effectiveness across the following areas: 1) accessibility of NSPs based on studies of geographical proximity; 2) distribution of injecting equipment in different settings including community site, pharmacies, hospitals, vending machines and prisons; and 3) different polices on the return and distribution of needles and syringes (e.g. one-for-one exchange). In addition, one CEA was identified that sought to determine the optimal allocation of resources within a multi-site needle exchange programme.

Two cross-sectional studies that examined the impact of geographical proximity to NSPs found that IDUs living in close proximity to NSPs were more likely to utilise NSP services and report lower levels of injection risk behaviours.

Eight studies were identified which examined a variety of outcomes among IDUs depending on their main source of needles. Two RCTs, one that compared pharmacy sales only with NSP exchange plus pharmacy sales and one that compared a hospital and a community-based NSP reported no effect of setting on injection risk behaviours. However, participants who attended a hospital-based NSP had improved access to inpatient and outpatient services compared to those attending a community-based NSP. Findings from six observational studies were inconsistent and difficult to interpret, but three studies demonstrated that mobile van sites and vending machines attracted younger IDU and IDUs with higher risk profiles. Two uncontrolled before and after studies were identified that examined the role of needle exchange in prisons. The needle exchange intervention consisted of a vending machine in two evaluations and in a third evaluation social workers from a non-governmental organisation exchanged sterile syringes and equipment. Reductions in syringe sharing and HIV incidence were found.

Three cross-sectional studies examined the impact of different syringe dispensation policies on injection risk behaviours among IDUs. These studies found that syringe dispensation policies had a limited impact on behavioural outcomes such as sharing but had some impact on syringe re-use.

Evidence statements

Availability and accessibility

6.2a. There is evidence from two poor quality (-) cross-sectional studies to tentatively suggest that close proximity to NSPs can lead to greater utilisation of NSP facilities, resulting in reduced syringe sharing.

Applicability: Both studies were conducted in the USA and it is unclear whether the findings are applicable to the UK given the differences in the political acceptance of NSPs and wider harm reduction services for IDUs.

Setting

6.2b. There is evidence from two RCTs, one good quality (++) and one moderate quality (+), to suggest that NSP setting does not impact on injection risk behaviours. The evidence from six poor quality (-) observational studies is inconsistent; however there is evidence from three poor quality cross-sectional studies that mobile van sites and vending machines may attract younger IDUs and IDUs with higher risk profiles.

Applicability: As all of these studies were conducted in countries where the pharmacy sale of needles to IDUs predominated (i.e. USA, Russia and France), rather than free distribution as is the norm in the UK, it is unclear whether the findings are applicable to the UK given the differences in the political acceptance of NSPs and wider harm reduction services for IDUs.

6.2c. There is evidence from one good quality (++) RCT to suggest that providing hospital-based NSP services may increase accessibility to outpatient services among IDUs attending NSPs.

Applicability: As this study was conducted in the USA, it is unclear whether the findings are applicable to the UK given the differences in the political acceptance of NSPs and wider harm reduction services for IDUs. However, as NSPs are available in A&E departments in some areas of the UK this finding may be applicable to NSP provision in the UK.

Syringe dispensation policy

6.2d. There is evidence from one moderate quality (+) and two poor quality (-) cross-sectional studies to suggest that syringe dispensation policies have a limited impact on behavioural outcomes such as sharing but some impact on syringe re-use.

Applicability: As all three studies were conducted in the USA, it is unclear whether the findings are applicable to the UK given the differences in the political acceptance of NSPs and wider harm reduction services for IDUs. In addition, the majority of needle exchange services in the UK do not place limits on the amount of equipment exchanged.

Prison-based NSPs

5.1d. There is evidence from one moderate quality (+) systematic review that prison-based syringe exchange may be feasible in small prisons, but there is insufficient evidence to determine the effectiveness of these programmes on a larger scale.

6.2e. There is limited evidence from two poor quality (-) uncontrolled before and after studies to tentatively suggest that the provision of vending machines in prisons does not have adverse effects on HIV and HCV seroconversion and reduces syringe sharing and other injection risk behaviours.

Applicability: Both uncontrolled before and after studies were conducted in Europe, however, these findings are currently of limited applicability to the UK because of the political and ethical issues surrounding prison-based NSPs.

Question 3: Which additional harm-reduction services offered by NSPs are effective and cost effective?

Few studies were identified that directly examined the effectiveness of additional harm reduction services offered by NSPs. However, it was clear from the literature that few NSP services only distributed sterile needles and syringes, in fact the large majority were linked into wider HIV prevention services including outreach, distribution of harm reduction materials and counselling and testing.

Seven studies were identified that addressed the provision of additional services offered by NSPs beyond needle and syringe exchange, two RCTs examined

interventions to encourage IDUs into drug treatment, and one cohort study compared users and non-users of NSP-based health care services. Strength-based case management was found to support drug treatment entry among IDUs who were seeking treatment. However, the primary outcome reported was based on IDUs entering into treatment within seven days, and therefore the impact of the intervention on treatment retention was not clear. A second RCT found that motivational interviewing (MI) had no impact on the treatment interest and enrolment of NSP participants. One cohort study examined the provision of a range of health care services delivered alongside an NSP and found that emergency department use among IDUs who utilised these services was lower than among those who did not.

Four studies examined secondary distribution of needles and syringes to IDUs. Two studies found that IDUs who exclusively obtained their needles from NSPs were less likely to engage in high risk injection behaviours than those who obtained them via secondary distribution. However these studies also found that IDUs who obtained needles via secondary distribution engaged in high risk injection behaviours less than IDU who obtained no needles directly or indirectly from NSPs.

None of the economic evaluation studies identified examined the cost-effectiveness of additional harm reduction services offered by NSPs.

Evidence statements

6.3a. There is evidence from one poor quality (-) RCT to suggest that strength-based case management delivered via NSPs may support drug treatment entry among clients who request drug treatment. There is evidence from one poor quality (-) RCT to suggest that MI has no impact on the treatment interest and enrolment of NSP participants.

6.3b. There is evidence from one moderate (+) quality cohort study to suggest that the provision of NSP-based health care services may decrease emergency department utilisation.

Applicability: As all these study were conducted in the USA, it is unclear whether the findings are applicable to the UK given the differences in the political acceptance of NSPs and wider harm reduction services for IDUs. In addition, differences in the funding of drug treatment services between the UK and USA limit the applicability of these findings.

6.3c. There is evidence from one moderate quality (+) cohort study and one poor quality (-) cross-sectional study to suggest that IDUs who exclusively obtain their needles from NSPs are less likely to engage in high risk injection behaviours than those who obtain them via secondary distribution. However, there is evidence from two poor quality (-) cross-sectional studies to suggest that IDUs who obtain needles via secondary distribution engage in high risk injection behaviours less than IDU who do not obtain any needles, directly or indirectly, from NSPs.

Applicability: As all these study were conducted in the USA, it is unclear whether the findings are applicable to the UK given the differences in the political acceptance of NSPs and wider harm reduction services for IDUs. In addition, the majority of needle exchange services in the UK do not place limits on the amount of equipment exchanged, but there is little consistency regarding service providers' attitudes towards secondary distribution (NTA 2007).

Question 4: Are NSPs delivered in parallel with, or alongside, opiate substitution therapy (OST) effective and cost-effective?

Two studies were identified that examined needle and syringe distribution delivered in parallel to, or alongside OST. One study assessed the effects of enrolment in two low-threshold methodone maintenance treatment (MMT) programmes delivered via

NSPs. At six-month follow-up, the proportion of participants who were injecting drugs, sharing needles, sharing drug equipment and indirectly sharing (e.g. frontloading and backloading) had declined significantly over the whole cohort. However, within a subgroup of participants who continued to inject during follow-up, only the sharing of injection equipment declined significantly. The second study examined the impact of different levels of harm reduction on HIV and HCV incidence in a cohort of drug users in Amsterdam. A comprehensive programme of harm reduction, which the authors defined as adequate methadone therapy (≥60mg) and full participation in NSP, contributed substantially to the reduction of the incidence of HIV and HCV among drug users in Amsterdam. However, a statistically significant effect was not seen when either intervention was considered separately.

None of the economic evaluation studies identified examined the cost-effectiveness of NSPs delivered in parallel with, or alongside, OST.

Evidence statements

6.4a. There is evidence from one poor quality (-) uncontrolled before and after study to suggest that participation in low-threshold MMT programmes delivered by NSPs can reduce injection risk behaviours among drug users.

Applicability: This study was conducted in Canada and given the broad similarities in approaches to harm reduction between the UK and Canada, this finding is likely to have good applicability to the UK.

6.4b. There is evidence from one moderate quality (+) cohort study to suggest that the combination of methadone treatment and full participation in NSPs reduces the incidence of HIV and HCV among drug users.

Applicability: This study was conducted in the Netherlands and given the similarities in approaches to harm reduction between the UK and the Netherlands this finding has good applicability to the UK.

Conclusions

There is a paucity of evidence with regards to the optimal provision of NSPs and it is therefore difficult to draw conclusions on 'what works best' within the range of harm reduction services available to IDUs. However, it is apparent from the literature that the distribution of sterile needles and syringes alone is not sufficient to reduce the transmission of BBVs among IDUs, especially the transmission of HCV. Programmes that deliver a comprehensive range of harm reduction services and which are easily accessible to IDUs may prove to be effective and cost-effective but further high quality research is urgently required.

1 INTRODUCTION

1.1 Aims and objectives

This review was undertaken to support the development of guidance on the optimal provision of needle exchange schemes among injecting drug users.

1.2 Research question

The following key research questions were addressed:

1. What level of coverage of needle and syringe programmes (NSPs) is the most effective and cost-effective?

Sub-questions considered the impact of the following components on effectiveness and cost effectiveness:

- Diversity of the population (e.g. age, gender and ethnicity);
- Types of drugs injected;
- The injecting environment;
- Whether or not users are homeless.

2. What types of NSPs are effective and cost effective?

Sub-questions considered the impact of the following components on effectiveness and cost effectiveness:

- Provider (including skill mix and level of training/competency of staff), site and size of setting;
- Availability (opening times) and accessibility;
- Geographical setting;
- Type of injecting equipment supplied;
- Return policies on used equipment.

3. Which additional harm-reduction services offered by NSPs are effective and cost effective?

Sub-questions considered the impact of the following components on effectiveness and cost effectiveness:

- Provision of additional harm-reduction equipment such as filters, mixing containers, sterile water;
- Availability of additional harm-reduction interventions such as advice and information on safer injecting practices, treatment for injection site infections,

onsite vaccination services, testing for hepatitis B and C and HIV, pre- and post-diagnostic counselling and general health advice;

- Provision of spoken vs. printed advice and information;
- Services which promote, or refer people to, a range of additional support services (including drug and alcohol treatment and support services, specialist support for those engaged in high-risk injecting methods, emergency referrals to secondary care, GP registration, dental care, safer sex/sexual health advice and condom distribution; referral to primary care services, and welfare, housing and legal advice);
- Encouraging current (or employing former) injecting drug users to deliver injecting equipment to their peers.

4. Are NSPs delivered in parallel with, or alongside, opiate substitution therapy (OST) effective and cost-effective?

2 BACKGROUND

2.1 Prevalence of injection drug use

Although the true extent of injecting drug use in the population is difficult to determine, national estimates for 2005/06 suggest that there are 129,977 (95% CI: 125,786 to 137,034) injecting opiate and/or crack cocaine users in England (Hay et al 2007), approximating to 3.90 per 1,000 of the population aged 15 to 64. The prevalence of injecting drug use varies across regions, ranging from around six per thousand in Yorkshire and the Humber to around three per thousand in London, the East of England and the South East. However, these estimates do not account for injectors of other drugs such as amphetamines and anabolic steroids. Although data on the number of amphetamine injectors is not readily available, according to the 2007 British Crime Survey, 0.2% of 16-24 year olds and 0.1% of 16-59 year olds in the United Kingdom have used anabolic steroids in the last year. Of these, a high proportion inject, with around 60% of anabolic steroid users reporting that they inject the drug (Korkia & Stimson 1993).

Data also suggest that injecting drug use prevalence is increasing over the long term (HPA 2007a). While there is some uncertainty about the size of the current IDU population in England, it has increased substantially since the 1986 Advisory Council for the Misuse of Drugs (ACMD) estimate of 37,000-75,000 IDUs for England and Wales (ACMD 1988).

2.2 Morbidity and mortality associated with injecting drug use

Injecting drug users (IDUs) experience high levels of morbidity and mortality. In 2006, there were 1,469 deaths relating to drug misuse in England including those who died as a result of accidental overdose, intentional self-poisoning and from drug abuse and drug dependence (ONS 2007). In addition, IDUs may experience poor health from a range of conditions including infectious diseases and injection site infections (HPA 2007a).

2.2.1 Blood borne viruses

HIV

HIV and AIDS remain a major concern in the UK, with 6,393 new HIV diagnoses in 2007, but HIV infection among IDUs is relatively uncommon. As shown in Table 1, 110 (2%) new diagnoses of HIV were thought to have occurred as a result of injecting drug use in 2007 (HPA 2007b). The proportion of new HIV diagnoses

thought to have been acquired through injecting drug use has fallen from around 7% in 1993 to around 2% in 2006. HIV prevalence rates among IDUs remain low with a cumulative total of 4,790 HIV diagnoses reported in the UK up to the end of 2007 (HPA 2007b).

Table 1. Individuals newly diagnosed with HIV in the UK, 2007

Exposure category	N (%)
Heterosexual contact	2732 (43%)
Sex between men	2145 (34%)
Injecting drug users	110 (2%)
Other/undetermined reasons	1406 (22%)

However, there is some evidence of ongoing and possibly increased incidence among active IDUs. Hope et al (2005) reported that although HIV prevalence among IDUs declined between 1990 and 1996, and remained stable at this level until 1999, HIV rates rose in 2003 and rates are still higher than those seen in the 1990s.

Hepatitis C

While HIV prevalence rates remain relatively low and stable among IDU populations in the UK, the same cannot be said for HCV. The majority of the 62,424 reported laboratory diagnoses of HCV infection in England reported up to the end of 2006 were probably acquired through injecting drug use and over 90% of those diagnoses with risk factor information reported injecting drug use as the route of infection (HPA 2007a). There has been a substantial rise in the number of diagnoses since HCV testing was introduced in the early 1990s, however this rise is more likely to reflect an increase in numbers tested, rather than in transmission. To counter this, HCV rates among recent IDU initiates can also be used as a measure of recent transmission. Among participants in the Unlinked Anonymous Prevalence Monitoring Programme (UAPMP) survey, the prevalence rate prior to 2001 was 11%, but has increased to – although remained stable at – 21% in the period 2001 to 2005. The UAPMP survey reported a HCV prevalence rate of 56% among IDUs in London and 37% outside London, the same prevalence rates as for 1998, although absolute numbers of infections have decreased since then.

Hepatitis B

The UAPMP survey also found increased prevalence of HBV among IDUs. Rates of infection have risen from 3.4% in 1997 to 10% in 2006. In 2006, within London the prevalence of hepatitis B among IDUs was 34% and 18% outside of London. Whereas HCV prevalence appears to have remained relatively stable, HBV

prevalence among IDUs outside of London has decreased since 1996 (from 23% to 18%) but continued to rise among London IDUs (from 22% to 34%).

2.2.2 Overdose

Data on the number of drug-related deaths in England have been reported since 1993. After a general increase in the number of deaths up to 2001, followed by a general decline and then an increase in 2004, currently drug related deaths are at their lowest since 1995. In 2006, 1,782 male and 788 female drug related deaths were recorded (ONS 2007). Although the number of heroin-related deaths has decreased over the years, it remains the largest cause of drug-related deaths and there continues to be a long term upward trend in deaths involving cocaine. In a study of drug-related overdose deaths in London in 2003, Hickman et al (2006) found that the majority of deaths were among people with a history of dependent drug use and injecting drug use.

2.2.3 Other health risks

IDUs are also at risk of wound site infections resulting from injecting contaminated drugs and/or non-sterile injecting equipment. Thirty-five percent of IDUs participating in the 2006 UAPMP survey reported experiencing an abscess, sore or open wound, or possible symptoms of an injecting site infection during the previous year. Elevated levels of wound site infections appear to be associated with homelessness, injecting in the legs, injecting in the hands and injecting crack cocaine within the previous four weeks.

Wound site infections to which IDUs are particularly vulnerable include tetanus, *Staphylococcus aureus*, Group A streptococcus and wound botulism. The prevalence of tetanus among IDUs in the UK is low, with only two of the 175 reported cases of tetanus identified in England and Wales between 1984 and 2000 known to have occurred in IDUs. This is in contrast to the USA, where IDUs accounted for 17% of cases between 1995 and 2000 (CDC 2003). However, in 2003 there was an outbreak of tetanus among UK IDUs, with most of those infected reporting ‘skin popping’ (the subcutaneous injection of heroin). Many were un-immunised or partially immunised and the distribution of the cases suggests that the outbreak may have been due to heroin contamination, rather than injection practices. This outbreak has led to an updating of vaccination guidance for IDUs to ensure tetanus immunisation status is actively checked (HPA 2007a).

Wound botulism occurs when wounds, such as injecting sites, are infected with *Clostridium botulinum*. Wound botulism among UK IDUs is rare, and prior to 2000 no cases had been reported among IDUs although by the end of 2006, 134 cases had been reported, with at least seven fatalities. *Staphylococcus aureus*, on the other hand, is a common pathogen among IDUs, and causes infections which can vary in severity from minor skin and soft tissue infections to life-threatening invasive disease such as bacteraemia and endocarditis. Between April 2003 and March 2007, 60 cases of sepsis due to MRSA were identified among IDUs in England and Wales, 50% of whom presented with injection site abscesses or skin infection. Group A streptococci can also cause skin sepsis and bacteraemia, and injecting drug use is a key risk factor with 20% of reports of Group A streptococcus in the UK being related to injecting drug use. However, the numbers of infected IDUs are diminishing and reported cases of Group A streptococcus have decreased in recent years (HPA 2007a).

2.3 Risk behaviours

Injection risk behaviours among IDUs have a wider public health impact, as the sharing of injection equipment and paraphernalia can be important risk factors for the transmission of blood borne viruses such as HIV, HBV and HCV both within the IDU population, through sexual transmission to the wider non-IDU population and vertically through pregnancy and childbirth.

The transmission of blood borne viruses among IDUs occurs primarily as a result of blood contact, particularly when IDUs share syringes and/or needles, but also potentially through the sharing of other types of injecting equipment such as spoons, filters, swabs or water (Van Beek et al 1998). Box 1 gives an overview of how the major drugs are prepared for injection and describes the role of injecting paraphernalia in the preparation process.

Box 1. Preparing drugs for injection

Preparing different drugs for injection

Heroin – The drug is mixed with water in a suitable receptacle, usually a spoon. An acidifying agent is added and the solution heated to help the heroin dissolve. Once cool the solution is drawn into the syringe, usually through a filter.

Amphetamine – Amphetamine sulphate powder does not need to be heated or acidified in order to dissolve for injection. The preparation process is otherwise similar to that of heroin for injection, although it may also be mixed in the syringe.

Cocaine – The preparation of cocaine hydrochloride for injection is similar to that of amphetamine, although some cocaine injectors may mix the solution in the syringe. An acidifier is needed to prepare crack cocaine for injection.

Injecting paraphernalia

Water – Used to dissolve certain drugs and for cleansing injection sites. Drawing up from a pot of communal water represents a risk behaviour for the transmission of hepatitis and HIV.

Swabs – Used to wipe and cleanse injection sites prior to injecting to reduce bacteria which may be present on the skin.

Spoons or other mixing containers – Used for mixing drugs (e.g. with water and/or citric acid) to prepare them for injection. Contact of the spoon with another person's needle, which has previously been used, may be enough to transmit some infections such as HCV.

Acidifiers (e.g. citric acid) – Used to dissolve brown heroin and crack cocaine for injection. Acids such as lemon juice and vinegar may contain bacteria or already be contaminated with HIV or hepatitis. Lemon juice has been associated with thrush and other fungal infections, leading to retinal damage. Ascorbic acid and citric acid, which can have been legally supplied by NSPs since 2005, are safer but can cause irritation to veins and tissues.

Filters – To filter out solid debris before injecting. IDUs may use improvised filters such as cotton wool, cigarette filters or filters obtained from NSP. Filters may be saved after injecting and re-used or shared and thus spread BBVs and/or bacterial infections. Also loose fibres can be drawn into the syringe and injected, causing circulatory problems.

Tourniquets – Used to raise veins. Tourniquets can cause limbs to be deprived of their blood supply if left in place too long. If not loosened prior to injection, the pressure in the veins may be raised risking rupture or leakage of the drug into the tissue. Tourniquets contaminated with blood and subsequently shared represent a HCV transmission risk.

Adapted from *The Safer Injecting Briefing* (Derricott et al 1999)

Almost a quarter (23%) of UAPMP respondents reported sharing needles and syringes in the previous four weeks. Sharing filters, mixing containers and water was more common, and almost half of UAPMP respondents (45%) reported that they had

shared these types of paraphernalia within the previous four weeks. Different transmission rates for HIV and HCV have been identified. In a longitudinal study (1983-1994) of HIV positive IDUs and their HIV negative heterosexual partners in Scotland, Wyld et al (1997) found that among 31 injecting drug using couples, 52% seroconverted for HIV and 80% seroconverted for HCV, whereas among 30 non-injecting couples, 40% seroconverted for HIV and there were no seroconversions for HCV.

2.4 Special populations

2.4.1 Female injectors

Estimates for 2005/06 indicate that approximately one quarter of all problem drug users (opiate and crack cocaine users) are female (Hay et al 2007), and drug use among females may be linked to specific behaviours and lifestyles that put them at an increased risk of HIV and hepatitis infection (NTA 2002). Studies have found that female injectors are more likely to require help injecting (Krall et al 1999; O'Connell et al 2005), that they are more likely than males to report injecting with used equipment which they obtained from a sexual partner (Davies et al, 1996), and that they are more likely than men to have a sexual partner who also injects drugs (Davies et al, 1996, Gossop et al, 1994).

Female drug users have been identified as being underserved by drug misuse services by the NTA and women are likely to be underrepresented in the majority of needle exchanges as they may be reluctant to use these services due to fears of stigmatisation or embarrassment (Barnard 1993). Further discussion of the barriers to use of NSPs by women is presented in the Qualitative review (Cattan et al 2008).

2.4.2 Steroid injectors

A high proportion of anabolic steroid users inject, although there does appear to be gender bias, with more women using oral steroids only and more men combining injection and oral routes of transmission (Korkia and Stimson 1993). Among 'hardcore' gym users in the North West ('hardcore' here defined as being characterised by having predominantly heavy weight training equipment, competitive body building and relatively few female members), the majority (81%) injected anabolic steroids. Of these injectors, approximately a third reported only injecting and almost half combined oral and injection routes of transmission (Lenehan et al 1996). A recent study of 50 anabolic steroid users, also found that the vast majority (94%)

were currently injecting the drug (Midgley et al 2000) and 66% reported using needle exchanges as a source of clean injecting equipment.

McVeigh et al (2003) identified a statistically significant decrease in the proportion of new NSP clients in the North West of England reporting heroin use. However, the proportion reporting anabolic steroid use over the same period increased (from 6% to 44%). In addition, Lenehan and McVeigh (1996) reported that anabolic steroids were the second most commonly injected drug among needle exchange clients in the North West in 1995. Thus an increasing proportion of NSP users are anabolic steroid/PIED users. However, there is evidence to suggest that these injectors use NSPs differently to other client groups, making fewer visits per year and collecting large numbers of syringes in a single visit (over a quarter of all NSP transactions by anabolic steroid users involved the provision of 100-1,000 syringes) (McVeigh et al 2003). This has implications for secondary exchange and syringe sharing. Midgley et al (2000) report that in terms of injection risk behaviours among anabolic steroid users, the most widely-reported risk practice was having ever shared multi-dose vials followed by dividing drugs using syringes. They note that these practices are only risky if injectors are re-using injecting equipment and few reported these behaviours.

McVeigh et al (2003) suggest that the increasing presentation and attendance of anabolic steroid users at NSPs raise issues regarding current knowledge, skills and resources provided by NSP staff for this client group. While some services have been proactive in attracting this client group, many have not. The differences between this groups and other IDUs (in terms of lifestyle, injection frequency and preference for intramuscular over intravenous injection) indicate a need for the implementation of specific harm reduction advice targeted towards this group. For significant numbers of anabolic steroid injectors, NSPs constituted the only point of contact for harm reduction and health intervention relating to their drug use (McVeigh et al 1996).

2.4.3 Recent initiates to injecting

In 2006, 90% of current and ex-IDUs participating in UAPMP reported that they had ever accessed an NSP, however among recent initiates (those who reported first injecting within the previous three years), the rate was lower at 85% (HPA 2007). Studies in the UK have observed higher rates of HCV infection in younger injectors and those in the early years of their injecting career (Hickman et al 2007). Studies conducted internationally have also found that recently initiated IDU have higher HIV and HCV seroincidence than IDU with longer duration of use (Garfein et al 1998; Nicolosi et al 1992; van Ameijden et al 1992). A Canadian study (Miller et al 2007),

which explored longitudinal drug use and sexual risk patterns among IDUs, identified that factors associated with younger age included borrowing syringes, and frequent injection of heroin, cocaine, and speedballs. In addition, young IDUs were found to be less likely to access drug treatment or methadone maintenance therapy. These studies highlight the need for services to intervene early in drug users' careers and the need for intervention tailored to young people.

2.4.4 Crack cocaine injectors

There is concern about the associations between crack cocaine use and higher levels of HCV infection and injection risk behaviours (HPA 2007a); 59% of crack cocaine injectors interviewed in the UAPMP survey had HCV, compared to 34% of those who did not inject this drug. There is evidence that the use and injection of crack cocaine is becoming increasingly common, with around one third of UAPMP respondents reporting that they had injected the drug (HPA 2007a). Crack cocaine injection is associated with high risk behaviours such as equipment sharing and frequent injection (HPA 2007a). As frequent injection can lead to vein collapse, frequent injectors are more likely to inject in higher risk parts of the body (e.g. the legs, hands, feet and groin). There is some evidence that high risk injection practices are becoming increasingly common and acceptable, with 45% reporting groin (femoral vein) injecting in a survey of IDUs in English cities (Rhodes et al 2006).

2.4.5 Homeless injectors

Homelessness is another risk factor for BBV transmission, with 25% of homeless UAPMP respondents reporting equipment sharing in the previous four weeks compared to 16% of non-homeless/securely housed respondents (HPA 2007a). Similarly, the results of the National Public Health Service for Wales, 2004 cohort study showed that 29% of those who reported having been homeless in the previous year also reporting sharing equipment in the previous year, compared to only 14% of housed respondents. In a study of injecting practices in homelessness hostels in Glasgow, Wadd et al (2006) reported a significant association between living mostly in a hostel in the six months prior to interview and high-risk injecting behaviour, such as injecting with and passing on previously used needles and syringes. In addition to homelessness being associated with elevated levels of HCV and increased levels of high risk behaviours such as receptive and distributive equipment sharing, among UAPMP respondents, those who had been homeless during the previous year were more likely to report wound site infections at injecting sites, abscesses and open sores (HPA 2007a).

2.5 A brief history of harm reduction and the emergence of NSPs

In response to the global HIV epidemic, the first needle exchange was opened in Amsterdam in 1985 by the drug user organisation Junkie's Union, which soon came to be supported by the Municipal Health Department of Amsterdam. This exchange had the goal of providing clean injection equipment to IDUs in order to reduce the transmission of HIV among IDUs and therefore between IDUs and the wider population through sexual transmission (van den Hoek et al 1989).

According to Stimson (1995), the first case of AIDS in an IDU in the UK was reported in March 1985. The first UK-based needle exchange was opened in Peterborough in April 1986 and followed that same year by a further five across England and Scotland (Surrey, Dundee, Swindon, Sheffield and Liverpool). Early in 1985 the ACMD had considered syringe distribution but rejected it following a lack of evidence that injectors shared needles and syringes due to a lack of access to clean equipment. Later in the year, following the opening of these six NSPs, the Department of Health and Social Security and the Scottish Home and Health Department supported 12 pilot needle exchanges in England and three in Scotland, mandated to provide advice and counselling on drug misuse, HIV risk and safer sex as well as distribute clean syringes.

The early history of NSPs in the UK is characterised by more than simply the opening of needle exchanges. The emergence of HIV (with prevalence rates as high as 51% among Edinburgh IDUs) marked a profound shift in attitudes and government policy from encouraging abstinence to advocating harm reduction or harm minimisation policies. As the ACMD reported in *AIDS and drug misuse* (1988),

> 'The spread of HIV is a greater danger to individual and public health than drug misuse. Accordingly, services that aim to minimise HIV risk behaviour by all available means, should take precedence in development plans…. In particular, we must recognise that, for the time being, many drug misusers will not be sufficiently motivated to consider abstinence and that many drug injectors will not be sufficiently motivated to change their routes of administration' (1988: 17).

Concurrently with this, although syringe sales were and are legal in the UK, in 1982 pharmacists initiated a voluntary ban on sales, a decision which was rescinded in 1986. This paradigm shift moved attention away from dependence and addiction to the health of drug users, and these early NSPs often distributed alcohol wipes with

clean syringes to reduce the incidence of bacterial site infections as well as the transmission of blood borne viruses.

Following the opening of the 15 pilot schemes in 1987, the number of agencies providing syringes grew from 15 in 1987 to over 200 in 1990. About two-thirds of all drug agencies were involved in some kind of syringe distribution, including some which also initiated outreach services, with drugs workers taking syringes to IDUs' homes and to popular drug using venues. It is important to note that alongside this change in attitude away from encouraging abstinence towards harm reduction, the reinstating of pharmacy syringe sales and the piloting and expansion of syringe-exchanges, a range of literature including posters, leaflets and comics emerged which promoted and encouraged safer injection practices. Since then, NSPs have gone on to expand in number and in terms of the services provided, with many offering condoms, referrals, hepatitis B vaccination and HIV and hepatitis testing in addition to providing clean injecting equipment and paraphernalia. In addition to providing a range of injection harm reduction measures, some NSPs also offer (supervised) methadone maintenance treatment (MMT). The use of methadone as an abstinence and maintenance measure has expanded significantly in the years since 1986.

In 2003, changes were made to section 9a of the Misuse of Drugs Act 1971 (Anon 2003) to allow providers of needle exchange services to supply five types of injection equipment to IDUs: ampoules of water for injection, swabs, utensils (spoons, bowls, cups, dishes), citric acid and filters. Previously it had been an offence to supply or offer to supply these items to IDUs. In addition, in 2005 ascorbic acid was permitted as an alternative acidifier to citric acid (Anon 2005a) and the supply of water for injection ampoules of 2 mls or less without prescription was allowed (Anon 2005b).

2.6 NSPs and pharmacies

Following the decision in 1986 to rescind the voluntary ban on pharmacy sales of syringes to IDUs in the UK, it has remained possible to purchase syringes from pharmacies, and additionally, many pharmacies also participate now in needle exchange. According to the EMCDDA, in 2004 there were a total of 1,764 pharmacies participating in needle exchange in England, Scotland and Northern Ireland (and 162 in Wales, 2003). While syringe sales are legally permitted in UK law, according to the 2001 update of the Code of Ethics and Standards for the Royal Pharmaceutical Society for Great Britain,

> 'Only in exceptional circumstances should pharmacists supply clean injecting equipment for drug misusers if the pharmacy has no arrangements for taking back contaminated equipment. Purchasers of injecting equipment should be advised of the availability of disposal facilities at the pharmacy and should always be encouraged to dispose of used syringes and needles safely'.

Therefore, while pharmacy sales of syringes may take place in the UK the lack of arrangement for the return of used equipment places the pharmacist in contravention of the RPSGH Code of Ethics and Standards. By contrast, in some parts of the USA, Canada and elsewhere in the world, pharmacy sales are legal, potentially limiting the applicability of some of the findings discussed here to the UK.

2.7 Current levels of provision

A 2005 survey of needle exchanges in England by the NTA identified that needle exchange services in England were based in specialist services, pharmacies, outreach/mobile services, custody suites and A&E departments (NTA 2007a). However, over 70% of services were provided by pharmacies. Service provision and the range of harm reduction interventions differed between regions. While there were no regional differences in the provision of injecting paraphernalia, face-to-face harm reduction advice and referral to structured treatment, there were significant differences in the provision of BBV-related interventions, including on-site hepatitis B immunisation, and hepatitis B and C testing on-site. Services in the South West and West Midlands regions were least likely to provide these interventions.

Results from the survey of drug services indicated that the majority of services offered needle exchange during 9 to 5, Monday to Friday, with a much smaller number of services available at the weekends. Services reported variation in the types of paraphernalia distributed to service users. The majority of services surveyed provided sharps bins and condoms, but there were significant differences across regions in the provision of citric acid and spoons. The majority of services had a returns policy whereby the service encouraged returns but this was not a condition for assessing sterile injecting equipment. There was variation between services in the maximum number of syringes distributed at any one contact. The results of the survey of pharmacists indicated that there was little uniformity in the services provided across England. Pharmacy schemes on the whole tended to provide needles and syringes, sharps bins, wipes, swabs and condoms, but fewer schemes provided other types of paraphernalia, and provision of BBV-related interventions and other harm reduction initiatives was limited. Pharmacy schemes provided good

access Monday to Friday, but as with specialist needle exchange services, services were significantly reduced at evenings and weekends.

A recent joint report by the Healthcare Commission and the NTA (2008) of a three-year review of drug treatment and harm reduction services concluded that there was good progress relating to harm reduction services in England and that generally pharmacy and specialist needle exchanges provided a wide range of harm reduction information and advice. However, the report also highlighted that there was a clear national shortfall in the provision of out-of-hours needle exchange, and that vaccination for hepatitis B, and testing and treatment for hepatitis C was not provided widely enough by local drug treatment partnerships.

A national hepatitis B vaccination strategy for IDUs was first recommended in 1988 but uptake among IDUs in England has previously been found to be poor (Lamagni et al 2001). Since then, additional funding has been allocated to local health authorities to expand hepatitis B vaccination provision and a prison vaccination programme established. Hope et al (2007) reported that uptake and course completion of the hepatitis B vaccine rose significantly between 1998 and 2004 indicating a considerable improvement on previous levels. The authors considered that the introduction of the prison vaccination programme was likely to have made a substantive contribution in recent years.

2.8 Government policy overview

Since the late 1990s the focus of policy around drug use has broadened from a public health perspective to also include the minimisation of wider social harm, including crime and anti-social behaviour. The 1998 government ten year drugs strategy, *Tackling drugs to build a better Britain*, identified the need for further action to 'improve the health of drug misusers and drive forward action to reduce the risk of death'. The 2008 updated drugs strategy, *Drugs: Protecting families and communities*, continues in the same vein, stating an intention to:

> 'Continu[e] to promote harm minimisation measures including needle exchange and drug-assisted treatments that encourage drug users to enter treatment, in order to reduce the risk of overdose for drug users and the risk of infection for the wider community' (2008: 29).

Following a rise in drug-related deaths in 2005, the government launched an action plan to reduce drug-related harm, which was aimed at directly reducing the number of drug-related deaths and BBV with wider goals of preventing drug misuse and encouraging stabilisation in treatment and support for abstinence (DH 2007). In

addition, there has been growing recognition of the need to reduce HCV transmission in IDU populations. Since the publication of *Getting ahead of the curve* (DH 2002), hepatitis C has been identified as needing 'intensified action' to improve its prevention, diagnosis and treatment. IDUs have been identified as a particular target due to the high rates of transmission as a result of injection equipment and paraphernalia sharing. Initiatives include developing clinical networks for the assessment and treatment of patients with HCV and the provision of services for particular groups of patients, including those who may experience social exclusion, such as prisoners and IDUs. Increased monitoring will enhance the targeted delivery of treatment in the future.

Harm reduction recognises the importance of reducing the risks associated with drug misuse by providing means of reducing sharing of injecting equipment, providing support in stopping injecting, providing opioid substitution therapies (OSTs) for heroin users and supporting the transition to abstinence from illegal drugs. Most harm reduction interventions specifically aim to prevent the transmission of BBV infections and other drug related harms, including overdose and drug-related deaths. These include: needle exchange services offering injecting equipment and paraphernalia; advice and support on safer injecting; reducing injection frequency and reducing initiation of others into injecting; advice and information on preventing the transmission of BBVs and other IDU-related infections; advice, information, counselling and testing for hepatitis and HIV; the provision of hepatitis A and hepatitis B vaccinations; advise and support on prevents risk of overdose and drug-related death; risk assessment and referral to other treatment services (Abdulrahim et al 2006).

3 METHODOLOGY

3.1 Search strategy

A database of published and unpublished literature was compiled in the Reference Manager software package from systematic searches of electronic sources and websites, searching reference lists of relevant systematic reviews. Relevant articles, published since 1990, were identified by searching the following health and social care databases and relevant websites:

- Medline
- Embase
- PsycINFO
- International Bibliography of the Social Sciences (IBSS)
- CINAHL
- Health Information Management Consortium
- The Cochrane Library (Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effect, Health Technology Assessment and Cochrane Controlled Trials Register)
- American College of Physicians (ACP) Journal Club
- Applied Social Science Index and Abstracts (ASSIA)
- Sociological Abstracts
- Evidence for Policy and Practice Information and Co-ordinating Centre (EPPI-Centre) databases
- National Research Register Archive
- OpenSIGLE (System for Information on Grey Literature in Europe)
- Project CORK
- SozialMedizin (SOMED)

Economic evaluation studies were identified by searching the following major health economic databases:

- EconLit
- NHS Economic Evaluation Database (NHS EED)
- Health Economic Evaluation Database (HEED)

All search strategies were developed and executed by information staff at the Support Unit for Research Evidence (SURE) at the University of Cardiff.

3.2 Inclusion and exclusion criteria

3.2.1 Population

Studies were eligible for inclusion if they included people who were currently injecting drug users[2] including those who inject:

- Opiates (e.g. heroin), stimulants (e.g. cocaine) and other illicit substances;
- Prescribed methadone and other opiate substitutes;
- Non-prescribed anabolic steroids and other performance and image enhancing drugs (PIED).

Studies which included the following participants were not eligible for inclusion:

- Non-injecting drug users (including those who formerly injected drugs);
- Those who inject drugs that have been prescribed for a medical condition (except methadone and other opiate substitutes).

3.2.2 Intervention

Studies were eligible for inclusion if they examined the distribution of needles, syringes and other injection equipment (e.g. filters, mixing containers and sterile water). Needle and syringe exchange programmes (NSPs) were defined as the supply of needles, syringes and other injection equipment for the preparation and consumption of drugs.

Question 1 considered the effectiveness and cost-effectiveness of different levels of coverage. We sought to examine the impact of

- Diversity of the population (e.g. age, gender and ethnicity);
- Types of drugs injected;
- The injecting environment;
- Whether or not users were homeless.

Question 2 considered the effectiveness and cost-effectiveness of different approaches to the distribution of injection equipment. We sought to examine the following:

[2] We used the definition of current injecting drug users as reported in the study.

- Setting (e.g. whether programmes were based within specialist drug treatment services, pharmacies, accident and emergency departments);
- Provider (e.g. whether services were delivered by a community pharmacist, specialist drugs worker, social worker or nurse);
- Policies and procedures relating to syringe distribution and return and accessibility.

Question 3 considered the effectiveness and cost-effectiveness of additional harm reduction interventions provided by NSP additional to the supply of injecting equipment. Other harm reduction interventions provided by NSP may include:

- Information/advice on safer injecting practices and safe disposal of used equipment;
- Supply of additional harm reduction equipment (e.g. filters, mixing containers and sterile water);
- On-site testing for BBVs, pre- and post-diagnostic counselling, hepatitis B immunisation;
- General health advice;
- Referral to additional support services (e.g. drug and alcohol treatment, primary care services, welfare, housing and legal advice);
- Safer sex/sexual health advice.

Question 4 considered the effectiveness and cost-effectiveness of NSPs that are delivered in parallel to, or alongside, opiate substitution therapy (OST). OST was defined as the prescription of substitute drugs for drug dependence, such as methadone and buprenorphine for a sustained period (maintenance therapy).

3.2.3 Comparator(s)

Studies were eligible for inclusion if they compared the intervention of interest against a no intervention control or against another intervention approach.

3.2.4 Outcomes

Studies were eligible for inclusion if they reported changes in drug injecting behaviour, including:

- Incidence and prevalence of blood-borne viral (BBV) infections (i.e. HIV, hepatitis B and C);

- Morbidity and mortality among injecting drug users (e.g. injecting site bacterial infections);
- Self-reported injecting risk-behaviour (e.g. sharing or re-using injection equipment), frequency of injection;
- Additional outcomes of interest included entry into drug treatment and utilisation of health care service.

3.2.5 Study design

For all questions, good quality systematic reviews of experimental and observational studies, randomised controlled trials, controlled non-randomised studies, controlled and uncontrolled before and after studies, cross-sectional studies, cohort studies, case-control studies and ecological studies were considered for inclusion in the assessment of effectiveness.

Studies that were considered for inclusion in the assessment of cost-effectiveness included economic evaluations conducted alongside trials, modelling studies and analyses of administrative databases. Only full economic evaluations that compared two or more options and considered both costs and consequences (including cost-effectiveness, cost-utility and cost-benefit analyses) were included.

3.3 Study inclusion

Titles and abstracts were screened independently by two reviewers (LJ, LP and HS). Full copies of included studies were assessed independently by two reviewers according to the inclusion criteria described above. Studies not meeting the inclusion criteria for the review were excluded and the reasons for exclusion noted. All disagreements relating to study inclusion were resolved through consensus and where necessary through consultation with a third reviewer.

3.4 Data extraction strategy

Data relating to study design, population details, intervention details, analysis and results were extracted by one reviewer into an Access database and independently checked for accuracy by a second reviewer.

3.5 Quality assessment strategy

One reviewer independently assessed the quality of the individual studies in an Access database. A second reviewer independently checked the accuracy of the quality assessment. Disagreements were resolved through consensus. The quality of the studies was assessed according to criteria set out in the NICE Centre for Public

Health Excellence Methods Manual except in relation to study designs where quality checklists were not available (e.g. cross-sectional studies, uncontrolled before and after studies). For these studies we used the Quality Assessment Tool for Quantitative Studies, developed by the Effective Public Health Practice Project, Canada (www.city.hamilton.on.ca/phcs/EPHPP/).

Each of the effectiveness and cost-effectiveness studies were graded using a code, ++, + or –, based on the extent to which the potential sources of bias had been minimised:

++ All or most of the criteria have been fulfilled. Where they have not been fulfilled the conclusions are thought very unlikely to alter.

\+ Some of the criteria have been fulfilled. Those criteria that have not been fulfilled or are not adequately described are thought unlikely to alter the conclusions.

\- Few or no criteria have been fulfilled. The conclusions of the study are thought likely or very likely to alter.

3.6 Assessing applicability

Applicability was assessed across each individual study by examining the population and intervention, and by referring to the legislative and political similarities between each of these factors and practice and policy in the UK. Using the ratings described below, applicability statements were generated for each evidence statement derived from the evidence of effectiveness and cost-effectiveness. Applicability of the included studies was rated using the following statements adapted from the NICE Methods Manual (version 1 2006):

A Studies of NSPs carried out in the UK AND likely to be applicable across a broad range of settings and populations;

B Studies of NSPs carried out in non-UK countries that have similar legislation and policy to the UK (e.g. The Netherlands) AND likely to be applicable across a broad range of settings and populations, assuming appropriately adapted;

C Studies of NSPs carried out in non-UK countries that have similar legislation and policy to the UK (e.g. Canada) BUT broader applicability is uncertain;

D Studies of NSPs carried out in non-UK countries that do not have similar legislation and policy to the UK (e.g. USA) AND broader applicability is uncertain.

3.7 Methods of analysis/synthesis

3.7.1 Assessment of effectiveness

The results of the data extraction and quality assessment for each study of effectiveness are presented in structured tables and as a narrative summary. The possible effects of study quality on the effectiveness data and review findings were also discussed within the text of the review.

Studies were grouped according to the broad research question they addressed and the outcomes reported. Where sufficient data were reported in the study publication, intervention effects were presented as adjusted odds ratios for dichotomous data.

3.7.2 Assessment of cost-effectiveness

Details of each identified published economic evaluation, together with a critical appraisal of its quality, were presented in structured tables and as a narrative summary.

4 SUMMARY OF STUDY IDENTIFICATION

4.1 Review of effectiveness

The database searches located approximately 4,591 references[3]. The initial screen of titles and abstracts by two reviewers identified 413 references, which were judged to be eligible for further screening as full text articles. It was not possible to retrieve seven references because they were not available through the British Library or other sources. Therefore, a total of 406 full text articles were screened for inclusion by two reviewers. The process of study identification is shown in Figure 1.

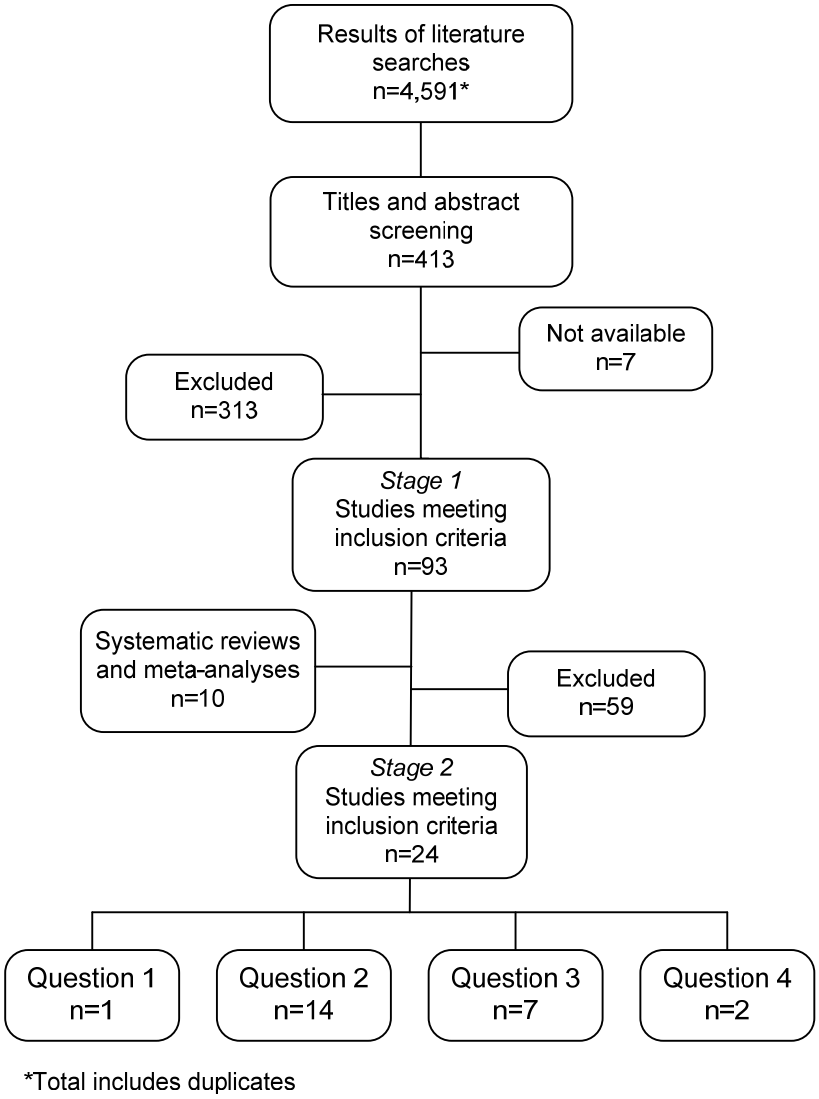


Figure 1. Flowchart of study identification for review of effectiveness

[3] As not all references could be imported into bibliographic software it was not possible to determine the final number of duplicates.

4.1.1 Included studies

Following the screening of full text studies for inclusion it was apparent that few studies addressed the research questions of interest for the review and thus work proceeded in two stages. Initially, studies were screened to determine whether the study was about the effectiveness of NSPs *per se*. Following the first stage of assessment by two reviewers, 93 full text articles were found to meet the inclusion criteria including 10 systematic reviews and meta-analyses and 83 primary studies.

None of the systematic reviews and meta-analyses identified for inclusion in the review directly addressed the research questions of interest; however these articles were included as they provided a good summary of the effectiveness of NSPs in reducing HIV and HCV infection.

In the second stage of assessment, the 83 primary studies identified were assessed to determine whether they answered one or more of the four key research questions or sub-questions. A total of 24 primary studies were judged to be eligible against these criteria; one study examined issues related to coverage, 14 studies examined different types of NSPs, seven studies examined additional harm reduction services offered by NSPs, and two studies examined NSPs delivered alongside OST. Table 2 gives an overview of the types of study designs identified for and their quality rating.

Table 2. Overview of study designs identified

Study design	N identified	Quality rating		
		++	+	-
Systematic reviews and meta-analyses (SR)	10	2	7	1
RCTs	4	1	1	2
Uncontrolled before and after studies (UBA)	3	-	-	3
Cohort studies (CT)	3	-	3	-
Cross-sectional surveys and studies (CS)	14	-	1	13

Of the 22 primary studies that addressed one of the key research questions, the largest proportion of studies focused on injection risk behaviours. Table 3 provides an overview of the outcome of interest and the number of studies identified.

Table 3. Outcomes of interest reported

Outcome of Interest	N Identified
Injection Risk Behaviours	15
HIV infection	7
HCV infection	3
HBV infection	1
Other	
Entry into Drug Treatment	2
Health care utilisation	2

Although inclusion was limited to English language publications, the included articles nonetheless covered a wide geographical range and settings with different policies regarding harm reduction in IDU populations. Nineteen studies were conducted in North America including three studies conducted in Canadian cities and 16 studies conducted in the USA. The remaining five studies were conducted across Europe, in France, Germany, the Netherlands, Russia and Switzerland. All of the included studies focused on provision of needle exchange among urban populations of IDUs.

4.1.2 Excluded studies

A total of 372 articles did not meet the criteria for inclusion in the review. Of these, 313 were excluded as they did not directly examine the effectiveness of NSPs, and a further 59 were excluded at the second state of full text screening as they did not address one or more of the four research questions or sub-questions. Bibliographic details of the excluded studies and reasons for exclusion are presented in Appendix 7.

4.2 Review of cost-effectiveness

A total of 166 references were identified from the literature searches conducted for the review of published economic evaluation studies. Thirty two articles were retrieved for assessment as full text articles. The process of study identification is shown in Figure 2.

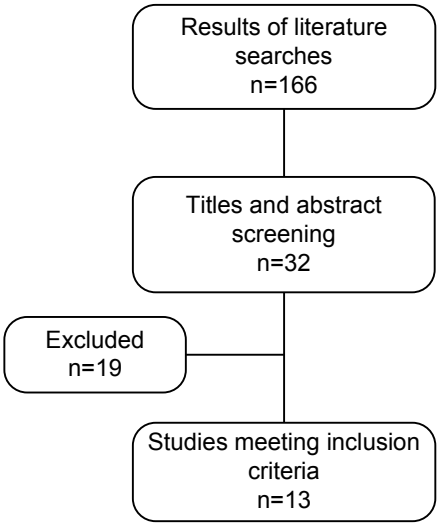


Figure 2. Flowchart of study identification for review of cost-effectiveness

4.2.1 Included studies

A total of 13 economic evaluation studies were identified for inclusion in the review, including 12 cost-effectiveness analyses (CEAs) and one cost-benefit analysis (CBA). As with the studies identified for inclusion in the review of effectiveness, the majority

of the included economic evaluations originated from North America. Seven studies originated from the USA, two were from Canada, and one each from Australia, Belarus, Spain and the Ukraine.

4.2.2 Excluded studies

Nineteen articles did not meet the criteria for inclusion in the review of published economic evaluations. Six articles were excluded as they were not full economic evaluations, six were review articles and the remaining seven studies were related to HIV prevention or other interventions for IDUs but did not examine NSPs.

5 REVIEW OF SYSTEMATIC REVIEWS AND META-ANALYSES

Ten reviews (Cross et al 1998 SR+; Dolan et al 2003 SR+; Gibson et al 2001 SR+; Kall et al 2007 SR-; Ksobiech 2003 SR+; Ksobiech 2006 SR+; Ritter & Cameron 2006 SR+; Tilson et al 2006 SR++; Wodak & Cooney 2004 SR+; Wright et al 2005 SR++) were identified that examined the effectiveness of NSPs. One review (Dolan et al 2003 SR+) examined prison-based exchange programmes, while the other nine reviews examined NSPs across a range of community settings.

5.1 Quality assessment

Overall the quality of the reviews identified was adequate. All of the included articles addressed an appropriate and focused question, and adequate descriptions of the methodology were reported. However, the majority of the included reviews lacked adequate assessment of study quality and few took study quality into account in their discussions. The two highest quality systematic reviews identified (rated ++) were by Tilson et al (2006) and Wright et al (2005).

Three studies (Cross et al 1998 SR+; Ksobiech 2003 SR+; Ksobiech 2006 SR+) used formal methods to combine studies. Ksobiech (2003 SR+, 2006 SR+) combined a range of studies across different designs and outcome measures without undertaking a full assessment of heterogeneity. Although chi-squared tests for heterogeneity were presented the author did not discuss the impact of heterogeneity on the findings, nor undertake sensitivity analyses. The meta-analysis by Cross et al (1998 SR+) also combined data across a range of study designs but effect sizes were presented for different outcomes. In addition, the authors considered how the strength of the effect sizes presented were affected by study design.

5.2 Needle and syringe exchange programmes

5.2.1 Injection risk behaviours

Cross et al (1998 SR+) examined the effects of educational interventions and needle exchange programmes on behavioural outcomes associated with injecting drug use. They combined data from 10 studies which had examined needle exchange programmes, finding that the largest group effect of NSPs was in reducing sharing, followed by lending and injecting. The authors concluded that NSPs were effective in reducing drug use in IDUs. However, both outcome and study design affected the strength of the effect size; sharing had a greater effect when measured using pre-post-test designs rather than randomised assignment.

Ksobiech (2003 SR+) examined the effects of NSPs across three broad categories of sharing behaviours: 'pure needle sharing', which included outcomes identified only as needle/syringe sharing; 'extended needle sharing', which included multiple variables of needle sharing behaviours including sharing with two or more people, and sharing with sexual partner; and 'borrowing/lending', which included outcomes such as never borrowing, using others' needles, reusing own needles/syringes. The author reported that each of the risk behaviours examined decreased over time, when comparing NSP attenders with non-attenders, or across groups, when comparing frequent with infrequent NSP attenders. A second meta-analysis by Ksobiech (2006 SR+) examined the impact of NSPs on social context risk behaviours of IDUs including injection frequency, risky drug-related contextual behaviours (e.g. using shooting galleries) and risky drug-related paraphernalia sharing behaviours. The author reported that NSP attendance had no impact upon risky contextual behaviours (e.g. using a shooting gallery) and that there was no difference in injection frequency among NSP attenders. NSP attenders were less likely to repeatedly re-use syringes, and were also slightly less likely to share drug paraphernalia. There was a moderately negative correlation between NSP use and drug preparation behaviours (e.g. disinfecting equipment, using bleach), indicating that NSP attendance was associated with a decline in risky drug preparation behaviours.

The Institute of Medicine undertook a review of the evidence for strategies to reduce HIV risk behaviours among IDUs (Tilson et al 2006 SR++). Examining the impact of needle and syringe exchange, the committee concluded that there was moderate evidence to show that participation in multicomponent HIV prevention programmes that included needle and syringe exchange was associated with reduction in drug-related HIV risk behaviour, including self-reported sharing of needle and syringes, safer injecting and disposal practices, and frequency of injection.

Ritter and Cameron (2006 SR+) reported that in terms of self-reported changes in risk behaviour there was a good body of literature supporting reductions in risk behaviour associated with NSPs. They also stated that research has demonstrated the efficacy of NSPs in reducing HIV seroconversion and that there was no evidence for the potential iatrogenic effects of NSPs. They concluded that the body of evidence for NSPs is very strongly weighed towards their efficacy and cost-effectiveness.

5.2.2 HIV prevention

Gibson et al (2001 SR+) reviewed 42 studies: 23 were community studies in which behaviour and HIV status of NSP users were compared with those IDU not using

NSPs; 11 studies were conducted exclusively with NSP clients; two studies were conducted with both community samples and with NSP clients; and six studies evaluated the ecological impact of NSPs. The authors reported that there was substantial evidence that NSPs are effective in preventing HIV risk behaviour and HIV seroconversion among IDUs. Of the 42 studies reviewed, 28 found positive effects associated with the use of NSPs, two found negative associations, and 14 found either no association or a mix of positive and negative effects. The authors commented that negative or null findings were concentrated in the studies conducted with community samples of IDUs, compared to studies of NSP-using IDUs. All of the studies with NSP clients reported positive associations. The authors concluded that the methodological rigor of evaluations of NSPs needs to be improved.

Wodak & Cooney (2004 SR+) concluded that overall there was convincing evidence that NSPs, assessed conservatively, fulfilled six of the nine Bradford Hill criteria (strength of association, replication of findings, temporal sequence, biological plausibility, coherence of the evidence and argument by analogy) and all of the five additional criteria specified for the review (cost-effectiveness, absence of negative consequences, feasibility of implementation, expansion and coverage, unanticipated benefits and special populations). The authors stated that measured against any objective standards, the evidence to support the effectiveness of NSPs in substantially reducing HIV must be regarded as overwhelming. The authors found no evidence that needle syringe programmes increased the initiation, duration or frequency of illicit drug use or drug injecting. However, the authors found no evidence to suggest that any single intervention was strong enough to guarantee HIV control but that the aggregate effect of several harm reduction interventions appeared to be generally successful in maintaining HIV control. They stated a need for sterile needle and syringe availability to be considered as a system that has to be supported by a range of complementary measures if communities wished to control HIV infection among and from IDUs.

Kall et al (2007 SR-) reported that most of the studies included in their review of HIV seroincidence found that the effect of NSPs was not significant. The authors were also of the opinion that of the few studies which did find positive effects (such as Des Jarlais et al 1996 and MacDonald et al 2003) confounders had not been adequately controlled for. The authors also highlighted the weaknesses in the design of studies which have examined NSPs and stated the studies reviewed ‘presented a very confused and contradictory picture’. Overall, the authors concluded that the effectiveness of NSPs to reduce HIV among IDUs is overrated.

The committee reviewing the evidence for the Institute of Medicine (Tilson et al 2006 SR++) considered the evidence of the effectiveness of NSPs in reducing HIV incidence among IDUs as modest. Their findings were based on the results of four ecological studies, which compared changes over time in HIV seroprevalence in IDUs in populations with or without access to needle and syringe exchange programmes. They concluded that although many of the studies had design limitations the consistency of the results supported the committee's conclusions.

5.2.3 HCV prevention

Wright et al (2005 SR++) undertook a systematic review of the effectiveness of primary prevention interventions to reduce incidence or prevalence of HCV. Following a narrative summary of the evidence the authors concluded that provision of clean needles and syringes are interventions for which there is an evidence base. Results presented in the review found that although incidence of HCV had reduced in the presence of NSPs in some countries, overall incidence remained high among IDUs. The authors reported that US studies have failed to identify a causal link between NSPs and HCV incidence.

The review by the Institute of Medicine (Tilson et al 2006 SR++) also considered the impact of NSPs on HCV prevention. The committee concluded that there was moderate evidence that NSPs have significantly less impact on transmission and acquisition of hepatitis C virus than on HIV.

5.3 Other outcomes

The review by the Institute for Medicine (Tilson et al 2006 SR++) examined the effects of NSPs in linking IDUs to ancillary health and social services. They found that few studies have evaluated this outcome but that the few studies examining this issue showed a moderate uptake of these services among NSP attendees. However, none of the studies had comparison or control groups.

5.4 Alternative access to needles and syringes

5.4.1 Pharmacy

Wodak and Cooney (2004 SR+) considered there to be reasonable evidence that pharmacy availability of sterile injecting equipment does provide specific benefits in addition to those derived from NSPs.

In relation to pharmacy access to needle and syringes, the Institute of Medicine (Tilson et al 2006 SR++) reviewed the evidence for pharmacy sales and physician-

based prescriptions. They concluded that there was moderate evidence that the elimination of criminal penalties for possessing needles and syringes, and the enhancement of legal access via pharmacy sales, voucher schemes, and physician prescription programmes, were alternative avenues for making sterile needles and syringes available to IDUs.

5.4.2 Vending machines

The review by the Institute for Health (Tilson et al 2006 SR++) also examined access to needles and syringes via vending machines. They stated, that while the evidence was encouraging, it was insufficient for drawing conclusions on the effectiveness of this intervention in reducing drug-related HIV risks among IDUs.

5.4.3 Prison-based syringe exchange

Dolan et al (2003 SR+) identified a total of 19 prison-based syringe exchange (PSE) programmes in Switzerland, Germany and Spain. Three different methods of distributing injecting equipment were identified: doctors; prison or external staff; and vending machines. Of the programmes identified, evaluations were available for six and all reported positive results. The authors reported that no new cases of HIV, hepatitis C or hepatitis B were reported in any of the evaluations identified. Rates of drug use reported from four prisons were stable or decreased, and evaluations conducted in Swiss prisons found a reduction in drug use at two follow-ups. Dolan et al (2003 SR+) concluded that prison syringe exchange programmes were feasible and did provide some benefit in the reduction of risk behaviour without any unintended negative consequences. However, they noted that there was a need for a PSE programme to be evaluated in a large prison before the viability of implementing such a programme could be confirmed.

5.5 Summary and evidence statements

The majority of the reviews identified considered there to be good evidence that NSPs reduce injection risk behaviours among IDUs, in particular self-reported syringe sharing. However the evidence is less clear in relation to HIV incidence. Wodak and Cooney (2004 SR+) and Gibson et al (2001 SR+) both considered there to be good evidence to support the effectiveness of NSPs in reducing HIV incidence but other reviews (e.g. Tilson et al 2006 SR++) have concluded that the evidence is less robust. One review in particular, by Kall et al (2007 SR-), was sceptical about the role that NSPs play in reducing HIV incidence. The authors of that review considered there to be only one study which presented a strong case in favour of NSPs (Des

Jarlais et al 1996) and that in other reviews, studies claiming positive results have not been adequately scrutinised. The evidence from ecological studies which have examined HIV seroprevalence in populations with and without access to NSPs have been criticised for failing to adequately control for confounding (Amundsen 2006).

Only two reviews, Tilson et al (2006 SR++) and Wright et al (2005 SR++) examined the impact of NSPs on HCV incidence. Tilson et al (2006 SR++) concluded that NSPs have less of an impact on HCV infection than HIV infection. This finding was supported by a review of reviews (Palmateer et al in press) conducted for the ACMD. They concluded that there was insufficient evidence for the effectiveness of NSPs in the prevention of HCV transmission.

Although the alternative access to free sterile needles and syringes through community pharmacies has long been a part of harm reduction services in the UK, other countries, such as the USA have imposed criminal penalties on IDUs for possessing needles and syringes. Two systematic reviews examined the evidence for pharmacy availability of sterile needles and syringes (Wodak & Cooney 2004 SR+; Tilson et al 2006 SR++). Both concluded that pharmacy access was a beneficial mode of access to sterile injecting equipment. There has only been limited implementation of vending machines for distributing needles and syringes in England and the rest of the UK, and the evidence in relation to vending machines was found to be insufficient (Tilson et al 2006 SR++).

Prison-based syringe exchange services have not been implemented in the UK because of wide-ranging political, practical and ethical issues (Hughes 2000). Based on data from European countries, Dolan et al (2003 SR+) concluded that prison syringe exchange programmes are feasible and do provide some benefits in the reduction of risk behaviour without any unintended negative consequences.

Evidence statement 5.1

5.1a. There is evidence from one good quality and five moderate quality systematic reviews and meta-analyses[1] that participation in NSPs reduces injection risk behaviours among IDUs, in particular self-reported syringe sharing of needle and syringes, and frequency of injection. The evidence is not clear in relation to the impact of participation in NSPs on sharing of other injection equipment such as cookers, filters or water because few studies have examined these outcomes.

5.1b. There is evidence from two good-quality systematic reviews[2] to support the

effectiveness of NSPs in reducing HIV infection among IDUs. However, findings from two other systematic reviews[3], including one good quality review, suggest that the evidence may be less convincing. There is insufficient evidence from two systematic reviews[4] to determine the impact of NSPs on hepatitis C infection in IDUs.

5.1c. There is evidence from two good quality systematic reviews[5] that access to sterile needles and syringes via pharmacies provides specific benefits in addition to those available through specialist NSPs.

5.1d. There is evidence from one moderate quality systematic review[6] that prison-based syringe exchange may be feasible in small prisons, but there is insufficient evidence to determine the effectiveness of these programmes on a larger scale.

1 Tilson et al 2006 (SR ++); Gibson et al 2001 (SR +); Cross et al 1998 (SR +); Ksobiech 2003 (SR +); Ksobiech 2006 (SR +); Ritter & Cameron 2006 (SR +)

2 Wodak & Cooney 2004 (SR +); Gibson et al 2001 (SR +)

3 Tilson et al 2006 (SR ++); Kall et al 2007 (SR -)

4 Tilson et al 2006 (SR ++); Wright et al 2005 (SR ++)

5 Wodak & Cooney 2004 (SR +); Tilson et al 2006 (SR ++)

6 Dolan et al 2003 (SR +)

6 REVIEW OF PRIMARY STUDIES

6.1 Question 1: What level of coverage of needle and syringe programmes (NSPs) is the most effective and cost-effective?

Research-based definitions of coverage are usually concerned with the number of syringes distributed per injector per injection (Burrows 2006) but syringe coverage may also refer to the proportion of services reaching a particular population. The UN uses the following definition with regard to IDUs: 'the number of sterile syringes provided to an injecting drug user divided by the estimated number of injections during a specified time frame'. Hickman et al (2004) estimated the annual number of syringes distributed per IDU per year for three English cities (Brighton, London and Liverpool), finding that coverage in Brighton and Liverpool was around 27% and 20% in London. However, there is little evidence on the coverage of syringe distribution among IDUs required to effectively prevent BBVs (Vickerman et al 2006).

6.1.1 Overview of evidence identified

One study (Bluthenthal et al 2007 CS-) was identified that examined adequate syringe coverage, defined as one injection per syringe, among NSP participants in a study of 24 of the 25 NSPs in California. Syringe coverage was calculated by multiplying the number of monthly NSP visits by the number of syringes retained from the last visit, then dividing by the number of illicit drug injections in the last thirty days, and multiplying the result by 100 to obtain a percentage. Research participants were then classified into coverage groups of 150% coverage or more, 100-149% coverage, 50-99% and under 50%. These groupings were used to examine the relative impact of different levels of syringe coverage on injection-related HIV risk and syringe disposal.

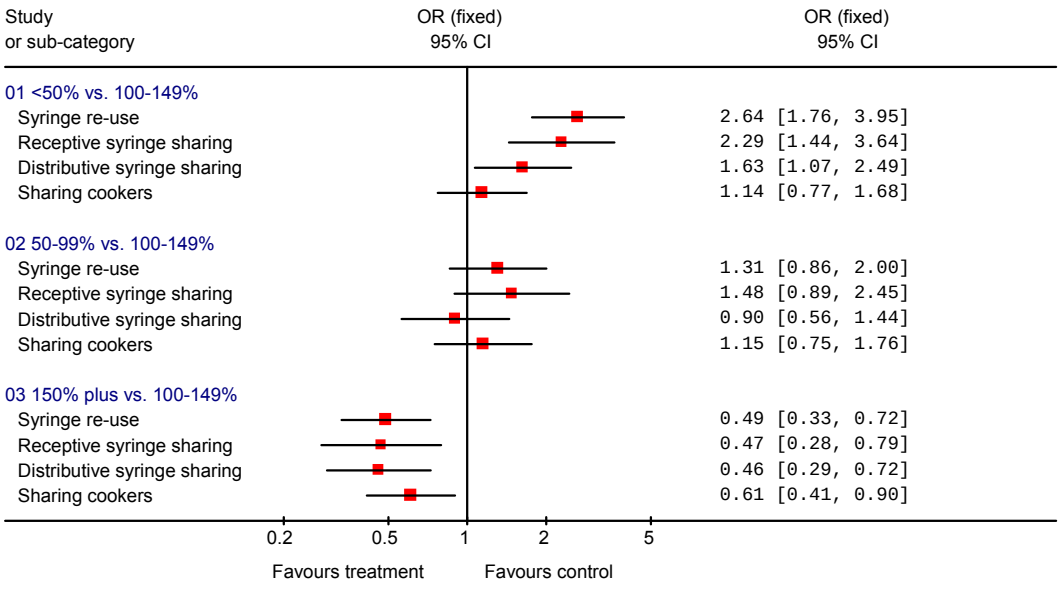
Quality assessment

Syringe coverage was calculated for samples from 24 California NSPs in annual cross-sectional waves in 2001, 2002 and 2003. Generally, the methodology used to examine individual syringe coverage was adequately reported, however some important details were missing and the study was consequently rated '–'. For example it was not clear whether the study sample was representative of the wider population of IDUs and the proportion of sampled participants meeting the eligibility criteria or giving consent were not reported.

Injection risk behaviours

The authors found that those with coverage of less than 50% had significantly higher odds of reporting syringe re-use and receptive syringe sharing than the referent group, those with coverage of 100-149%, (syringe re-use: OR 2.64; 95% CI 1.76, 3.95; receptive syringe sharing: OR 2.29; 95% CI 1.44, 3.63). There were no significant statistical differences in terms of risk behaviours between clients with 50-99% and 100-149% coverage levels. Compared to the referent group, NSP clients with coverage of over 150% reported significantly lower odds of syringe re-use and receptive and distributive syringe sharing (syringe re-use: OR 0.49; 95% CI 0.33, 0.72; receptive syringe sharing: OR 0.47; 95% CI 0.28, 0.80; distributive syringe sharing OR 0.46; 95% CI 0.29, 0.72). Additionally, only clients with coverage of over 150% reported significantly lower odds of sharing cookers compared to their referent group, clients with coverage of 100-149%, (OR 0.61, 95% CI 0.41-0.89). These findings are shown in Figure 3. Syringe coverage of 100% or more was inversely associated with being homeless, injecting heroin in the last 30 days, using crack cocaine in the last 30 days and being injected by another IDU. In addition, participants who reported being currently in drug treatment were more likely to report syringe coverage of 100% or more.

Figure 3. Coverage: Injection risk behaviours



6.1.2 Summary and evidence statements

Bluthenthal et al (2007 CS-) found that individual syringe coverage was associated with safer injection risk behaviours. Although the authors did not examine how NSPs

can increase coverage among clients, the authors suggested that NSP dispensation policy might be related to coverage. In further analyses, Bluthenthal et al (2007) found that NSPs that had less restrictive dispensation policies had more clients with adequate syringe coverage; clients of unlimited needs-based distribution and unlimited one-for-one plus exchange had a higher prevalence of adequate syringe coverage compared to clients of more restrictive syringe dispensation models. Further discussion of the impact of syringe dispensation policies on injection risk behaviours is presented in Section 6.2.4.

Vickerman et al (2006) developed a mathematical model to explore the relationship between an IDU population's endemic HIV prevalence and the coverage of syringe distribution based on data from the UK and Belarus. The results of the model suggested that although the results did not support the existence of a universal coverage target, there are critical coverage thresholds for syringe distribution that need to be reached to substantially reduce HIV prevalence among IDU populations. For example, to reduce the HIV prevalence in London to less than 1%, the coverage of syringe distribution would need to increase to 27%.

Evidence statement 6.1

6.1a. There is evidence from one poor quality cross-sectional study[1] to suggest that higher syringe coverage was associated with lower injection risk behaviours among IDUs who participated in NSPs, including sharing needles and syringes, sharing cookers and syringe re-use.

6.1b. There is evidence from one poor quality cross-sectional study[1] to suggest that IDUs who were homeless, reported recent heroin injection or crack cocaine use, or were not in treatment had lower levels of syringe coverage.

Applicability: As this study was conducted in the USA, it is unclear whether the findings are applicable to the UK given the differences in the political acceptance of NSPs and wider harm reduction services for IDUs. However, the concept of coverage is applicable in terms of NSP provision in the UK.

[1] Bluthenthal et al 2007a (CS -)

Table 4. Studies that examined coverage

Author (Year)	Design	Intervention details	Population	Outcomes	Applicability
Bluthenthal et al (2007)	CS-	24 of 25 NSPs in San Francisco area	California, USA n=1,570 IDUs	Significantly lower odds of syringe re-use and receptive and distributive syringe sharing among NSP clients with coverage >150% compared to clients with 100-149% coverage. Clients with <50% coverage had significantly higher odds of reporting syringe re-use, receptive syringe sharing and distributive syringe sharing, but not sharing cookers. No statistically significant differences in risk behaviours were observed between clients with 50-99% and 100-149% coverage levels.	D

6.2 Question 2: What types of NSPs are effective and cost effective?

The term NSP may be applied to a wide variety of harm reduction programmes targeted at IDUs, which have at their core the distribution of sterile injecting equipment and the collection and safe disposal of used needles and syringes. NSPs may be located in a variety of settings. In England, although the majority of services are pharmacy-based, other services may be stand-alone or operate as part of mixed-service provision, located alongside other drug treatment services (HPA 2007a; Abdulrahim et al 2006). Specialist services may be fixed site, mobile or both and often operate with very different opening hours. Distributions and returns policies at NSPs vary not only by country but also within them. In England, the majority of NSPs have a returns policy whereby the service encourages returns but this is not a condition for exchanging sterile injecting equipment (Abdulrahim et al 2006). However, there are large variations between services in the maximum number of syringes distributed at any one contact.

6.2.1 Overview of evidence identified

Fourteen studies were identified that addressed different types of NSPs and their impact on effectiveness. Four were based in Europe (Germany: Stark et al 2006 UBA-; France: Obadia et al 1999 CS-; Switzerland: Nelles et al 1997 UBA-; Russia: Rhodes et al 2004 CS-). The remaining ten were based in North America (Alaska: Fisher et al 2003 RCT+; Baltimore: Riley et al 2000 CS-; California: Masson et al 2007 RCT++, Kral et al 2004 CS+; Connecticut: Singer et al 1997 CS-, Khoshnood et al 2000 CS-; New York: Schilling et al 2004 CS-, Rockwell et al 1999 CS-; comparison of Chicago, IL, Hartford, CT and Oakland, CA: Bluthenthal et al 2004 CS-; Vancouver: Miller et al 2002 CS-).

Two studies (Schilling et al 2004 CS-; Rockwell et al 1999 CS-) conducted in New York focused on distance from NSP and utilisation and three studies compared the impact of NSP distribution and exchange policies on needle sharing behaviours (Kral et al 2004 CS+; Bluthenthal et al 2004 CS-; Singer et al 1997 CS-). Eight studies[4] compared characteristics and behaviours of IDUs based on syringe source (Fisher et al 2003; Knoshnood et al 2000; Masson et al 2007; Miller et al 2002; Obadia et al 1999; Rhodes et al 2004; Riley et al 2000; Singer et al 1997). Five studies compared NSP use, pharmacy sales, both and neither, comprising one RCT (Fisher et al 2003

[4] Singer et al (1997 CS-) examined both the effects of setting and different syringe dispensation policies.

RCT+) and four cross-sectional studies (Khoshnood et al 2000 CS-; Miller et al 2002 CS-; Rhodes et al 2004 CS-; Singer et al 1997 CS-). Masson et al (2007 RCT++) compared outcomes in IDUs assigned to community-based NSPs to those assigned to a hospital-based NSP. Riley et al 2000 (CS-) compared the characteristics of first time NSP participants who enrolled at mobile van-based NSP with those who enrolled at a pharmacy-based exchange. Obadia et al (1999 CS-) compared characteristics of IDUs whose primary source of clean syringes were street vending machines with those whose primary source were NSPs and pharmacy sales. Two studies discussed outcomes relating to placing syringe vending machines in prisons (Nelles et al 1997 UBA-; Stark et al 2006 UBA-).

6.2.2 Accessibility and geographical distance

Schilling et al (2004 CS-) compared needle sharing behaviours, sexual risk behaviours and entry into drug treatment based on whether research participants were recruited at the NSP, from the streets within ten blocks of the NSP or more than ten blocks away. Rockwell et al (1999 CS-) analysed data collected for the Center for Disease Control and Prevention's Collaborative Intravenous Drug Users Study (CIDUS) and classified respondents into more than ten minutes walk and less than ten minutes walk distance from an NSP based upon their answers to the question 'how long would it take you to get to an exchange from where you usually stay?'.

Quality Assessment

Rockwell et al (1999 CS-) was a cross-sectional analysis of data gathered as part of CIDUS. The study methodology was poorly reported and consequently the study was rated '-'. No details were offered about how those meeting eligibility criteria for the study differed from those who did not, or how consenters compared with non-consenters. There was limited controlling for confounders and differences between those who travelled for more or less than ten minutes to get to an NSP at baseline were not explored. Schilling et al (2004 CS-) reported their methodology reasonably well but some details were missing, and this study was also rated '-'. The study design was weak (cross-sectional) and selection bias was only moderately controlled for. As with Rockwell et al (1999), there were limitations due to a lack of comparison between those meeting eligibility criteria for the study differed from those who did not, and how consenters compared with non-consenters. Additionally, the significance of (dis)similarity between groups at baseline was not presented.

Injection risk behaviour

Schilling et al (2004 CS-) found that NSP-recruited participants were less likely to use needles others had injected drugs into (e.g. frontloading or backloading) (adjusted mean 0.24 for NSP users, compared to 0.65 for proximal NSP access and 0.62 distal NSP access; $p<0.01$) and that they were less likely to use dirty needles by themselves (adjusted mean 0.21 for NSP users, compared to 0.36, $p<0.05$ for proximal NSP access and 0.62, $p<0.01$ for distal NSP access). Compared to the street-recruited samples, NSP users were also less likely to share the same cooker ($p=0.031$).

Supporting this, Rockwell et al (1999 CS-) found that after controlling for drug injection frequency and sociodemographic variables, respondents who were ten or fewer minutes walk from an NSP were less likely to report injecting with a used needle at their last injection (OR 0.45; 95% CI 0.24, 0.86; $p=0.01$). Also, respondents who reported using an NSP within the previous six months were less likely than non-NSP users to reporting injecting with a used syringe at their last injection (OR 0.30; 95% CI 0.16, 0.55; $p=0.001$). These two findings are linked by virtue of their additional finding that living within a ten minute walk of an NSP was significantly associated with typical use of an NSP (OR 2.89; 95% CI 2.06, 4.06; $p=0.001$).

6.2.3 Setting

Eight studies compared different NSP settings (Fisher et al 2003; Knoshnood et al 2000; Masson et al 2007; Miller et al 2002; Obadia et al 1999; Rhodes et al 2004; Riley et al 2000; Singer et al 1997). Two were RCTs, one comparing pharmacy sales only with NSP exchange plus pharmacy sales (Fisher et al 2003 RCT+) and the other comparing differences between IDUs attending a hospital- and community-based NSP (Masson et al 2007 RCT++). The remaining six studies were cross-sectional in design and compared characteristics of IDUs according to their primary source of clean needles and syringes across the following types of setting: NSPs only, pharmacies only, both or neither (Khoshnood et al 2000 CS-; Singer et al 1997 CS-), NSP/outreach, pharmacy/shop, or street (Rhodes et al 2004 CS-); pharmacy, fixed site or van-based services (Miller et al 2002 CS-; Riley et al 2000 CS-); and NSP, pharmacy or vending machine (Obadia et al 1999 CS-). All studies included pharmacy sales in their analysis, as all studies originated in countries where the pharmacy sale of needles to IDUs predominated (USA, Russia and France). Thus the applicability of the findings of these studies to the United Kingdom may be limited in part by the cultural difference of pharmacy exchange compared to pharmacy sales.

It is worth noting that Khoshnood et al (2000 CS-) reported on differences in success in purchasing syringes from pharmacies based on gender. Of those who were refused purchase, 79% were male (21% females) and of those allowed purchase 69% were male (31% female). Even allowing for the greater number of males in the sample than females (69% male among those who used pharmacies), women had greater success in purchasing syringes from pharmacies. Additionally, as part of their RCT of pharmacy versus NSP, Fisher et al (2003 RCT+) provided those randomly allocated to the pharmacy arm an envelope containing advice on buying needles in pharmacies, as pharmacists exercise discretion in whether or not to serve IDUs, which is not the case for NSPs.

Quality Assessment

The two RCTs were of superior study design and both described their methodologies well. Both Fisher et al (2003 RCT+) and Masson et al (2007 RCT++), minimised differences between the control and intervention arms of the trials and efforts to control bias were made, although Fisher et al (2003 RCT+) was somewhat limited by the use of an inadequate concealment method (opaque envelopes) and was consequently rated to be of moderate quality.

Obadia et al (1999 CS-) had a reasonably well reported study methodology, but details were missing regarding study recruitment and how representative of the study population the participants were. In the analysis, confounders were not well accounted for, limiting the applicability of the study. Similarly, Rhodes et al (2004 CS-) did not discuss or quantify how well their sampled participants reflected the study population nor details such as the proportion of sampled participants meeting the eligibility criteria. Neither Singer et al (1997 CS-) nor Miller et al (2002 CS-) reported on how representative the study participants were of their target populations, nor how consenters compared with non-consenters or how those not meeting the eligibility criteria differed from those who did. Because Khoshnood et al (2000 CS-) used respondent-driven sampling to recruit participants it was not possible to identify consent rates or how representative the sample were of the target population. Riley et al (2000 CS-) accounted well for confounders but did not show data collection tools to be validated, nor were differences between consenters and non-consenters quantified or discussed.

Injection risk behaviours

a) NSP vs. pharmacy sales

Fisher et al (2003 RCT+) found that participants reduced their injecting drug use over time in both the NSP plus pharmacy sales group and the pharmacy sales only group, but that group assignment did not modify this reduction.

Singer et al (1997 CS-) reported that in terms of receptive sharing (using syringes or needles previously used by another IDU), compared to using neither sources or NSPs or pharmacies alone, the percentage of IDUs who shared receptively was lowest among those who used both NSPs and pharmacies (18.5%). This compared to 30.8% among those who used only NSPs and 32.1% among those who used only pharmacies, with the highest rate (39.5%) among those who used neither source ($p<0.005$). The authors noted that the patterns of drug use in the sample suggested the existence of different subgroups of IDUs based on drug patterns and that these subgroups differentially accessed the NSP and pharmacies. IDUs who were injecting heroin or speedballs were more likely to report using the NSP alone or the NSP combined with pharmacy purchase compared to those just using the pharmacy.

Rhodes et al (2004 CS-) identified several 'risk factors' based on primary source of clean syringes (NSP/outreach; pharmacy/shop; other) among IDUs in Togliatti, Russia. After controlling for a range of potential confounders (district of residence, injection frequency, average number of times injected with the same syringe within the previous four weeks, last time arrested or detained and self-reported HIV status), IDUs who reported NSPs or outreach as their primary source of needles had lower odds of sharing in the last four weeks compared with those who obtained them from a pharmacy or shop (OR 0.3; 95% CI 0.1, 1.1). IDUs who bought syringes on the street or sourced them from sex partner, friends, other IDUs or drug dealers had greater odds of sharing relative to IDUs with pharmacy or shop as their primary source (OR 12.4; 95% CI: 2.6, 58.5).

Knoshnood et al (2000 CS-) examined syringe source, use and discard practices among 268 IDUs in New Haven, Connecticut, USA. The majority of the sample reported pharmacies and NSPs as their usual source of syringes in the past six months; 41% reported pharmacies as their main source, 13% reported the NSP and not pharmacies, 34% reported both the NSP and pharmacies, and 10% reported neither of these sources. IDUs who reported using neither pharmacies nor NSPs as their usual source of syringes were more likely to be female, African-American or Latino/a, and less likely to have been in drug treatment in the previous last year,

compared to IDUs whose main source of syringes was pharmacies or the NSP. Of the 211 (79%) who had attempted to purchase syringes from a pharmacy in the previous six months, 28 (13%) had been refused. Those who were refused were more likely to be white and to report 'sometimes to always' sharing. In terms of syringe sharing and syringe re-use, Khoshnood et al (2000 CS-) reported that there were no statistically significant differences in frequency of syringe sharing or syringe re-use between IDUs who used NSPs and IDUs who used pharmacies as their primary sources of syringes. Participants who did not rely on either source were less likely to report syringe sharing (significance not reported) and were significantly less likely to report re-using syringes ($p<0.05$ compared to pharmacy and NSP groups).

Miller et al (2002 CS-) characterised risk-taking behaviour among an open cohort of 1,020 IDUs in Vancouver, according to their primary source of clean needles within the previous six months. Primary sources of needles were pharmacies, fixed site NSPs and van-based NSPs. The majority of participants reported that they primarily obtained needles from fixed-site programmes, though most of the participants reported accessing two or more of the distribution modalities. Across these three groupings there was no significant trend for needle borrowing or lending, although pharmacy users were more likely to report needle sharing behaviours. The authors reported that mobile van site users were more likely to be younger and have fewer years of injecting drug use. In addition, they were significantly more likely to report frequent cocaine use and sex trade work. Van users were also more likely to be female and Aboriginal.

Riley et al (2000 CS-) identified that in Baltimore, USA when NSP provision expanded from van-based mobile NSP only to van-based NSP plus pharmacy-based fixed-site NSP, these different sites attracted users with different demographic and injection risk behaviour characteristics. While pharmacy users were like likely to be African-American, they were more likely to be cocaine injectors, to inject more frequently and to use a needle already used by someone else. Controlling for other independent variables, Riley et al (2000 CS-) found race and injection frequency to be predictors of NSP venue type.

b) Hospital vs. community

Only one study directly examined the effectiveness of NSPs in different locations. Masson et al (2007 RCT++) examined the effects of a hospital-based and a community-based syringe exchange programme on the injection practices, health status, and health service utilisation of IDUs. The authors found that NSP condition

did not influence risk behaviours, health status or self-reported NSP use. Drug use risk behaviours decreased over time in both groups (p<0.0001). At the six month assessment, 59% of participants assigned to the hospital-based NSP reported using syringe exchange in the previous 30 days, compared to 52% of those assigned to the community NSP (p=0.61). The portion of participants reporting NSP use did not differ between the hospital and community NSP groups at the 12 month assessment (47% v 46%; p=0.11). However, among participants assigned to the hospital NSP, participants with stable housing were more likely to attend than those who were homeless.

c) Vending machines

Obadia et al (1999 CS-) compared IDUs whose primary source of syringes was vending machines to those whose primary source was pharmacies or NSPs in Marseilles, France. They identified no differences between vending machine users and others in terms of sharing needles in the previous six months (OR 1.0; 95% CI 0.5, 2.4), although vending machine users were significantly less likely to have shared cookers, filters and water during the previous six months compared to non-users (OR 0.3; 95% CI 0.2, 0.7). Primary users of vending machines were significantly younger, less likely to live in a house that they owned or personally rented and less likely to have been in drug treatment.

Blood borne viruses

Miller et al (2002 CS-) also examined the impact of primary needle source on HIV and HCV prevalence. Primary sources of needles were pharmacies, fixed site NSPs and van-based NSPs. The authors found that there was no significant trend for HIV or HCV prevalence across any of the groupings, although HIV prevalence was lower among pharmacy users than participants who reported using the van or fixed site NSPs as their primary source of needles.

Other outcomes

b) Hospital vs. community

Masson et al (2007 RCT++) examined health care utilisation, finding that participants assigned to the hospital NSP had 83% (95% CI: 29%, 160%) more inpatient admissions and 22% (95% CI: 13%, 32%) more ambulatory care visits (i.e. outpatient visits) than those assigned to the community NSP. Among participants who accessed healthcare, there were significantly fewer inpatient admissions among participants who were white, HIV positive or who had higher mental or physical functioning, and

fewer outpatient visits among participants who were younger, female, white, homeless and those with higher mental or physical functioning.

6.2.4 Returns and Exchange Policies

Three studies (Bluthenthal et al 2004 CS-; Kral et al 2004 CS+; Singer et al 1997 CS-) examined the impact of different syringe dispensation policies. Kral et al (2004 CS+) compared the policies of 23 of the 24 NSPs in California in 2001 and categorised them into those which distributed on a one-for-one (NSPs had a stated policy of giving clients the same number of sterile syringes as were turned in by the client), one-for-one plus (NSPs had a stated policy of giving clients a few more syringes as were turned in by the client) and distributive (NSPs had a policy of giving clients the number of syringes that the client requested, regardless of who many they turned in) basis. The authors reported that NSPs with differing policies had different operational characteristics. Distributive NSPs provided more syringes and were open more days and hours than one-for-one and one-for-one plus programmes, therefore these sites differed on more than just distribution policy. Bluthenthal et al (2004 CS-) compared the policies of three NSPs in Chicago, Hartford and Oakland, USA. In Chicago, pharmacy purchase was not available but NSP users could carry syringes and use a large NSP that provided syringes on a one for two basis (i.e. for every one syringe returned by the client they received two back). In Hartford, IDUs could carry a limited number of syringes, receive up to ten syringes from the NSP and participate in pharmacy purchase, and in Oakland, IDUs could neither carry syringes nor make pharmacy purchases, although they could exchange syringes at the NSP on a one-for-one plus five basis. Singer et al (1997 CS-) conducted a serial cross-sectional analysis of baseline entry data from a cohort study conducted in Hartford, USA. They examined three periods over which different syringe dispensation policies operated in the city: 1) when non-prescription pharmacy syringe sales were permitted but there was no NSP; 2) an NSP with a five syringe limit; and 3) when the five syringe limit was increased to ten syringes.

Quality assessment

Bluthenthal et al (2004 CS-) and Kral et al (2004 CS+) used cross-sectional study designs and were therefore unable to examine behaviour change over time. The participants in Bluthenthal et al (2004 CS-) appeared to be representative of the target population, and the analysis accounted well for confounders. However, the data collection tools were not shown to be validated. Similarly, participants in the study by Kral et al (2004 CS+) appeared to be representative of the target population,

and the analysis accounted well for confounders. In addition, in contrast to Bluthenthal et al (2004 CS), the data collection tools were shown to be both valid and reliable. Singer et al (1997 CS-) conducted a repeated cross-sectional study and a discussion of the quality assessment of this study is reported under Section 6.2.3.

Injection Risk Behaviours

Bluthenthal et al (2004 CS-) found no significant differences in receptive syringe sharing between the cities examined (Chicago vs. Hartford: AOR 0.29; 95% CI 0.08, 1.05 / Oakland vs. Hartford: AOR 0.49; 95% CI 0.15, 1.62). Receptive sharing was found to be predicted by homelessness and less than high school education. Kral et al (2004 CS+) also found no statistically significant differences in receptive or distributive sharing by policy (one-for-one, one-for-one plus, distributive). After controlling for confounders, participation in distributive programmes was not statistically significantly associated with receptive or distributive sharing, or sharing filters.

Kral et al (2004 CS+) reported that participants in distributive programmes had lower odds for syringe re-use than other participants (AOR 0.43; 95% CI 0.27, 0.71). Bluthenthal et al (2004 CS-) found that in multivariate analysis, Chicago and Oakland IDUs (with no pharmacy purchase allowed but two-for-one and one-for-one plus five NSP policies respectively) were less likely to report syringe re-use than IDUs in Hartford, which had limits on the number of syringes exchanged at the NSP and on the number IDUs were permitted to carry (Oakland vs. Hartford: OR 0.10; 95% CI 0.03-0.30, $p<0.01$). Older age was also associated with lower odds of syringe re-use.

Singer et al (1997 CS-) found that over the three periods examined, that there was a steady and statistically significant decrease in the percentage of IDUs who reported using pre-used syringes (41.6% to 23.3%; $p<0.005$) and pre-used supplies (45.6% to 36.1%; NS). They also noted a significant decrease in the number of IDUs who reported injecting at shooting galleries during the time when IDUs could exchange up to 10 needles per visit to the NSP (27.1% to 7.5%; $p<0.05$).

Blood borne viruses

Singer et al (1997 CS-) noted a decrease in self-reported HIV prevalence between the period of legal pharmacy syringe purchase and when up to five needles could be exchanged at the newly established NSP (35% to 22%; $p<0.05$). However, data collected when the limit increased from five to ten syringes showed a 25% increase in HIV seroprevalence, differentiated by age with a significant increase among those

aged 36-45 and no change among those aged 26-35. As a repeated cross-sectional study, this shift could have been due to demographic changes, and these potential confounding factors were not accounted for in the analysis, limiting the applicability of these findings.

Other outcomes

Kral et al (2004 CS+) reported that frequency of NSP use did not differ significantly by programme type, however clients of distribution programmes reported that they had received more needles on their last visit to the NSP (median 100) compared to clients of one-for-one (median 20) and one-for-one plus (median 20) programmes.

6.2.5 Prisons

Two articles were identified which examined the role of needle exchange in prisons: one based in a prison in Switzerland (Nelles et al 1997 UBA-) and one was based one male and one female prison in Germany (Stark et al 2006 UBA-). In both Switzerland and the female prison in Germany this consisted of a vending machine located out of sight of prison guards, and in the male German prison of social workers from an NGO exchanging sterile syringes and equipment three times a week. Both studies were of an uncontrolled before and after design, and considered the feasibility and impact of the implantation of NSPs in these prisons.

Quality Assessment

Nelles et al (1997 UBA-) had a poorly reported methodology, with few details offered regarding drop out rates and characteristics of consenters in relation to non-consenters. Stark et al (2006 UBA-) was similarly an uncontrolled before and after study, however, drop out rates were reported and in multivariate analysis confounders were adequately accounted for.

Injection risk behaviours

Stark et al (2006 UBA-) reported that 95% of inmates reported drug use at baseline (gender and drug choice breakdown not provided), compared to 67% of females and 90% of males at follow up (95% using heroin, 26% using cocaine). At baseline 17% of inmates reported sharing in the previous six months, compared to 11% at follow up.

Blood borne viruses

Stark et al (2006 UBA-) reported baseline rates of 18% for HIV, 53% for HBV and 82% for HCV. In multivariate analysis, injecting drug use during previous imprisonment was found to be an independent predictor of HIV seroconversion (AOR

2.3; 95% CI 1.2, 4.9) and HCV seroconversion (AOR 2.0; 95% CI 1.1, 5.6). During follow up, no HIV or HBV seroconversions were observed. However four out of 22 participants who were seronegative at baseline developed HCV antibodies (incidence rate of 18 per 100 person years). All IDUs who seroconverted denied sharing syringes while in prison, but three quarters reported frontloading or sharing cookers.

Nelles et al (1997 UBA-) reported that the results of the pilot project carried out at Hindelbank prison in Switzerland did not provide arguments against the continuation of the distribution of sterile injecting equipment, as there was no increase in drug consumption and no syringe-related incidents were observed. Further, there were no new cases of HIV, HBV or HCV identified between baseline and follow up, and no abscesses related to drug injection were observed.

6.2.6 Summary and evidence statements

Few studies examined how different types of approaches to the distribution of injecting equipment impacted on effectiveness. However, based on the literature identified effectiveness was examined across the following areas: 1) accessibility of NSPs based on studies of geographical proximity; 2) distribution of injecting equipment in different settings including community sites, pharmacies, hospitals, mobile exchanges, vending machines, and prisons; and 3) different polices on the return and distribution of needles and syringes (e.g. one-for-one exchange).

Two cross-sectional studies (Schilling et al 2004 CS- and Rockwell et al 1999 CS-) examined the impact of geographical proximity to NSPs on risk behaviours among IDUs. IDUs living within close proximity to NSPs were more likely to utilise NSP services and report lower levels of injection risk behaviours.

Eight studies were identified which examined a variety of outcomes among IDUs depending on their main source of needles. Two RCTs were identified; Fisher et al (2003 RCT+) compared pharmacy sales only with NSP exchange plus pharmacy sales and Masson et al (2007 RCT++) compared a hospital and a community-based NSP. Four studies (Khoshnood et al 2000 CS-; Singer et al 1997 CS- ; Rhodes et al 2004 CS-; Miller et al 2002 CS-) compared characteristics of IDUs according to whether their primary source of clean needles was from pharmacies or NSPs. One study (Obadia et al 1999 CS-) examined the characteristics of IDUs who used vending machines as their primary source of needles and a further study (Riley et al 2000 CS-) compared the characteristics of first time NSP participants who enrolled at mobile van-based NSP with those who enrolled at a pharmacy-based exchange.. The two RCTs by Fisher et al (2003 RCT+) and Masson et al (2007 RCT++) reported

that setting did not impact on injection risk behaviours including injection frequency and HIV risk behaviours, respectively. However, Masson et al (2007 RCT++) found that participants assigned to the hospital-based NSP had improved access to inpatient and outpatient services. The results from the observational studies that examined the characteristics of IDUs according to their primary source of sterile needles and syringes were inconsistent and difficult to interpret. However, it appears that mobile van services and vending machines attract younger users and users with higher risk profiles.

Three cross-sectional studies (Bluthenthal et al 2004 CS-; Kral et al 2004 CS+; Singer et al 1997 CS-) examined the impact of different syringe dispensation policies on injection risk behaviours among IDUs. These studies found that syringe dispensation policies had a limited impact on behavioural outcomes such as sharing but had some impact on syringe re-use.

Two uncontrolled before and after studies were identified that examined the role of needle exchange in prisons. The needle exchange intervention consisted of a vending machine in two evaluations and in a third evaluation social workers from an NGO exchanged sterile syringes and equipment. Reductions in syringe sharing and HIV incidence were found.

Evidence statement 6.2

6.2a. There is evidence from two poor quality cross-sectional studies[1] to tentatively suggest that close proximity to NSPs can lead to greater utilisation of NSP facilities, resulting in reduced syringe sharing.

Applicability: Both studies were conducted in the USA and it is unclear whether the findings are applicable to the UK given the differences in the political acceptance of NSPs and wider harm reduction services for IDUs.

6.2b. There is evidence from two RCTs[2], one good quality and one moderate quality, to suggest that NSP setting does not impact on injection risk behaviours. The evidence from six poor quality observational studies[3] is inconsistent; however there is evidence from three poor quality cross-sectional studies[4] that mobile van sites and vending machines may attract younger IDUs and IDUs with higher risk profiles.

Applicability: As all of these studies were conducted in countries where the pharmacy sale of needles to IDUs predominated (USA, Russia and France), rather than free distribution as is the norm in the UK, it is unclear whether the findings are applicable

to the UK given the differences in the political acceptance of NSPs and wider harm reduction services for IDUs.

6.2c. There is evidence from one good quality RCT[5] to suggest that providing hospital-based NSP services may increase accessibility to outpatient services among IDUs attending NSPs.

Applicability: As this study was conducted in the USA, it is unclear whether the findings are applicable to the UK given the differences in the political acceptance of NSPs and wider harm reduction services for IDUs. However, as NSPs are available in A&E departments in some areas of the UK this finding may be applicable to NSP provision in the UK.

6.2d. There is evidence from one moderate quality and two poor quality cross-sectional studies[6] to suggest that syringe dispensation policies have a limited impact on behavioural outcomes such as sharing but some impact on syringe re-use.

Applicability: All three studies were conducted in the USA, and it is unclear whether the findings are applicable to the UK given the differences in the political acceptance of NSPs and wider harm reduction services for IDUs.

6.2e. There is limited evidence from two poor quality uncontrolled before and after studies[7] to tentatively suggest that the provision of vending machines in prisons does not have adverse effects on HIV and HCV seroconversion and reduces syringe sharing and other injection risk behaviours.

Applicability: Both studies were conducted in Europe, however these findings are currently of limited applicability to the UK because of the political and ethical issues surrounding prison-based NSPs.

1 Schilling et al 2004 (CS-); Rockwell et al 1999 (CS-)

2 Fisher et al 2003 (RCT+); Masson et al 2007 (RCT++)

3 Khoshnood et al 2000 (CS-); Singer et al 1997 (CS-); Rhodes et al 2004 (CS-); Miller et al 2002 (CS-); Obadia et al 1999 (CS-); Riley et al 2000 (CS-)

4 Miller et al 2002 (CS-) ; Obadia et al 1999 (CS -); Riley et al 2000 (CS-)

5 Masson et al 2007 (RCT++)

6 Bluthenthal et al 2004 (CS-); Kral et al 2004 (CS+); Singer et al 1997 (CS-)

7 Nelles et al 1997 (UBA-); Stark et al 2006 (UBA-)

Table 5. Studies that examined different types of NSPs

Author (Year)	Design	Intervention details	Population	Outcomes	Applicability
Availability and accessibility					
Rockwell et al (1999)	CS-	Not described	New York City, USA N=776 active IDUs	Respondents who were ≤10 min walk from an NSP were less likely to report injecting with a used syringe at last injection. Respondents who reported use of an NSP in the previous six months were less likely than non-exchangers to reported injecting with a used syringe at last injection.	D
Schilling et al (2004)	CS-	NSP that provided pre- and post-diagnostic counselling, safer sexual health advice and referrals to drug treatment, social services, and soup kitchens.	Harlem (NYC), USA N=587 IDUs; 186 recruited at NSPs, 203 recruited ≤10 blocks of the NSP, and 198 recruited >10 blocks of the NSP	Post-hoc analyses indicated that the NSP recruited participants engaged in HIV risk behaviours less frequently than street recruited participants. NSP sample were less likely to inject with a needle that someone else had squirted drugs into; less likely to use dirty needles by themselves; and less likely to share a cooker.	D
Setting					
Fisher et al (2003)	RCT+	NSP vs. pharmacy sales	Alaska, USA 296 IDUs assigned to NSP vs. 304 assigned to pharmacy sales	Neither NSP or pharmacy sales groups modified the association between time and injection frequency (i.e. did not reduce or increase injection frequency over 12 month course of study).	D
Khoshnood et al (2000)	CS-	NSP vs. pharmacy	New Haven, USA N=264 active IDUs; 111 pharmacy users, 36 NSP users, 90 both NSP and pharmacy user and 27 neither	No statistically significant differences in frequency of syringe sharing or syringe re-use between those who used NSPs and pharmacies as their primary source of syringes. Participants who did not rely on either source were less likely to report syringe sharing (significance not reported) and were significantly less likely to report re-using syringes ($p<0.05$ compared to pharmacy and NSP groups).	D
Masson et al (2007)	RCT++	Community NSP vs. hospital NSP	San Francisco, USA 83 IDUs assigned to community-based NSPs vs. 83 assigned to hospital-based NSP	NSP condition did not influence risk behaviours, health status, or self-reported NSP programme use. Drug use risk behaviours decreased over time in both groups ($p<0.0001$). Persons assigned to the hospital NSP had 83% (CI: 29% to 160%) more inpatient admissions and 22% (CI: 13% to 32%) more ambulatory care visits than those assigned to community NSPs.	D

Author (Year)	Design	Intervention details	Population	Outcomes	Applicability
Miller et al (2002)	CS-	Pharmacy sales, fixed site and mobile van NSPs	Vancouver, Canada N=1,020 IDUs who had ever accessed an NSP; 62 pharmacy users, 768 fixed site users and 190 mobile van users	No significant trend for needle borrowing or lending, but pharmacy users were more likely to report needle sharing behaviours (NS). HIV prevalence was lower among pharmacy users than participants who reported using the van or fixed sites NSPs.	C
Obadia et al (1999)	CS-	Sterile needles and syringes were available for purchase from pharmacies, from four NSPs and at seven vending machines	Marseille, France N=373 IDUs; 73 primary users of vending machines and 270 primary users of other programmes	No differences between vending machine users and users of other sources in terms of sharing needles in the previous six months. Vending machine users reported that they were significantly less likely to have shared cookers, cotton and water during the previous 6 months compared to non-users.	C
Rhodes et al (2004)	CS-	Not described	Togliatti City, Russia N=426 IDUs who had injected in previous 4 weeks	IDUs who reported NSPs or outreach workers as their main source of new needles and syringes in the last four weeks were less likely to share compared with those obtaining them from a pharmacy or shop. Participants whose main source was buying needles and syringes on the streets or obtaining them from a sex partner, friend, other drug user, or drug dealer were morel likely to have shared needles and syringes in the last four weeks.	D
Riley et al (2000)	CS-	Mobile van-based NSP and fixed site pharmacy-based NSP.	Baltimore, USA N=286 IDUs, 124 primary users of van-based NSP and 162 users of pharmacy-based NSP	The different sites attracted first-time NSP users with different characteristics. Compared with pharmacy-based NSPs, van based sites attracted twice as many high-frequency injectors.	D

Author (Year)	Design	Intervention details	Population	Outcomes	Applicability
Singer et al (1997)	CS-	Pharmacy sales and community NSP (mobile van)	Hartford, USA N=571 IDUs	Percentage of IDUs that injected with pre-used syringes was lowest among those that used both the NSP and pharmacy (18.5%) and highest among those who accessed neither programme (39.5%; p<0.005). Significant drop in the number of IDUs who were HIV positive (based on testing or self-report) between the periods of legal syringe purchase and when up to five needles could be exchanged at the NSP (35% to 22%; p<0.05).	D
Syringe dispensation policy					
Bluthenthal et al (2004)	CS-	Comparison of NSPs and legal over-the-counter pharmacy access with limits of syringes that can be purchased, exchanged or possessed to IDUs with no pharmacy sales but unlimited syringe access through NSPs	Chicago, Hartford, Oakland, USA N=584 current IDUs (injected illegal drugs at least once in previous 30 days)	Chicago and Oakland IDUs were both less likely to report syringe re-use than IDUs in Hartford. No significant differences in receptive syringe sharing were observed by city.	D
Kral et al (2004)	CS+	Comparison of 23 of the 24 NSPs in San Francisco	California, USA N=531 IDUs who had injected drugs and used NSP in previous 30 days	Participation in a distribution programme was not statistically significantly associated with receptive sharing, distributive syringe sharing or sharing filters. Participants of distribution programmes had lower odds of re-using syringes than other participants.	D
Singer et al (1997)	CS-	Three periods with different syringe dispensation policies: 1) non-prescription pharmacy syringe sales permitted but no NSP; 2) NSP with a five syringe limit; and 3) five syringe limit was increased to ten syringes.	Hartford, USA N=571 IDUs	Over the three periods examined, there was a steady and statistically significant decrease in the percentage of IDUs who reported using pre-used syringes and pre-used supplies. They also noted a significant decrease in the number of IDUs who reported injecting at shooting galleries during the time when IDUs could exchange up to 10 needles per visit to the NSP.	D

Author (Year)	Design	Intervention details	Population	Outcomes	Applicability
Prison-based NSPs					
Nelles et al (1997)	UBA-	Vending machine	Hindelbank prison, Switzerland N=86	No increase in drug consumption and no syringe-related incidents observed. No new cases of HIV, HBV or HCV identified between baseline and follow up, and no abscesses related to drug injection.	C
Stark at al (2006)	UBA-	Vending machine in female prison, and social workers from NGO exchanged equipment in male prison	Berlin, Germany N=166 inmates who had ever used illicit drugs	At baseline 17% of inmates reported sharing in the previous six months, compared to 11% at follow up. Injecting drug use during previous imprisonment was found to be an independent predictor of HIV seroconversion and HCV seroconversion. During follow up, no HIV or HBV seroconversions were observed.	C

6.3 Question 3: Which additional harm-reduction services offered by NSPs are effective and cost effective?

NSPs often offer other harm reduction interventions in addition to needle and syringe exchange, including provision of injecting paraphernalia, advice and information on safer injecting practices, onsite vaccination services, testing for HBV, HCV and HIV and referrals. However, service provision and the range of harm reduction interventions has been found to differ between regions in England (Abdulrahim et al 2006). The majority of needle exchange services in England are pharmacy-based, and since 2003 and the passing of the amendment to Section 9a of the 1971 Misuse of Drugs Act, NSP providers can now supply swabs, utensils, citric acid, filters and ampoules of clean water. Nonetheless, the range of additional services offered by pharmacists is often more restricted than those offered by specialist services.

6.3.1 Overview of evidence identified

Seven studies were identified which addressed the provision of additional services offered by NSPs beyond needle and syringe exchange. Six of the studies (Huo et al 2005 CS-; Kidorf et al 2005 RCT-; Pollack et al 2002 CT+; Sears et al 2001 CS-; Strathdee et al 2006 RCT-; Valente et al 2001 CS-) were based in the USA, and one (Tyndall et al 2002 CT+) in Canada.

Two RCTs (Kidorf et al 2005 RCT-; Strathdee et al 2006 RCT-) examined interventions to encourage IDUs into drug treatment, and one cohort studies (Pollack et al 2002 CT+) compared users and non-users of NSP-based health care services. The remaining studies (Huo et al 2005 CS-; Sears et al 2001 CS-; Tyndall et al 2002 CT+; Valente et al 2001 CS-) all addressed the subject of secondary exchange, whereby IDUs collect and return more syringes than they use personally and distribute them to other IDUs. This practice raises a number of ethical questions, primarily weighing up the benefits of distributing clean injecting equipment as widely as possible among IDUs against the benefits of access to additional goods and services (such as condoms, referrals, BBV testing and counselling), which derive from personally attending NSPs, which Valente et al (2001 CS-) articulate in terms of (competing) individual and community benefits.

Evaluating research in secondary exchange (or distribution) can be hampered by the lack of consistency of terms. Thus while Huo et al (2005 CS-) use secondary exchange in the sense used here, Tyndall et al (2002 CT+) and Valente et al (2001 CS-) used ‘satellite exchange’ to refer to the same practice. Additionally, Valente et al (2001 CS-) use ‘secondary exchange’ to refer to the practice of a network of IDUs

sending one person to the NSP to get needles for the group, but neither they, nor any other contributing authors, provide any evidence of this practice. Finally, Sears et al (2001 CS-) use secondary exchange to refer to an altogether different practice: that of formalised peer-led exchange.

6.3.2 Additional harm reduction services

Strathdee et al (2006 RCT-) conducted a cluster, cross-over RCT to compare the effectiveness of free strengths-based case management (intervention) with passive referral (control) among NSP attenders requesting and receiving referrals to publicly funded drug treatment in Baltimore. The intervention consisted of case managers assisting clients in setting treatment goals and helping them achieve those goals by helping them handle potential barriers to treatment such as transportation or childcare. Passive referral consisted of participants being provided only with a voucher stating the time and date of their intake appointment at the drug treatment programme in accordance with standard operating procedure at the Baltimore NSP.

Kidorf et al (2005 RCT-) evaluated the effectiveness of motivational interviewing (MI) on the treatment interest and enrolment of NSP participants. Study participants were randomly assigned to one of three intervention conditions: 1) 50 minute structured intervention (MI); 2) 50 minute structured interview to address job seeking readiness (JR); and 3) the standard care referral in which participants were instructed to contact the Baltimore NSP themselves if interested in pursing substance abuse treatment.

Pollack et al (2002 CT+) conducted a cohort study examining the impact of a Community Health Care Van (CHCV) accompanying the NSP outreach van on emergency department use by IDUs in New Haven. Services available included acute medical care, HIV counselling and testing and social work referrals. Over the study period, the facilities offered by the CHCV expanded to include diagnosis and treatment of tuberculosis and sexually transmitted infections, a vaccination programme for influenza, tetanus and pneumococcal infections (which can lead to serious diseases such as pneumonia, blood poisoning and meningitis), general health education/counselling and distribution of condoms. It should be noted that the van was not designed or intended to reduce emergency room use. As the authors noted, CHCV staff actively referred (and sometimes transported) patients to the emergency room for services that could not be provided on site. They add, ‘Many of these individuals would not have presented to the ED [Emergency Department] were it not for their clinical interaction with CHCV staff’ (2002: 342). Thus measuring the ‘success’ of the van is difficult since the range of services it could offer expanded

over the study period and attracting difficult-to-reach health care users both reduced and increased ED utilisation. Pollack et al (2002 CT+) noted that some CHCV staff suggested that CHCV emergency room referrals were particularly common before full-scale implementation, when CHCV staff had more limited capacity to care for minor emergency treatments.

Quality Assessment

Both RCTs (Strathdee et al 2006 RCT-; Kidorf et al 2005 RCT-) reported their methodology poorly and were limited somewhat by the possibility of selection bias as the methods of randomisation was not reported by Strathdee et al (2006 RCT-) and poorly reported by Kidorf et al (2005 RCT-). Consequently both RCTs were rated poor quality. Pollack et al (2002 CT+) was a moderately well conducted cohort study, with qualitative assessment of the impact of biases and a well-reported methodology, although loss to follow up and comparisons with non-consenters was not discussed in sufficient detail.

Entry into drug treatment

Strathdee et al (2006 RCT-) reported that, overall, 34% of participants entered treatment within seven days of referral. Participation rates were higher among the intervention arm, who received case management (40%), compared with the control arm (26%; p=0.03). Factors associated with greater odds of entering treatment were receiving case management (OR 1.84; 95% CI 1.07, 3.16), having two or more contacts with the case manager before intake visit (OR 2.47; 95% CI 1.33, 4.59), having received more time with a case manager (OR 1.10; 95% CI 1.03, 1.17) and being driven to treatments by a case manager (OR 4.94; 95% CI 2.19, 11.14). In an 'intention to treat' analysis, participants randomised to case management were more likely to enter treatment after adjusting for farther travel, access to a car and clustering by NSP site (AOR 1.87; 95% CI 0.91, 3.86). Having received more case management time was independently predictive of treatment entry; participants who received 30 minutes or more of case management within seven days were 33% more likely to enter treatment. However, further analysis suggests that the 'active ingredient' of case management was the provision of transportation to the treatment programme.

Kidorf et al (2005 RCT-) included a total of 302 participants in their final analyses. Overall, 33 participants (10.9%) enrolled in treatment, of which 28 participants enrolled in methadone maintenance treatment (MMT). The authors found that there were no group differences in treatment enrolment, and no effect of MI on treatment

enrolment; 10% of the participants assigned to the MI group entered treatment (8% MMT) compared to 13% of those assigned to the JR group (10% MMT) and 10% of standard care participants (9% MMT). There was no difference in methadone treatment retention over the first 90 days of treatment across the three groups. Race and psychiatric co-morbidity were associated with treatment enrolment; participants who enrolled in treatment were more likely to have been diagnosed with major depression and African-American participants were less likely to enrol.

Emergency department use

The results of the cohort study (Pollack et al 2002 CT+), comparing CHCV users with non-users, showed that over the full study period CHCV users made more frequent ED visits. Emergency department use by this group peaked in February 1996, just before the implementation of the full range of CHCV services. After this, ED use by this group slowed markedly. By contrast, the non-user group exhibited increased ED use over 1996 and 1997. Overall, CHCV use was significantly associated with a reduction in the rate of emergency room use (IRR 0.79; 95% CI 0.66, 0.95; $p<0.05$). The authors examined ED utilisation across a range of subgroups, finding statistically significant reduction in overall ED use for five of the ten subgroups examined (Hispanic, male, HIV negative or unknown, health insured and self-reported mental illness).

6.3.3 Secondary Exchange

Of the studies addressing secondary exchange, three were cross-sectional studies conducted in the USA (Huo et al 2005 CS-; Sears et al 2001 CS-; Valente et al 2001 CS-) and one was a cohort study conducted in Canada (Tyndall et al 2002 CT+).

Valente et al (2001 CS-) examined secondary exchange through the analysis of what they termed ‘syringe relay’, where NSP users returned syringes distributed to a different NSP user. They extrapolated that IDUs with lower syringe relay were participating to a lesser extent in secondary exchange, used the NSP more frequently and thus derived a greater level of individual benefit, as measured by HIV seroconversion. Tyndall et al (2002 CT+) compared sources of needles and trends in needle distribution among IDU in Vancouver and Montreal, which have very different policies towards secondary needle exchange. Secondary needle exchange was defined as receiving a new syringe from another individual through trading, purchasing, borrowing, or being given the syringe outright. At the time of the study, needle exchange was restricted to the individual and secondary needle exchange strongly discouraged in Vancouver. By contrast, in Montreal policies had been

developed that allowed individuals to exchange needles for others and secondary exchange was actively promoted. Huo et al (2005 CS-) compared needle sharing behaviours among those who reported always obtaining syringes from NSP personally (primary NSP users), those who obtained at least some of their syringes through other NSP users (mixed/secondary NSP users), and those who obtained no needles – either directly or indirectly – from NSPs (NSP non-users). Sears et al (2001 CS-) evaluated a particular form of secondary needle exchange – that of formalised exchange by trained peer distributors with additional community level activities in San Francisco. The intervention targeted a community of young adult IDUs who were homeless and consisted of four core peer leaders who received training in syringe exchange (including distribution of syringes and other injection equipment such as cookers, filters and containers for sharps) and HIV test counselling.

Quality Assessment

Tyndall et al (2002 CT+) was a moderately well conducted cohort study. The study methodology was fairly well reported although some methodological details were missing, particularly in relation to study recruitment. It was difficult to judge whether the participants included in the analysis were representative of the target population as numbers and reasons of those not meeting the eligibility criteria and non-consenters were not stated.

Huo et al (2005 CS-), Sears et al (2001 CS-) and Valente et al (2001 CS-) were all cross-sectional studies. Huo et al (2005 CS-) reported their methodology poorly and important details were missing. These were mainly in regard to study recruitment, and details such as the proportion of sampled participants meeting the eligibility criteria were not reported. In addition, the peer-driven recruitment method made it difficult to judge what proportion consented and reasons for consenting or not. Sears et al (2001 CS-) reported their methodology poorly. Numbers of participants meeting eligibility criteria and consenting were reported, although the recruitment method was interviewers approaching IDUs on the street, and so may have been subject to some recruitment bias. The methodology in Valente et al (2001 CS-) was poorly presented and although they included details on study recruitment and confounders, they did not report using established data collection tools.

Injection risk behaviours

Tyndall et al (2002 CT+) compared individuals who reported secondary needle distribution in the past six months with individuals who obtained syringes exclusively

from fixed site NSPs, mobile NSPs, pharmacies or health clinics. Combined data from Montreal and Vancouver showed that secondary needle distribution was associated with borrowing used injection equipment/paraphernalia (AOR 2.62; 95% CI: 1.85, 3.71). Participants who reported secondary needle distribution were stratified according to whether they exclusively received clean needles through secondary needle exchange (n=95) or exclusively provided them (n=196). Compared with those who did not report secondary distribution, both exclusively receiving (AOR 2.44; 95% CI: 1.41, 4.23) and exclusively providing (AOR 2.41; 95% CI: 1.56, 3.69) clean needles was associated with borrowing used equipment. For Vancouver, factors associated with secondary needle exchange included borrowing used needles (OR 4.16; 95% CI 2.60, 6.66), borrowing used injecting equipment (OR 3.93; 95% CI 2.59, 5.96), bulk needle exchanges (OR 1.91; 95% CI 1.33, 2.74), at least weekly visits to the NSP (OR 1.58; 95% CI 1.12, 2.23) and obtaining needles from a pharmacy (OR 1.57; 95% CI 1.06, 2.34). For Montreal, the factors associated with secondary needle exchange were borrowing used needles (OR 1.76; 95% CI 1.18, 2.63) and borrowing used injecting equipment (OR 3.09; 95% CI 2.05, 4.67). Tyndall et al (2002 CT+) found that IDUs in Montreal and Vancouver displayed very similar patterns of needle use despite very different distribution policies. They point out that across both cities high risk individuals participated in secondary needle exchange and that the availability of new syringes through alternative sources was an important consideration in reducing the transmission of BBVs.

Huo et al (2005 CS-) reported that of primary and mixed/secondary NSP users, fewer primary exchangers (15.3%) had exchanged needles for others within the previous four weeks compared to secondary exchangers (42.0%; $p<0.001$). Among secondary exchangers, more than half stated a friend as the person who most often went to the NSP on their behalf, and a further third stated a spouse or boy/girlfriend. In terms of syringe sharing, the proportion of IDUs engaging in high risk behaviours increased across the three groupings of IDUs: primary, secondary and non-NSP users. For receptive and distributive needle sharing, 30.0% and 38.8% of primary users reported this behaviour respectively, compared to 42.4% and 52.2% of mixed/secondary NSP users and 51.7% and 54.1% of non-NSP users. Thus, the proportion of study participants who reported needle sharing was significantly lower among primary-only NSP users than secondary and non-users. Similarly, in terms of backloading, fewer primary-only NSP users reported this behaviour (18.6% of primary users compared to 33.9% of secondary users and 40.1% of non-NSP users).

The odds of receptive needle sharing were 61% and 47% lower in primary and mixed/secondary users, respectively, compared with non-users.

Sears et al (2001 CS-) examined an organised programme of secondary exchange combined with community-level activities among homeless young adult IDUs. In logistic regression analysis, comparison site IDUs were more likely than intervention site IDU to report syringe sharing (AOR 3.75; 95% CI 1.41, 9.99) and syringe re-use (AOR 2.77; 95% CI 1.12, 6.85). No independent association was found between intervention site and using someone else's filter.

Blood borne viruses

Valente et al (2001 CS-) reported that among low frequency NSP users the average period of time between distribution and return of a given syringe was 31.2 days, compared to an average 26.8 days among high frequency NSP users. Low frequency users of the NSP were more likely to return syringes originally distributed to someone else, and those syringes circulated in the community about four days (14%) longer compared to high frequency users. Results of the multivariate analysis showed that participants who returned their own syringes ($p<0.001$) and who returned them more quickly ($p<0.05$) used the NSP more. In a subsample of HIV negative NSP users systematically recruited for additional HIV testing (n=262), neither NSP use (OR 1.18; 95% CI 0.65, 2.15) nor circulation time (OR 0.98; 95% CI 0.93, 1.02) were associated with HIV seroconversion. Gender played a role in the likelihood of seroconversion. There was no difference between relay and non-relay males (OR 1.07; 95% CI 0.19, 6.00) and between non-relay males and non-relay females (OR 0.36; 95% CI 0.04, 3.22). However, there was a significance difference in seroconversion among relay females compared to non-relay males (OR 8.53; 95% CI 1.83, 39.79), indicating that relaying females were at particular risk of HIV seroconversion.

Other outcomes

Sears et al (2001 CS-) identified a number of positive associations with living proximately to the peer-run secondary exchange, such as having used any NSP (i.e., primary, secondary or underground) more than three times (86.6% v 52.7; p=0.001); exchanging with friends any time (11.9% v 72.7%; p=0.001); contact with an outreach worker (94.0% v 61.8%; p=0.001) and use of a drop in centre (73.1% v 44.4%; p=0.001). Sears et al (2001 CS-) noted that although all youth in the study had reliable access to new syringes through nearby NSPs, the exceptionally high rate of any NSP use among those living close to the secondary NSP (97.0% v 80.0%) suggested that it is significant that this secondary NSP was designed and

implemented by peers, available most hours of the day and accompanied by community-subculture-specific media and community activities that reinforced the HIV message.

6.3.4 Summary and evidence statements

Few studies were identified that directly examined the effectiveness of additional harm reduction services offered by NSPs. However, it was clear from the literature that few NSP services only distributed sterile needles and syringes, in fact the large majority were linked into wider HIV prevention services including outreach, distribution of harm reduction materials, counselling and testing, and referrals. However, few studies compared NSPs with and without these services.

Seven studies were identified that addressed the provision of additional services offered by NSPs beyond needle and syringe exchange, two RCTs examined interventions to encourage IDUs into drug treatment, and one cohort study compared users and non-users of NSP-based health care services. Strength-based case management was found to support drug treatment entry among IDUs who were seeking treatment (Strathdee et al 2006 RCT-). However, the primary outcome reported was based on IDUs entering into treatment within seven days, and therefore the impact of the intervention on treatment retention and outcome was not clear. Kidorf et al (2005 RCT-) found that MI had no impact on the treatment interest and enrolment of NSP participants. Pollack et al (2002 CT+) reported that provision of a range of health care services delivered alongside an NSP reduced emergency department use among IDUs who utilised that service compared to those who did not.

Four studies examined secondary distribution of needles and syringes to IDUs. Tyndall et al (2001 CT+) identified that secondary needle distribution, defined as receiving a new syringe from another individual through trading, purchasing, borrowing or being given the syringe outright, was associated with high risk injection behaviours including sharing and syringe re-use. In addition, Huo et al (2005 CS-) found that primary only users of NSPs reported significantly lower levels of sharing than mixed/secondary NSPs users and non-users. However, Huo et al (2005 CS-) also found that mixed/secondary NSP users were less likely than non-NSP users to engage in injection risk behaviours and the authors suggested that secondary exchange may facilitate reductions in injection risk behaviours among IDUs. Sears et al (2001 CS-) found that an organised programme of secondary exchange was effective in delivering NSP services to homeless young adult IDUs, and that IDUs who accessed the service reported lower levels of injection risk behaviours than

those who did not access the service. Valente et al (2001 CS-) found that participants who returned their own syringes to the NSP, and who returned them more quickly, were more likely to be frequent NSP users. Among a subsample of HIV tested participants, returning syringes to the NSP originally acquired by someone else was associated with HIV conversion among female IDUs.

It is worth noting that although these articles were concerned with secondary needle exchange, they were in fact discussing rather divergent phenomena. Analysing the impact of encouraging or discouraging needle distribution by NSP users to IDUs not in contact with the NSP (Tyndall et al 2002 CT+) is rather different from comparing characteristics of IDUs who acquire their needles from NSPs directly, some or all indirectly through secondary exchange and no syringes directly or indirectly from NSPs (Tyndall et al 2002 CT+). In turn, both of these studies focused on very different questions to examining HIV seroconversion in relation to syringe relay (Valente et al 2001 CS-) or evaluating the effectiveness of a peer-driven exchange site with volunteers trained in needle exchange and HIV counselling (Sears et al 2001 CS-). However, they all addressed a common question regarding the efficacy and relative merits of encouraging IDUs to come into NSPs personally and thus potentially benefit from the range of additional services offered by NSPs and distributing clean needles as widely as possible. Valente et al (2001 CS-) described this conflict in terms of individual versus community benefit; contact with NSPs and thus access to additional services benefited the individual, whereas secondary exchange benefited the community through greater access to clean needles by IDUs who did not want/were unable to come into contact with NSPs. The results of these four studies have been mixed, with Tyndall et al (2002 CT+) finding there were few differences between different secondary exchange policies, Valente et al (2001 CS-) flagging up syringe relay and the importance of gender, Huo et al (2005 CS-) finding that those who directly used NSP displayed lower risk behaviours than secondary or non-users and Sears et al (2001 CS-) who suggested that a potentially fruitful area of further research lies in identifying and evaluating explicitly different NSP models.

Evidence statement 6.3

6.3a. There is evidence from one poor quality RCT[1] to suggest that strength-based case management delivered via NSPs may support drug treatment entry among clients who request drug treatment. There is evidence from one poor quality RCT[2] to suggest that MI has no impact on the treatment interest and enrolment of NSP participants.

Applicability: As both studies were conducted in the USA, it is unclear whether the findings are applicable to the UK given the differences in the political acceptance of NSPs and wider harm reduction services for IDUs. In addition, differences in the funding of drug treatment services between the UK and USA limit the applicability of this finding.

6.3b. There is evidence from one moderate quality cohort study[3] to suggest that the provision of NSP-based health care services may decrease emergency department utilisation.

Applicability: As all these study were conducted in the USA, it is unclear whether the findings are applicable to the UK given the differences in the political acceptance of NSPs and wider harm reduction services for IDUs. In addition, differences in the funding of drug treatment services between the UK and USA limit the applicability of these findings.

6.3c. There is evidence from one moderate quality cross-sectional study and one poor quality cohort study to suggest that IDUs who exclusively obtain their needles from NSPs are less likely to engage in high risk injection behaviours than those who obtain them via secondary distribution[4]. However, there is evidence from two poor quality cross-sectional studies[5] to suggest that IDUs who obtain needles via secondary distribution engage in high risk injection behaviours less than IDUs who do not use NSPs.

Applicability: As all these study were conducted in the USA, it is unclear whether the findings are applicable to the UK given the differences in the political acceptance of NSPs and wider harm reduction services for IDUs. In addition, the majority of needle exchange services in the UK do not place limits on the amount of equipment exchanged, but there is little consistency regarding service providers' attitudes towards secondary distribution (NTA 2007).

1 Strathdee et al 2006 (RCT-)

2 Kidorf et al 2005 (RCT-)

[3] Pollack et al 2002 (CT+)

[4] Tyndall et al 2001 (CT+); Huo et al 2005 (CS-)

[5] Sears et al 2001 (CS-); Huo et al 2005 (CS-)

Table 6. Studies that examined additional harm reduction services

Author (Year)	Design	Intervention details	Population	Outcomes	Applicability
Additional harm reduction services					
Strathdee et al (2006)	RCT-	Two mobile vans serving 10 NSP sites	Baltimore, USA N=245 treatment seeking IDUs; 128 assigned to case management services and 117 assigned to standard treatment	Participants randomised to case management were 87% more likely to enter treatment within seven days after adjusting for farther travel, access to a car and clustering by NSP site. Further analyses suggested that the 'active ingredient' of case management was the provision of transportation to the treatment programme.	D
Kidorf et al (2005)	RCT-	Mobile van	Baltimore, USA N=302 IDUs who had not arranged treatment; 98 assigned to MI; 96 assigned to job readiness intervention and 108 assigned to standard control	33 participants (10.9%) enrolled in treatment; 28 of which enrolled in MMT. There was no group difference in treatment enrolment, and no effect of MI on treatment enrolment.	D
Pollack et al (2002)	CT+	Health Care van (Community Health Care Van [CHCV]) that travelled in tandem with New Haven NSP	New Haven, USA N=373 active IDUs; 117 had used CHCV, 256 had not used CHCV	CHCV use was significantly associated with a reduction in the rate of emergency department use. Reductions were prominent at the largest local hospital, Yale-New Haven Hospital ED.	D
Secondary exchange					
Sears et al (2001)	CS-	HIV prevention programme for homeless young adult IDUs that combined secondary NSP with community-level activities	San Francisco, USA N=122 current IDU aged 15-25 yrs, homeless; 67 from NSP area and 55 from non-NSP area	Comparison/non-NSP site IDUs were more likely than intervention site IDU to report syringe sharing, syringe re-use, and inconsistent condom use with a casual partner. No independent association was found between intervention site and using someone else's filter.	D

Author (Year)	Design	Intervention details	Population	Outcomes	Applicability
Tyndall et al (2002)	CT+	Fixed site and mobile NSPs One-for-one unlimited at Vancouver NSPs; unlimited at Montreal NSPs. Bulk exchanges of >20 needles per visit were not permitted at Vancouver NSPs.	Montreal and Vancouver, Canada N=956 active IDUs; 391 Montreal and 565 Vancouver	Satellite needle distribution (SND) was associated with borrowing used injection equipment/paraphernalia. Exclusively receiving clean needles through SND (n=95) was associated with borrowing used equipment. Only providing needles through SND was also associated with borrowing used equipment and borrowing used needles.	C
Valente et al (2001)	CS-	Programme distributed clean needles and syringes. Secondary exchange was not accepted and the exchange operated a one-for-one exchange policy	Baltimore, USA N=2,574 NSP users who had visited NSP more than once and returned syringe from NSP; 770 low users, 941 medium users and 863 high users	Low users of the NSP were more likely to return syringes originally distributed to someone else, and those syringes circulated in the community about four days (14%) longer. Results of multivariate analysis showed that participants who returned their own syringes ($p<0.001$) and who returned them more quickly ($p<0.05$) used the NSP more. NSP use was not associated with seroconversion.	D
Huo et al (2005)	CS-	Three storefront locations and one mobile van	Chicago, USA N=886 IDUs; 490 primary only NSP users, 224 mixed/secondary NSP users and 172 non-users	Receptive needle sharing was significantly lower among primary-only NSP users than mixed/secondary and non-users. Among IDUs who shared needles, both primary-only and mixed/secondary NSP users were more likely than non-users to clean their needles with bleach. Primary–only NEP users had significantly lower rates of backloading, sharing injection paraphernalia other than needles (cookers, filters and water), and lending used needles compared with the other two groups. The likelihood of having shared injection paraphernalia other than needles was not significantly different between mixed/secondary NEP users and non-users.	D

6.4 Question 4: Are NSPs delivered in parallel with, or alongside, opiate substitution therapy (OST) effective and cost-effective?

Two studies (Millson et al 2007 UBA -; Van Den Berg et al 2007 CT+) were identified that examined OST delivered in parallel with or alongside NSP services. Millson et al (2007 UBA-) assessed the effects of enrolment in two low-threshold methadone maintenance treatment (MMT) programmes delivered via NSPs on injection risk behaviours. In Canada, where the study was set, low-threshold programmes aim to not necessarily eliminate drug use but to establish and maintain contact with opioid drug users to reduce health and social risks associated with drug use. As part of their participation in low-threshold programmes, clients were exposed to a range of medical and social support services. Van Den Berg et al (2007 CT+) examined the impact of different levels of harm reduction on HIV and HCV incidence in a cohort of drug users in Amsterdam. Harm reduction programmes were initiated in the Netherlands at the end of the 1970s, providing methadone in combination with social and medical care, and needle-exchange facilities across low, medium and high threshold programmes. The effects of harm reduction were measured across five levels in this study. Participants who had received daily methadone (≥60 mg) in the past six months and, if they reported injecting drug use in the past six months, had obtained all of their needles via an NSP were defined as having received full harm reduction. Incomplete harm reduction was defined as: 1) any methadone dose in the past six months, injecting drug use in the past six months and irregular or no NSP use; or 2) 0-59mg methadone daily in the past six months, injecting daily in the past six months and always obtained needles via an NSP.

Quality assessment

Millson et al (2007 UBA-) used a before and after study design to examine the effects of low threshold MMT on injection risk behaviours. However, the study lacked an untreated comparison group and was therefore uncontrolled. Although the overall assessment of the study resulted in a poor quality rating, selection bias was largely minimised as a high proportion agreed to participate in the study. In addition, losses to follow-up were very low. Van Den Berg et al (2007 CT+) examined the effects of harm reduction among participants in the Amsterdam Cohort Study. The study is an ongoing, prospective cohort study which was initiated in 1985. On the whole the study methodology was well reported but some details were missing and the study was rated to be of moderate quality. This was mainly in regard to study recruitment and it was difficult to judge whether the participants included in the analysis were

representative of the population as details such as the proportion of sampled participants meeting the eligibility criteria were not reported.

Injection risk behaviours

Millson et al (2007 UBA-) found that six months after entry into low-threshold MMT programmes delivered through NSPs, there were statistically significant declines in drug injection, needle and paraphernalia sharing and indirect sharing (e.g. backloading or frontloading). Among a subgroup of participants who continued to inject, declines were seen in needle sharing (21.7% vs. 14.2%; OR 0.50; 95% CI 0.23, 1.11) and indirect sharing (10.0% vs. 5.0%; OR 0.40; 95% CI 0.13, 1.28) over the six months, although these findings were not significant. However, significant declines were seen in sharing of injection equipment (37.3% vs. 20.8%; OR 0.27; 95% CI 0.12, 0.62).

Blood borne viruses

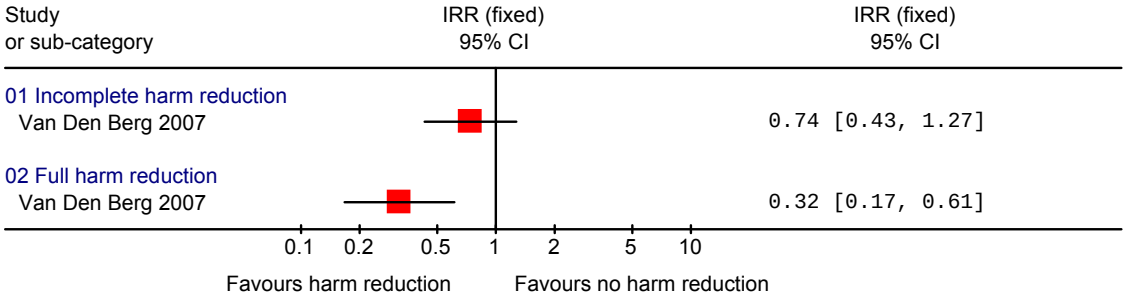
In total, 714 HIV- and/or HCV-negative ever-injecting drug users entered the Amsterdam cohort at study entry and were followed-up until seroconversion for HIV or HCV, or until the end of follow up in November 2005 (Van Den Berg et al 2007 CT+). The authors found that, although not statistically significant, any prescribed dose of methadone was associated with lower incidence rates of HIV and HCV infection (p=0.084 and p=0.21, respectively), but that the use of NSPs was associated with a higher risk of HIV and HCV seroconversion. However, when the authors restricted the sample to participants who had injected in the preceding six months this finding was shown to be non-significant.

HIV incidence was 1.22 per 100 person-year (PY) in the full harm reduction group, compared to 2.80 per 100 PY in the incomplete harm reduction group and 3.80 in the no harm reduction group. As shown in Table 7 and Figure 4, compared to no harm reduction, full participation in harm reduction programmes was associated with a significant reduction in HIV incidence (incidence rate ratio [IRR]: 0.32; 95% CI: 0.17, 0.62). Although incomplete harm reduction was also associated with a reduction in HIV incidence this finding did not reach significance (IRR: 0.74; 95% CI 0.43, 1.27).

Table 7. HIV seroconversion (Van Den Berg et al 2007)

	Incidence (/100 PY)	sc	PY	IRR	95% CI
No HR	3.80	18	473.6	1	
Incomplete HR	2.80	46	1640.8	0.74	(0.43, 1.27)
Full HR	1.22	18	1475.9	0.32	(0.17, 0.62)

Figure 4. HIV seroconversion (Van Den Berg et al 2007)

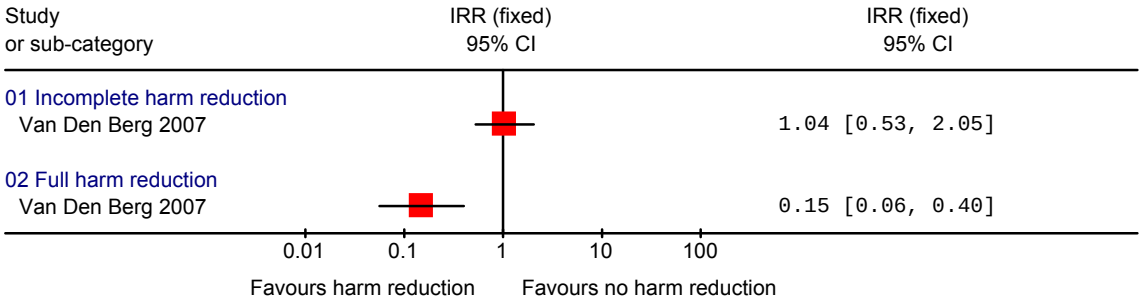


HCV incidence was 3.47 per 100 PY in the full harm reduction group, compared to 24.12 per 100 PY in the incomplete harm reduction group and 23.16 in the no harm reduction group. As shown in Table 8 and Figure 5, participation in full harm reduction was significantly associated with a lower incidence of HCV (IRR 0.15; 95% CI 0.056, 0.40) compared to no harm reduction. Incomplete harm reduction was associated with a higher incidence of HCV compared to no harm reduction, although this finding did not reach significance (IRR 1.04; 0.53, 2.05).

Table 8. HCV seroconversion (Van Den Berg et al 2007)

	Incidence (/100 PY)	sc	PY	IRR	95% CI
No HR	23.16	11	47.5	1	
Incomplete HR	24.12	34	141.0	1.04	(0.53, 2.05)
Full HR	3.47	6	173.0	0.15	(0.056, 0.40)

Figure 5. HCV seroconversion (Van Den Berg et al 2007)



6.4.1 Summary and evidence statements

Two studies were identified that examined needle and syringe distribution delivered alongside OST. Millson et al (2007 UBA-) found that after six months participation in low threshold MMT programmes, the proportion of participants who injected drugs, shared needles, shared drug equipment and indirectly shared had declined over the

whole cohort. However, within a subgroup of participants who continued to inject during follow-up, only the sharing of injection equipment declined significantly. Van Den Berg et al (2007 CT+) found that a comprehensive programme of adequate methadone therapy and full participation in NSP contributed substantially to the reduction of the incidence of HIV and HCV among drug users in Amsterdam. However, a statistically significant effect was not seen when either intervention was considered separately.

Evidence statement 6.4

6.4a. There is evidence from one poor quality uncontrolled before and after study[1] to suggest that participation in low-threshold MMT programmes delivered by NSPs can reduce injection risk behaviours among drug users.

Applicability: This study was conducted in Canada and given the broad similarities in approaches to harm reduction between the UK and Canada, this finding is likely to have good applicability to the UK.

6.4b. There is evidence from one moderate quality cohort study[1] to suggest that the combination of methadone treatment and full participation in NSPs reduces the incidence of HIV and HCV among IDUs.

Applicability: This study was conducted in the Netherlands and given the similarities in approaches to harm reduction between the UK and the Netherlands, this finding has good applicability to the UK.

1 Millson et al 2007 (UBA-)

2 Van Den Berg et al 2007 (CT+)

Table 9. Studies that examined NSP services delivered in parallel to OST

Author (Year)	Design	Intervention details	Population	Outcomes	Applicability
Millson et al (2007)	UBA -	Low-threshold MMT programme delivered via NSPs	Kingston and Toronto, Canada N=183 opioid users enrolled in two MMT programmes	At ix month follow-up, proportion of participants injecting drugs, sharing needles, sharing drug equipment and indirectly sharing declined over the whole cohort. Within a subgroup of participants who continued to inject, only the sharing of injection equipment declined significantly.	C
Van Den Berg et al (2007)	CT+	Harm reduction measured by combining methadone dose and NSP use	Amsterdam, The Netherlands N=878 HIV negative and/or HCV negative drug users	When methadone dose and NSP use were combined, full participation in harm reduction programmes was associated with a significant reduction in HIV and HCV seroconversion.	B

7 REVIEW OF PUBLISHED ECONOMIC EVALUATIONS

7.1 Overview of evidence identified

A total of 13 full economic evaluations were identified for inclusion, including 12 cost-effectiveness analyses and one cost-benefit analysis. All of the included studies examined the provision of access to sterile needles and syringes. The cost-effectiveness of specific/named interventions were examined in seven studies (Cabases & Sanchez 2003; Gold et al 1997; Harris 2006; Jacobs et al 1998; Kumaranayake et al 2004; Laufer 2001; Vickerman et al 2006). Cohen et al (2004; 2006) examined a range of HIV prevention interventions including needle exchange. Holtgrave et al (1998) examined a policy of increased availability of sterile syringes via NSPs and pharmacy sales across the USA. Lurie and Drucker (1997) estimated the number of HIV infections that could have been prevented in the USA had NSPs been implemented. Health Outcomes PTY Ltd et al (2002) examined the implementation of NSPs in Australia.

Eleven studies examined reduction in HIV incidence (Cabases & Sanchez 2003; Cohen et al 2004; Cohen et al 2006; Gold et al 1997; Harris 2006; Holtgrave et al 1998; Jacobs et al 1998; Kumaranayake et al 2004; Laufer 2001; Lurie and Drucker 1997; Vickerman et al 2006), one study examined HCV incidence (Pollack 2001) and one study examined reductions in both HIV and HCV incidence (Health Outcome International PTY Ltd et al 2002).

Four studies developed behavioural models using simplified Bernoulli process formulas (Holtgrave et al 1998; Cabases and Sanchez 2003; Cohen et al 2004; Cohen et al 2006). Cabases and Sanchez (2003) adapted the model developed by Holtgrave et al (1998). Kumaranayake et al (2004) and Vickerman et al (2006) were based on the same model that simulated the transmission of HIV resulting from syringe and needle sharing and heterosexual contact among groups of IDUs and their sexual partners. Four studies (Harris 2006; Jacobs et al 1998; Laufer 2001; Pollack 2001) developed models based on the theory of needle circulation originally developed by Kaplan and O'Keefe (1993). The circulation theory of needle exchange focuses on the behaviour of needles rather than IDU. In the model, needle exchange reduces needle circulation times, which in turns leads to a reduction in the fraction of needles infected with HIV because of reduced opportunities for sharing needles (Kaplan and Heimer 1994). The model assumes that HIV incidence via needle sharing is proportional to the level of infection in circulating needles. Vickerman et al (2006) have commented that the assumptions in this model did not reflect

observations in other IDU populations and therefore has limited relevant to other settings.

7.2 Review of cost-effectiveness evidence for HIV

7.2.1 Review of Cabases and Sanchez (2003 CEA+)

Overview

Cabases and Sanchez (2003 CEA+) estimated the costs and effectiveness of distributing 'anti-AIDS kits' to IDUs in Navarra, Spain via NSPs or pharmacy sales. The kits contained one syringe and needle, one condom, a paper towel and an ampoule of distilled water. Effectiveness was expressed as a function of the level of coverage of the programme. The authors compared programme costs with effectiveness, measured as the number of averted HIV infections due to needle use patterns among IDUs.

Summary of effectiveness data

The authors adapted a model of HIV transmission developed by Holtgrave et al (1998), in which effectiveness was expressed as a function of the level of coverage of the programme. Coverage was defined as the extent of substituting non-sterile syringes with sterile syringes provided to the IDU population as part of the programme. Information on the annual number of anti-AIDS kits supplied and estimates of the number of active IDUs in the population were provided by the Government. The mean number of injections per IDU was drawn from a survey of 120 IDUs in Navarra, Spain, and the fraction of lost and unused sterile syringes out of the total number supplied was taken from Holtgrave et al (1998). The authors estimated that the total number of HIV infections averted by the programme between 1993 and 2000 was 34.

Summary of resource utilisation and cost data

Total programme costs were estimated from the costs of production, management, distribution and disposal of the anti-AIDS kits and the programme running costs estimated from accounts. Unit costs of production were valued at the health authority purchasing price and commercial costs were valued at the price of the kit for the user (€0.3 per unit). Other costs considered included programme management costs, coordination costs (valued in Year 2000 prices and deflated at the consumer price index for each year), NGO costs, and syringe disposal costs. Out of pocket costs to

IDUs purchasing the kits were not included. Total programme costs ranged from €27,490 in 1993 through to €54,477 in 2000.

Summary of cost-effectiveness data

The authors described a CEA with calculations of incremental costs of syringe distribution per HIV infection averted per year. As shown in Table 10, annual ICERs ranged from €8,331 (1994) to €44,287 (2000). The annual cost per HIV infection averted was lower than the cost of treating one infected person (estimated at €99,371) and the results showed the programme to be cost saving for each of the eight years of the study period.

Table 10. Programme ICERs (Cabases & Sanchez 2003)

	Incremental programme costs	New HIV infections without NSP	New HIV infections with NSP	Number of HIV infections averted	ICER (cost per averted HIV infection)
1993	27,490	74.1	72.8	1.34	20,533
1994	60,505	71.6	64.3	7.26	8,331
1995	66,410	67.4	59.8	7.59	8,752
1996	75,405	46.2	40.3	5.88	12,826
1997	79,887	41.4	35.7	5.65	14,137
1998	77,445	27.7	24.0	3.67	21,080
1999	66,947	18.1	16.2	1.90	35,274
2000	54,478	14.2	13	1.23	44,287

Comments

The authors compared programme costs of an HIV prevention intervention targeting IDUs with effectiveness for the eight years since the programme was introduced, using no programme as the comparator. Effectiveness estimates were based on local survey data where available and from previous publications when not. The measure of benefit, HIV infections averted, was modelled using a simplified mathematical model of HIV transmission adapted from Holtgrave et al (1998), which required a number of assumptions to be made. The analysis was considered from the viewpoint of the health care system and a range of costs were included. However, it may have been relevant for the analysis to consider costs from the perspective of IDUs, which were relevant given the out of pocket costs for purchasing the anti-AIDS intervention in pharmacies (€0.3 per unit). Health care costs of HIV treatment were estimated from local data and appeared comprehensive.

7.2.2 Review of Cohen et al (2004 CEA+)

Overview

Cohen et al (2004 CEA+) estimated the relative cost-effectiveness of 26 HIV prevention interventions across four broad categories: individual, community and

social network, biomedical and structural. Structural interventions examined included needle exchange.

Summary of effectiveness

For assessing interventions that prevented HIV transmission through needle sharing, the authors adapted a Bernoulli process formula. The model calculated HIV infections prevented based on HIV prevalence in drug users, the number of injections and frequency of needle sharing. For each intervention, the authors selected one study that demonstrated its effectiveness in changing HIV incidence, STI incidence or risk behaviour (unprotected sex or needle sharing). Estimates of effectiveness for NSPs were drawn from two previously published studies that examined the numbers of needles exchanged over a three month period (Heimer et al 1998; Kaplan 1995).

Summary of resource utilisation and cost data

To estimate the costs for some interventions, the authors used published cost analyses or cost-benefit analyses. For other interventions, the authors estimated the cost of person-hours, supplies, and overheads needed to implement the intervention based on salary and subcontract figures supplied by HIV prevention staff at the Louisiana Office of Public Health and/or the LA County Department of Health.

Summary of cost-effectiveness data

The authors calculated incremental cost-effectiveness ratios for each intervention, compared to no intervention. An ICER of US$13,000 per HIV infection averted was calculated for needle exchange (adjusted to 12 months). The sensitivity analyses showed that the results were sensitive to variations in the prevalence of HIV infection. The averted lifetime costs of HIV treatment, at $20,000, were used as a threshold in the analysis for determining whether or not the intervention was cost-effective. Compared to HIV treatment, needle exchange was only cost-effective when HIV prevalence among IDUs was high (20%). Among targeted interventions for groups with high HIV prevalence, the most cost-effective interventions were opinion leader programme and community mobilisation using the Mpowerment model.

Comments

The authors examined a range of HIV prevention interventions including needle exchange, however interventions were not directly comparable as the authors were unable to use a single model across the interventions examined. Estimates of effectiveness were based on estimates derived from mathematical models of HIV

transmission among IDUs. The measure of benefit was the number of HIV infections prevented over 12 months, which was derived from a model based on a Bernoulli process formula. The duration of intervention effectiveness was adjusted from three months to 12 months in the case of NSPs, and it was unclear whether this adjustment was appropriate. The cost analysis was conducted from the viewpoint of the public health system and all relevant costs appear to have been included. However, some costs were estimated and in sensitivity analyses the cost per person reached by the intervention was found to have a large impact on cost-effectiveness.

7.2.3 Review of Cohen et al (2006 CEA-)

Overview

Cohen et al (2006 CEA-) examined whether structural HIV prevention interventions (e.g. needle exchange, condom availability) were cost-effective in reducing HIV among women in the Southern US states.

Summary of effectiveness data

The number that would be reached by the interventions (n=1,000) and intervention effectiveness (increase in proportion of needle exchanged from 34% to 63%) were drawn from previous evaluations. For NSPs, the number of HIV infections prevented was calculated at 1.1 per year.

Summary of resource utilisation and cost data

Costs were taken from the literature or estimated. The cost of NSPs was estimated at $10 per person for a three-month period (Heimer et al 1998; Lurie et al 1998). The authors arbitrarily chose a one time cost of $100,000 for needle deregulation to cover the lobbying and education of pharmacists.

Summary of cost-effectiveness data

For NSPs, a cost per HIV injection averted (over three months) of US$9,000 was calculated. The authors stated a cost-effectiveness threshold value of $200,000 per HIV infection averted as this was the amount required per person to treat HIV.

Comments

The authors examined the cost-effectiveness of six structural HIV prevention interventions including needle exchange. The methods used to examine the cost-effectiveness of NSPs were the same as those used in the previous study by Cohen et al (2004). See this study for comments.

7.2.4 Review of Gold et al (1997 CEA-)

Overview

Gold et al (1997 CEA-) examined whether a mobile needle exchange programme targeting IDUs in Hamilton, Canada was cost-effective. The programme operated across three sites, one mobile and two fixed. In addition to needle exchange, the programme provided other harm reduction services including substance abuse counselling and referral, HIV testing, HBV vaccination, safer-sex counselling and the provision of condoms and dental dams.

Summary of effectiveness data

To determine effectiveness, the authors developed an incidence outcome model to estimate the number of new cases of HIV infection expected over five years among IDUs using the NSP. Baseline HIV prevalence rates were drawn from five Canadian studies, from which the authors chose an estimate of 3%. HIV incidence without NSPs were drawn from two American studies and estimated at 4%. The estimate of HIV incidence with NSPs was drawn from Kaplan and Heimer (1994), from which the authors assumed an HIV incidence rate of 2%. For 275 programme users, it was estimated that 24 cases of HIV infection would be prevented over a five-year period.

Summary of resource utilisation and cost data

Programme costs for the NSPs were drawn from budgetary data, and estimates of health costs relating to HIV infection were based on data from a previously published study (1995 Canadian dollars). Costs were discounted (5%) and the authors included both direct and indirect costs. Indirect costs were productivity losses associated with time spent by the volunteers. Estimates of the costs of treating HIV infection were based on a previous Canadian study and included inpatient and outpatient hospital costs, and physician services and medication costs. Average lifetime costs of HIV treatment were estimated to be $100,167 (1991 Canadian dollars).

Summary of cost-effectiveness data

Over five years, the costs of the programme were CAN$349,012 at the baseline discount rate of 5%. The authors calculated the lifetime cost of illness for a person with HIV/AIDS to be $68,394. At the 5% discount rate and assuming 275 IDUs participated in the programme, total cost savings associated with the programme were CAN$1,292,44 resulting from the prevention of HIV cases. If HIV incidence in the absence of an NSP was higher (10.7%) this resulted in savings of

CAN$5,943,236 and increasing the number of IDUs using the service (n=550) resulted in cost savings of CAN$2,865,605. Varying the discount rate from 1% to 10% resulted in cost savings across the range (CAN$1.8 million to CAN $800,000, respectively).

Comments

A 'do-nothing' option was used as the comparator in this study which examined cost-effectiveness of a mobile NSP. Effectiveness estimates were drawn from Canadian and American studies, but no justification for using these studies was reported. The authors reported that these estimates were conservative and baseline estimates of HIV incidence without an NSP and the number of IDUs using the programme were increased in a one-way sensitivity analysis. The viewpoint of the cost analysis was not explicitly stated, but it broadly considered costs to the provider, including direct costs of the programme and 'non-market costs' relating to community volunteers and pharmacists. Costs were drawn from budgetary data.

7.2.5 Review of Harris (2006 CEA+)

Overview

Harris (2006 CEA+) sought to determine the optimal allocation of resources within a multi-site needle exchange programme. Prevention Point Philadelphia (PPP) operated across six sites and provided sterile needles and syringes and clean injection equipment supplies. It also provided HIV testing and counselling, referrals for drug treatment, medical care for HIV and social and legal services. The author adapted the circulation model of the spread of HIV among IDUs, originally developed by Kaplan and colleagues.

Summary of effectiveness data

The number of new infections per unit time that result from an NSP was written as a function of the rate of distribution of needles per unit time and two positive constants which were dependent on the following parameters: rate at which infected IDUs die or leave the community; the probability that an IDU will disinfect a needle prior to injection; the frequency of shared injections per IDU per year; and the prevalence of HIV in circulating needles in the absence of an NSP. Data for these parameters were drawn from 12 studies of NSPs, although parameters included in the model were largely drawn from the evaluation of the New Haven NSP by Kaplan et al.

Summary of resource utilisation and cost data

Data on total costs and costs directly related to the numbers of syringes distributed were obtained via personal communication with the executive director of the NSP, and based on unpublished budgetary data. Costs included in the analysis were not well described but included mobile vehicle operating costs, costs of client services (e.g. HIV testing and counselling, referrals for health care), costs of syringes and ancillary materials (e.g. bleach, sterile water, alcohol swabs and biohazard containers), and distribution and disposal costs. Total NSP costs were estimated at $371,000 annually. Costs per syringe distributed were estimated at $0.13.

Summary of cost-effectiveness data

The author reported that the NSP could spend the same budget more effectively by equalising the number of syringes exchanged per client (a mean of 22.08 per client across each site in the case of PPP) and that this implied that operating hours needed to be increased from 13 hours across the six sites to 13.8 hours; in particular at sites in areas of the city with a high density of IDUs. At the median estimate of the optimal total number of IDU clients (n=8,221), the estimated cost per HIV infection averted was US$2,757 as shown in Table 11. This corresponded to an approximate 28% increase in the size and cost of the programme.

Table 11. Optimal total number of IDU clients and estimated cost-effectiveness ratios, PPP

Estimated value	Low	Median	High
Optimal number of clients, N	14,734	8,221	5,295
Cost-effectiveness ratio ($ per HIV infection averted	2,258	2,757	4,229

Comments

The comparator in the analysis was the absence of the NSP. Effectiveness estimates were drawn from 12 studies of NSPs, but the use of these studies was not justified by the authors. Estimates incorporated into the model were derived from mathematical models of HIV transmission among IDUs. The measure of benefit, the number of HIV infections averted, was estimated using a model based on the theory of needle circulation. Costs included in the analysis were not reported in detail and the viewpoint of the analysis was not clear. It was therefore possible that some relevant costs were not considered. In the model the author distinguished between costs that varied with the number of clients and costs that varied with the number of syringes

exchanged, resulting in marginal costs per distributed syringe considerably lower than estimates from previous studies.

7.2.6 Review of Health Outcomes International PTY Ltd et al (2002 CBA+)

Overview

The authors developed an economic model to compare the costs of operating NSPs during the 1990s to the anticipated savings that would accrue from the number of cases of HIV and HCV avoided as a result of NSPs (Health Outcomes International PTY Ltd et al 2002 CBA+). The authors calculated return on investment by discounting future cashflows associated with the investment in the NSP program and treatment costs avoided by a range of agreed discount rates (5%, 3% and 0%). The impact of NSPs on both HIV and HCV was considered in the analysis.

Summary of effectiveness data

Estimates of the number of HIV and HCV infections avoided through the introduction of NSPs were calculated according to stage of disease. NSPs were assumed to have reduced HIV and HCV prevalence among IDUs from 1988 onwards. The effect of NSPs in reducing HIV transmission among IDUs was estimated to correspond to an annual reduction in (logit) HIV prevalence of 0.28, and therefore the pattern of HIV prevalence if NSPs had not been introduced was estimated by increasing (logit) HIV prevalence by 0.28 per year from 1988 onwards. The pattern of HCV incidence had NSPs not been introduced was derived by assuming that HCV prevalence would have remained constant at 1988 levels from 1988 onwards. The authors assumed that the introduction of NSPs had no effect on HCV transmission through routes other than injecting drug use (e.g. needle stick injuries in health care workers). The authors estimated that by the year 2000, approximately 25,000 HIV infections and 21,000 HCV infections had been prevented since the introduction of NSPs in 1988.

Summary of resource utilisation and cost data

Only direct costs were included. Direct costs included the costs of operating NSPs themselves, the infrastructure associated with their development and operation, and the costs of safe disposal of used syringes and needles. Data on the expenditure on operating NSPs in Australia during the 1990s was sought from all State and Territory health authorities.

Health care cost estimates for HIV and HCV were drawn from previously published studies. In determining the health care costs for HIV, the authors made the following

assumptions: all people who acquire HIV infection are at risk of progression to advanced HIV disease; and the health care costs of acute HIV are small, due to the often asymptomatic nature of newly acquired HIV infection, and therefore were not considered in the total costs. Costs included were the costs of antiretroviral therapy and HIV/AIDS management (e.g. hospitalisation costs, doctor visits, HIV viral load testing). The following assumptions were employed in determination of health care costs for hepatitis C: 75% of people who acquire HCV infection develop chronic hepatitis C; the health care costs of acute hepatitis C are small, due to the largely asymptomatic nature of newly acquired HCV infection, and therefore were not considered in the total costs; all people with chronic hepatitis C are at risk of progression to advanced liver disease complications; and people can either remain in disease states or progress forward but not regress. Costs were included for hospitalisation, doctor visits, pathology services, liver ultrasound, liver biopsy, liver failure with and without transplant, and hepatocellular carcinoma with and without surgery. Annual costs of treatment of HIV and HCV by stage of disease were converted to Year 2000 prices.

Summary of cost-effectiveness data

HIV: Net savings to government from its investment in NSPs over the lifetime of cases of HIV avoided (after deducting the value of the initial government investment) before discounting were AUS$6,896 million. Discounting these savings at 5% resulted in a Net Present Value (NPV) of their investment of AUS$2,277 million (AUS$3,415 million at 3% discount rate). Considering all expenditure, the equivalent returns were AUS$6,876 million undiscounted, and AUS$2,262 million and AUS$3,398 million at discount rates of 5% and 3%, respectively. Considering the return achieved to the end of the investment period (2000), the government had achieved net savings of AUS$373 million (after deducting the value of their investment), the NPV of which at a discount rate of 5% was AUS$242 million (AUS$287 million at a discount rate of 3%). The equivalent returns on the total investment in NSPs over the same period were AUS$353 million (undiscounted), AUS$227 million (5% discount rate) and AUS$270 million (3% discount rate).

HIV and HCV: The net savings to government from its investment in NSPs over the lifetime of cases of HIV and HCV avoided (after deducting the value of the initial government investment) before discounting were AUS$7,678 million. Discounting these savings at 5% resulted in a NPV of their investment of AUS$2,402 million (AUS$3,653 million at 3% discount rate). When considering total expenditure, the

equivalent returns were AUS$7,658 million (undiscounted), AUS$2,386 million (5% discount rate) and AUS$3,637 million (3% discount rate).

In sensitivity analysis the outcomes presented were most sensitive to the impact of NSPs on HIV incidence. Halving the rate of effect of NSPs on HIV incidence had a proportionally greater effect on the number of cases avoided over time. However, even at the most conservative estimate of effect (one quarter of the original effect estimate) the return on investment was positive.

Comments

The costs and benefits of operating NSPs in Australia during the 1990s were compared to the absence of NSPs. The measures of benefit used in the analysis were the number of HIV and HCV infections avoided. Effectiveness estimates were based on an ecological study design used to compare HIV and HCV incidence among IDUs in countries with and without NSPs. Several sources were used to identify studies and this increased the validity of the estimate, however ecological studies examine populations rather than individuals and should not be used to demonstrate causal links between exposure and outcomes. Further limitations of the methodology used in the ecological study were discussed by the authors. The analysis of costs only considered the direct costs and savings associated with NSPs. In addition, the estimates of future treatment costs were based on current treatment regimens. However, in sensitivity analyses the return on investment from NSPs was still positive when future treatment costs were halved.

7.2.7 Review of Holtgrave et al (1998 CEA-)

Overview

Holtgrave et al (1998 CEA-) estimated the costs and cost-effectiveness of a policy of increased availability of sterile syringes via NSPs and pharmacy sales by examining a variety of levels of programme coverage. Coverage was defined as the percentage of non-sterile injections by IDUs for which sterile syringes were made available by the programme.

Summary of effectiveness data

Effectiveness of a programme at a given level of coverage was based on a simplified mathematical model and expressed as the fraction reduction in disease at that coverage level.

Summary of resource utilisation and cost data

The authors used a one-year time frame for policy implementation costs and a multi-year analytic time horizon for estimating the lifetime medical costs saved when an HIV infection is averted. Gross unit costs per syringe distributed and disposed were calculated based on data from a previous study. The authors assumed that 25% of syringes were provided via NSPs (at a cost of $0.97 per syringe) and that 75% were provided via pharmacy sales (at a cost of $0.17 each). Costs were converted into 1996 prices to give a weighted average cost per syringe of $0.44. Total programme costs at 100% coverage were US$423 million ($277 million NSP costs and $145.8 million pharmacy-based sale costs).

Summary of cost-effectiveness data

The base case values for each parameter used in the analysis are shown in Table 12. At 100% coverage, the average cost-effectiveness ratio[5] was $34,278 per HIV infection averted. The authors reported that such a programme represented net savings of more than US$916 million in medical care and treatment costs for HIV. The authors also reported marginal cost effectiveness ratios[6]. The programme was marginally cost saving up to 88.4% coverage (cost-effectiveness ratio = $108,469 per HIV infection averted). Programme coverage rates above this were cost-effective, but were not cost saving in comparison to the medical care and treatment costs for HIV.

Table 12. Parameters and base case values (Holtgrave et al 1998)

Parameter	Base case value
Active IDUs in USA	1,000,000
Injection per IDU per year	1022
Injections with non-sterile syringe per IDU per year	868
Fraction of syringes lost or not used	0.1
Coverage of drug injections	0.0 to 1.0
Gross cost/syringe	$0.44
New HIV infections among IDUs per year	19,000
Proportion of new HIV infections among IDUs per year caused by injection behaviours	0.65

[5] The average cost-effectiveness ratio is used to compare a policy at a given level of coverage with the absence of that policy.

[6] The marginal cost-effectiveness ratio is used to compare a programme at a given level of coverage to a programme at a lower level of coverage; when the level of coverage is zero the marginal cost-effectiveness ratio is equal to the average cost-effectiveness ratio.

Comments

The study estimated the costs and benefits of NSPs over one-year at different levels of programme coverage ranging from 0 to 100%. Estimates of the effectiveness of NSPs were drawn from studies in three US cities, though the authors made a somewhat arbitrary estimate that 15% of IDU injections were made with sterile syringes. The measure of benefit, HIV infections averted, was based on a simplified mathematical model and several of the parameters in the model were estimated. The authors used a societal perspective but as few details of the costs included were provided it is difficult to judge whether all relevant costs had been considered. However, health service costs and out of pockets costs for IDUs were included. The findings of the study are likely to be sensitive to the parameter estimates used but the authors did not undertake any sensitivity analyses.

7.2.8 Review of Jacobs et al (1998 CEA-)

Overview

Jacobs et al (1998 CEA-) conducted a CEA of the Edmonton Streetworks NSP. The programme was based at two fixed site locations and included an outreach van.

Summary of effectiveness data

A model of programme effectiveness was developed based on circulation theory (Kaplan and O'Keefe 1993) using the parameters and base case values shown in Table 13. The model predicted the number of new infections which resulted from a year's supply of needles based on the number of needles distributed, sharing behaviours among IDUs, the number of uninfected IDUs, and on the infectivity of each shared needle. The amount of needle sharing and HIV seroprevalence within the IDU population, with and without an NSP, was determined from a survey of 100 IDUs who used the NSP. In the first year of the programme the authors estimated that 20.33 new HIV infections would have been averted.

Table 13. Parameters and base case values (Jacobs et al 1998)

Parameter	Base case value
Proportion of population susceptible to HIV infection	0.93
Total number of circulating needles (1997)	565,754
Proportion of needles shared without NSP	0.24
Proportion of needles shared with NSP	0.08
Proportion of shared needles which are uncleaned	0.5
Transmission rate	0.005
Rate of HIV infection in the IDU population	0.07
Number of sharing partners per shared injection	1.38

Summary of resource utilisation and cost data

Data on costs were obtained from the financial records for the NSP across five areas, needle exchange, condom provision, nursing, education and research, and administration/overheads. Costs of unpaid volunteers were included at a cost of $15.00 per hour and costs of donated facilities were included at the rate required to rent them. Total programme costs were estimated at CAN$194,916.

Summary of cost-effectiveness data

The operations of the NSP were examined over one year. Cost per HIV infection averted was CAN$9,537. When the rate of infection in the IDU population was adjusted to 13.9%, cost per HIV infection averted was CAN$4,829.

Comments

The authors considered a do-nothing approach as the comparator in an analysis that examined the costs and benefits of the Streetworks NSP over one year. Effectiveness estimates had limited validity as they were based on a behavioural survey among IDUs. IDUs who participated in the NSP were asked to estimate the number of used or shared needles they would use in the absence of the programme. The measure of benefit, HIV infections averted, was estimated from a model based on the circulation theory approach. The model only included HIV transmission via sharing but the authors did not discuss other limitations of the model. The viewpoint of the analysis was not stated, but it was assumed to be from the perspective of the health service based on the costs included. Direct costs and the costs of volunteer and donated services were considered.

7.2.9 Review of Kumaranayake et al (2004 CEA+)

Overview

Kumaranayake et al (2004 CEA+) undertook a CEA of a harm reduction and HIV prevention project in Belarus. Syringes, condoms and information, education and communication materials were distributed at two NSPs. In addition, mass media was used to inform the wider public about HIV/AIDS and the risks of injecting drugs. The project experienced an 8-month shortfall in funding both within and after the evaluation period of the study. A dynamic, deterministic mathematical model was developed to estimate how the intervention impacted on HIV transmission among IDUs and their sexual partners, the methods of which were adapted to consider the

effects of the funding gap. Model inputs included behavioural data, contextual inputs about the initial level of HIV infection, and intervention coverage.

Summary of effectiveness data

Intervention coverage was approximated by dividing the number of IDUs reached by the intervention (n=565) by the total number of registered IDUs (n=900 to 1,300). The impact of the programme on injecting and sexual behaviours was determined through two cross-sectional behavioural surveys. The first survey was conducted prior to the introduction of the intervention and the second survey was conducted at the two NSPs. The surveys identified significant increases in the number of IDUs who reported never sharing (8% in the first survey and 65% in the second) and in the number who reported cleaning syringes before re-use (16% in the first survey and 55% in the second).

Including the 8-month funding gap in the analysis, an estimated 176 HIV infections were averted among IDU and their sexual partners over two years (95% CI: 60, 270) equating to a 48% reduction in the number of HIV infections in the IDU population 95% CI: 35%, 62%). Without the funding gap, the authors reported that an additional 45 HIV infections over two years (95% CI: 27, 67) would have been averted.

Summary of resource utilisation and cost data

Costs of the intervention were analysed over two years (both with and without the eight-month shortfall in funding). Cost data were collected retrospectively and included capital and recurrent costs as shown in Table 14. A discount rate of 3% was used to obtain the annualised cost for capital items. All costs were presented in US 2002 dollars. Total programme costs with and without a gap in funding were estimated at $63,210 and $71,436, respectively.

Table 14. Data included in cost analysis (Kumaranayake et al 2004)

Cost category	Actual costs with gap in funding	Estimated costs with no gap in funding
Capital		
Start-up	612	612
Buildings	337	353
Equipment	716	716
Total capital costs	1,665	1,681
Recurrent		
Personnel	7,731	8,347
Mass media	34,213	38,902
Supplies	16,227	18,867
Vehicle operating and maintenance	1,845	2,116
Building operating and maintenance	220	214
Other	1,310	1,310
Total recurrent costs	61,545	69,756
Total costs US$	63,210	71,436

Summary of cost-effectiveness data

For the two year duration of the programme, the cost per HIV infection averted was $359 (95% CI $234 to $1054). Without the 8-month gap in funding the estimated cost-effectiveness ratio of the project would have been reduced; the authors estimated a cost per HIV infection averted of US$323 (95% CI $188 to $680). HIV infections averted and cost-effectiveness after two years of intervention activity are shown in Table 15. In sensitivity analysis, initial IDU HIV prevalence had the greatest effect on model outputs. For example, a 5% increase in HIV prevalence (from 74% to 78%) resulted in a 27% increase in the cost-effectiveness ratio.

Table 15. HIV infections averted and cost-effectiveness (Kumaranayake et al 2004)

Cumulative HIV infections averted among IDUs	Cumulative HIV infections averted among non-IDUs	Total cumulative HIV infections averted	Cost per HIV infection averted (US$2002)
With gap in funding 138 (70, 185)	38 (-40, 110)	176 (60, 270)	359 (234, 1054)
Without gap in funding 167 (105, 235)	54 (-15, 180)	221 (105, 380)	323 (188, 680)

Comments

The cost and benefits of an intervention for IDUs in Svetlogorsk, Belarus, were estimated relative to the absence of the intervention over a two year period. Effectiveness estimates were drawn from two behavioural surveys conducted before and after the introduction of the intervention. However, as both surveys were cross-sectional it limited the validity of the effectiveness estimates. The estimate of the measure of benefit, HIV infection averted, was modelled using a dynamic, deterministic mathematical model and this appears to have been appropriate to model the impact of the intervention on HIV prevalence. The perspective of the study was from the viewpoint of the provider and an appropriate range of costs were considered. Costs for two years were modelled with and without an eight-month gap in funding. The study was conducted in a setting that had experienced an HIV epidemic among its HIV population and HIV prevalence was high among IDUs (74%). Therefore, it is likely that the results of this study are not generalisble to the UK, where HIV prevalence among IDUs is relatively low.

7.2.10 Review of Laufer (2001 CEA+)

Overview

Laufer (2001 CEA+) analysed the cost-effectiveness of state-approved NSPs in New York. State regulations required that the programmes provide needle and syringe

exchange in the context of comprehensive harm reduction services such as outreach, distributing condoms and bleach kits, making referrals for HIV counselling and testing, and providing literature and instruction on HIV prevention and safer injection techniques. At the time of the study, 12 NSPs were legally operating in New York, though only data from seven were included in the analysis.

Summary of effectiveness data

Two methods were used to estimate effectiveness. However, the authors used the number of HIV infections averted as estimated by a simplified circulation model in the base case analysis. The simplified circulation model used the number of needles exchanged per IDU per year and the number of shared injections per IDU per year. The number of number of needles exchanged was estimated at 369.99 per IDU per year, by dividing the number of needles distributed by the NSPs by client-years of participation. The number of shared injections was estimated at 245.7 per IDU per year. This was calculated by multiplying IDUs' injection frequency by the proportion of injection that are shared; estimated at 780 and 31.5%, respectively. The authors reported that an estimated 87 HIV infections were averted.

Summary of resource utilisation and cost data

Costs were analysed over a 12-month period. Costs reported were for personal services (including fringe benefits) for the syringe exchange activities as well as for other activities required (e.g. condom and bleach distribution) and ancillary activities (e.g. counselling). Expenses relating to supplies, materials, travel, subcontracts and other non-personal services were also collected. Costs incurred by participants were not included in the analyses. Estimates of costs relating to treatment for HIV were drawn from a previously published study. Total costs across the seven programme sites were $1,822,426.

Summary of cost-effectiveness data

The cost-effectiveness ratio for the base case scenario was US$20,947 per HIV infection averted across all reported programmes. On a programme specific basis, costs per HIV infection averted ranged from US$11,648 to US$129,008. The authors calculated that averting 87 HIV infections through IDU participation in NSPs would save almost $17 million in treatment costs for HIV.

Comments

The authors did not explicitly state the comparator but it appeared to be a do-nothing approach. Estimates of the effectiveness of state-approved NSPs were based on a study conducted by Des Jarlais et al (1996) that used meta-analytic techniques to combine HIV incidence data from IDUs in New York who did and did not use NSPs. The measure of benefit, HIV infections averted, was estimated using a simplified circulation model, which required a number of assumptions to be made. A societal perspective was taken in the analysis, but the author acknowledged that they had not considered costs incurred by NSP users to participate in the programme or productivity losses. Direct costs of the seven programmes were based on survey data for a given year and combined to give the total programme costs. Prices and resource use were not reported separately. The author did not report how or why a particular estimate of the lifetime costs of HIV treatment was chosen.

7.2.11 Review of Lurie and Drucker (1997 CEA-)

Overview

Lurie and Drucker (1997 CEA-) attempted to estimate the number of HIV infections that could have been prevented and the costs to the US health care system, had NSPs been implemented during the early stages of the HIV epidemic in the USA (1987-1995).

Summary of effectiveness data

A model was developed based on the formula to estimate the percentage decline in HIV incidence that might have occurred in the presence of NSPs. Data for the model were drawn from previously published studies. The formula included: the proportion of incident HIV infections among IDUs from sexual transmission; the proportion of IDUs who could have used an NSP in each year; the reduction in HIV incidence among IDU participating in NSPs; and the ratio of primary HIV infections among IDUs plus secondary infections among sexual partners and children to primary HIV infections among IDUs.

The annual number of incident HIV infections among IDUs was estimated in 1987 and linear interpolation used to calculate the number of incident infections between 1987 and 1994. The number of infections was reduced by 35% (estimated from consultation and Kaplan et al) to account for the proportion of infections that were the result of sexual behaviour. The proportion of IDUs who could have used an NSP was drawn from an Australian study (Loxley et al). The authors assumed that 0% of IDUs

could have used an NSP in 1987 and that 49.2% could have used exchanges in 1994 and 1995. Use of NSPs in the intervening years was estimated by linear interpolation. The percentage decline in HIV incidence among IDUs who used NSPs was based on data from two modelling studies. One study based on the needle circulation theory model estimated that NSP participants had a 33% lower HIV incidence than non-participants. In the second study, three different models were constructed which yielded broad estimates of effectiveness. Lurie and Drucker used 15% as a lower limit and 33% as an upper limit (assumed constant over time) in their model. The ratio of primary plus secondary HIV infections to primary infections was estimated from data reported to the Centers for Disease Control.

Summary of resource utilisation and cost data

The authors calculated the direct medical costs of HIV infection. Indirect costs were not included. The lifetime cost of treating an HIV infection was drawn from a previously published study and estimated at US$55,640.

Summary of cost-effectiveness data

At the lower limit of effectiveness (15%), 4,394 HIV infections could have been prevented between 1987 and 1995 and at the higher estimate (33%), 9,666 infections could have been prevented. Costs savings ranged from US$244 million at the lower limit of effectiveness, to US$538 million at the higher estimate.

Assuming that all model variables were unchanged the authors estimated that between 1996 and 2000, 5,150-11,329 additional HIV infections could have been prevented had the US government expanded NSP coverage to Australian levels. Corresponding cost savings for 1996-2000 ranged from US$287 million to US$630 million.

Comments

The comparator in the study was a do-nothing approach. To determine the number of HIV infections that could have been prevented with a national NSP programme during the early stages of the AIDS epidemic in the USA a model was developed. Effectiveness estimates were based on data from modelling studies and estimates of the measure of benefit, the number of HIV infections that could have been averted, were derived from a model that incorporated epidemiological and effectiveness data from the US and Australia. Only the direct costs of HIV treatment were included in the model and the costs associated with NSPs were not considered. The results were of limited generalisibility to a UK setting.

7.2.12 Review of Vickerman et al (2006 CEA+)

Overview

Vickerman et al (2006 CEA+) estimated the cost-effectiveness of a harm reduction intervention for IDUs in Odessa, Ukraine. The intervention consisted of harm reduction and peer education across two mobile sites and one fixed site. Main activities were promotion of safe drug use practices and sexual behaviour through provision of condoms, syringes and information materials. At each visit IDUs attending the outreach points were counselled about routes of HIV/STI transmission, disease relating to drug use, and methods of HIV and STI prevention. After counselling, each IDU received information materials, syringes, condoms and bleach disinfectant. A dynamic, deterministic model was developed to estimate the impact of the intervention on HIV transmission among IDUs and their sexual partners. The same model was used in the study by Kumaranayake et al (2004).

Summary of effectiveness data

HIV prevalence in IDUs was estimated from the prevalence of HIV in syringes collected by the mobile outreach points. HIV incidence was estimated to be 20 infections per 100 susceptible IDU person-years in March 2000. Behavioural data were drawn from three cross-sectional surveys among IDUs in Odessa (October 1999, March 2000 and June 2001). Intervention coverage (20% to 38%) was estimated by dividing high and low estimates for the number of IDU that were 'effectively reached' by the intervention by high and low estimates for the size of Odessa IDU population. Over one year, 792 HIV infections were averted (95% CI 422, 1,019), compared with no intervention.

Summary of resource utilisation and cost data

Cost data were collected retrospectively for September 1999 to August 2000. Direct costs were estimated from the provider perspective and did not include costs borne by IDUs attending the intervention. Costs were obtained from interviews with the project co-ordinator and from observations of the resources used. Buildings costs were calculated based on square footage and the prevailing market rental rates for that space. For building space with multiple uses, an allocation factor was applied. Start-up activity and equipment costs included a calculation of the opportunity cost of the activity or equipment based on the discount rate and length of life of the item. To obtain personnel costs, full salary costs were multiplied by their time allocation on the project. The authors were not able to estimate costs for mass media or the time

spent by volunteer peer educators. Total programme costs were estimated at $76,797. One year costs of the intervention are presented in Table 16.

Table 16. Data included in cost analysis (Vickerman et al 2006)

Cost category	One year costs (US$ 1999)
Capital	
Start-up activities	$3518
Buildings	$11,519
Equipment	$258
Total capital costs	$15,296
Recurrent	
Personnel	$27,036
Supplies	$17,570
Vehicle repair and maintenance	$1,326
Building repair and maintenance	$3,054
Project management and training	$3,305
Information, education and communication materials	$2,908
Other	$6,301
Total recurrent costs	$61,501
Total costs US$	$76,797
Average cost per IDU reached	$10.21

Summary of cost-effectiveness data

Over one year, costs per HIV infection averted were US$97 (ranging from US$71 to US$272). The model developed projected that HIV prevalence would increase by 1.1%. In sensitivity analysis, the initial IDU prevalence and the factor increase in the HIV transmission probability during the initial high viraemia phase of infection had the greatest effect on model outputs. The authors reported that an increase in either parameter by 35% resulted in a doubling of the cost per HIV infection averted.

The authors examined the cost-effectiveness of scaling up the intervention. Assuming the same pattern of behaviour change, increasing coverage to 60%, the intervention would have decreased HIV incidence by 42% (16 infections per 100 person-years) and prevalence by 0.7% after one year. Reducing behaviour change by 15% resulted in a decrease in incidence of 39% and prevalence by 3% after five years.

Comments

The cost and benefits of a harm reduction intervention in Odessa, Ukraine, were estimated relative to the absence of the intervention for one-year. Effectiveness estimates were drawn from cross-sectional surveys among IDUs in Odessa, limiting the validity of the effectiveness estimates. The estimate of the measure of benefit, HIV infection averted, was modelled using a dynamic, deterministic mathematical model and this appears to have been appropriate to model the impact of the intervention on HIV prevalence. The perspective of the study was from the viewpoint of the provider and an appropriate range of costs were considered. The study was

conducted in a setting with high HIV prevalence among IDUs (47-60%) and therefore it is likely that the results are therefore not generalisble to the UK, where HIV prevalence among IDUs is relatively low.

7.3 Review of cost-effectiveness evidence for HCV

7.3.1 Review of Pollack (2001 CEA+)

Overview

Pollack (2001 CEA+) explored the potential of NSPs to reduce HCV incidence and prevalence among IDUs. A susceptible-infected, random-mixing model of disease spread was developed to explore the effectiveness and cost-effectiveness of NSPs. Within the framework for the model, NSPs reduced the infectivity (or frequency) associated with unsafe needle sharing, thereby reducing HCV incidence and prevalence. To provide a tractable analytic model, the authors made the following assumptions: 1) all IDUs had identical risk behaviours; 2) sexual risks were not considered; and 3) sharing occurred through a process of random mixing across the IDU population. Model parameters extracted from the research literature and their baseline values are shown in Table 17.

Table 17. Parameters and base case values (Pollack 2001)

Parameter	Baseline value for HCV
Arrival rate in IDU population of uninfected individuals	0.5/day
Arrival rates into shooting galleries	1/(7 days)
Infectivity	0.005 to 0.5
Exit rate from active IDU population	1/(4,000 days) (range 1/6,320 to 1/2,920)
Cost of intervention/client/day	$5
Proportional reduction in short-term disease incidence attributable to an NSP	1/3

Summary of effectiveness data

Effectiveness data were drawn from a previously published study based on the circulation theory model (Kaplan and Heimer 1994). It was assumed that the NSP created a one-third (1/3) proportional reduction in short-term disease incidence.

Summary of resource utilisation and cost data

The authors used a programme cost of $5 per client per day, but the source of these estimates was not clear.

Summary of cost-effectiveness data

At levels of the reproductive rate of infection equivalent to the range for HCV, NSPs only had a small impact on steady state prevalence. Costs per HCV infection averted

were high and exceeded US$1 million within the range of observed HCV prevalence in high-risk populations. In sensitivity analyses, the reproductive rate of infection emerged as a critical variable in the analysis. For example, a reduction in the frequency of high-risk needle sharing that lowered the reproductive rate of infection would have a small impact on steady state prevalence but would reduce the costs per averted infection of an NSP from $400,000 to $320,000.

Comments

NSPs were compared to a do-nothing approach. The author assessed the costs and benefits of NSPs in reducing the steady-state prevalence of HCV compared to the natural convergence to the steady state. Similar models have been used by Kaplan and colleagues to examine the impact of NSPs on HIV incidence among IDUs. Effectiveness estimates were based on estimates derived from mathematical models of HIV transmission among IDUs (Kaplan & Heimer 1994) and the estimation of benefits was modelled using an analytic model. The random-mixing model used is most appropriate to high-risk populations with prevalent random sharing. It was not possible to determine the validity of the costs used. The perspective of the study was not clear and it was possible that not all relevant costs had been included. Overall, although the values used in the model may not be generalisble to a UK setting, the article highlights that to reduce the incidence and prevalence of highly infectious BBVs among IDUs there is a need for more comprehensive harm reduction models in addition to NSPs.

7.4 Summary and evidence statements

A total of 12 published economic evaluations were identified that examined the impact of NSPs on HIV infection. The authors of all 12 studies concluded that NSPs were cost-effective, and compared to the lifetime costs of HIV/AIDS treatment were cost-saving. Two studies (Health Outcomes PTY Ltd et al 2002 and Pollack 2001) examined the impact of NSPs on HCV infection. Pollack (2002 CEA+) concluded that short term incidence analysis substantially overstates NSP effectiveness and cost-effectiveness in preventing HCV. The analysis presented by the author suggested that the costs of NSPs were much higher than current estimates of HCV treatment costs. However, the analysis conducted by Health Outcomes PTY Ltd et al (2002 CBA+) indicated that the effects of NSPs on HCV provided net savings in addition to those calculated in terms of cases of HIV avoided. Although the impact on costs was significantly lower than for HIV, the analysis indicated that the incorporation of HCV further increased the savings accruing to the Australian government. The studies

identified for inclusion were, on the whole, of limited generalisbility to a UK setting. Cost and benefit estimates were either based on locally derived data or from studies conducted in North America, and a range of assumptions were made often limiting the applicability of findings beyond the individual study.

Two studies (Holtgrave et al 1998 CEA - and Vickerman et al 2006 CEA+) examined the cost-effective of increasing the level of coverage of NSPs. Holtgrave et al (1998) considered a hypothetical cohort of one million active IDUs in the US. They found that the programme was cost-effective across all levels of coverage, and cost-saving compared to HIV treatment costs at levels of coverage up to 88.4%. Vickerman et al (2006) examined the effects of scaling up harm reduction activities for IDU in a population with high HIV prevalence in the Ukraine. The results of the model suggested that increasing intervention coverage to the 60% target recommended by WHO/UNAIDS resulted in reductions in both HIV incidence and prevalence and that the additional resources required to achieve this level of coverage represented a 'worthwhile use of resources'.

Harris (2006 CEA+) sought to determine the optimal allocation of resources within a multi-site needle exchange programme in Philadelphia, USA. The author found that the NSP examined could spend the same budget more effectively by equalising the number of syringes exchanged per client (a mean of 22.08 per client across each site in the case of PPP) and by increasing operating hours (by up to three hours per week in areas of the city with a high density of IDUs).

Evidence Statement 7.1

7.1a. There is evidence from 11 CEAs[1] and one CBA[2] to suggest that in terms of reducing HIV incidence and prevalence among IDUs, NSPs are cost-effective.

7.1b. There is evidence from two CEAs[3] to suggest that intervention coverage may be increased to higher levels at a low cost per HIV infection averted.

7.1c. There is evidence from one CEA[4] to suggest that cost-effective allocation within a multi-site NSP requires that sites are located where the density of IDUs is highest, and that the number of syringes exchanged per client is equal across sites.

7.1d. There is evidence from one CEA[5] to suggest that in terms of HCV incidence and prevalence among IDUs, NSPs are not cost-effective.

Applicability: The studies identified for inclusion are, on the whole, of limited generalisbility to a UK setting. Cost and benefit estimates were either based on

locally derived data or from studies conducted in North America, and a range of assumptions were made often limiting the applicability of the findings beyond individual studies.

[1] Cabases & Sanchez 2003 (CEA+); Cohen et al 2004 (CEA+); Cohen et al 2006 (CEA-); Gold et al 1997 (CEA-); Harris 2006 (CEA+); Holtgrave et al 1998 (CEA-); Jacobs et al 1998 (CEA-); Kumaranayake et al 2004 (CEA+); Laufer 2001 (CEA+); Lurie & Drucker 1997 (CEA-); Vickerman et al 2006 (CEA+)

[2] Health Outcomes PTY Ltd et al 2002 (CBA+)

[3] Holtgrave et al 1998 (CEA-); Vickerman et al 2006 (CEA+)

[4] Harris 2006 (CEA+)

[5] Pollack 2001 (CEA+)

8 DISCUSSION

8.1 Summary of the review of effectiveness and cost-effectiveness

The review of effectiveness included a total of 10 systematic reviews and meta-analyses, and 24 primary studies. Thirteen full economic evaluations were identified for inclusion, including 12 cost-effectiveness analyses and one cost-benefit analysis. Although we identified a large number of studies that had examined the effects of NSPs on risk behaviours and BBV incidence and prevalence among IDUs, few studies addressed the research questions of interest for this review.

8.1.1 Systematic reviews and meta-analyses

Ten systematic reviews and meta-analyses were identified that examined the effectiveness of NSPs, including one systematic review that examined prison-based exchange programmes. The majority of the reviews identified examined the effectiveness of NSP in terms of their role in the HIV prevention and considered there to be good evidence that NSPs reduce injection risk behaviours among IDUs. However, the evidence was less clear in relation to HIV incidence, whilst two reviews considered there to be good evidence to support the effectiveness of NSPs in reducing HIV incidence, another review concluded that the evidence was less robust. Two reviews considered the impact of NSPs on the prevalence and incidence of HCV, concluding that NSPs have less of an impact on HCV infection than HIV infection.

Few of the reviews identified for inclusion examined how different types of NSPs impact on effectiveness and no reviews examined additional services offered by NSPs. Pharmacy access to sterile needles and syringes was identified as beneficial in two reviews, but the evidence in relation to vending machines was found to be insufficient. Prison-based syringe exchange services have not been implemented in the UK because of wide-ranging political, practical and ethical issues (Hughes, 2000). However, a review based on data from European countries, found that such programmes are feasible and do provide some benefits but that large scale evaluations are required.

8.1.2 Primary studies

Twenty-four studies were identified that met the criteria for inclusion in the review and addressed one of the key research questions or sub-questions. One study was identified that examined whether adequate syringe coverage, defined as one injection per syringe, among NSP participants was associated with injection risk behaviours and syringe disposal. Fourteen studies were identified that addressed

different characteristics of NSPs and their impact on effectiveness. Seven studies were identified which addressed the provision of additional services offered by NSPs beyond needle and syringe exchange. Two studies were identified that examined OST delivered in parallel with or alongside NSP services.

8.1.3 Economic evaluation studies

Eleven studies examined reduction in HIV incidence, one study examined HCV incidence and one study examined reductions in both HIV and HCV incidence. All 12 studies that examined the impact of NSPs on HIV infection concluded that NSPs were cost-effective, and compared to the lifetime costs of HIV/AIDS treatment were cost-saving. Two studies examined the impact of NSPs on HCV infection but drew differing conclusions. One CEA concluded that short term incidence analysis substantially overstates NSP effectiveness and cost-effectiveness in preventing HCV, and that NSPs were not cost-saving compared to HCV treatment costs. One CBA found that although the impact on costs was significantly lower than for HIV, the analysis undertaken indicated that the incorporation of HCV further increased the savings accruing to the Australian government.

8.2 What level of coverage of needle and syringe programmes (NSPs) is the most effective and cost-effective?

One cross-sectional study was identified that examined individual syringe coverage among NSP participants in California. Individual syringe coverage was calculated by multiplying the number of monthly NSP visits by the participant by the number of syringes they had retained from their last visit. This was then divided by the number of illicit drug injections they reported in the last thirty days and multiplied by 100 to obtain a percentage. Participants were grouped into four categories based on syringe coverage: 150% coverage or more; 100-149%; 50-99%; and less than 50% coverage. High levels of individual syringe coverage (150% coverage or more) were found to be associated with safer injection risk behaviours. NSP participants who were homeless, reported recent heroin injection or crack cocaine use, or were not in treatment had lower levels of syringe coverage. In a further analysis of data from the same NSPs, Bluthenthal et al (2007b) found that NSPs that had less restrictive dispensation policies had more clients with adequate syringe coverage (100% or more); clients of unlimited needs-based distribution and unlimited one-for-one plus exchange had a higher prevalence of adequate syringe coverage compared to clients of more restrictive syringe dispensation models. Evidence relating to dispensation policies is reviewed under Section 8.3.

Two CEAs examined the cost-effectiveness of increasing the level of coverage of NSPs. Holtgrave et al (1998) considered a hypothetical cohort of IDUs in the USA, finding that the programme was cost-effective across all levels of coverage, and cost-saving compared to HIV treatment costs at levels of coverage up to 88.4%. Vickerman et al (2006a) examined the effects of scaling up harm reduction activities for IDU in a population with high HIV prevalence in the Ukraine. The results of the model suggested that increasing intervention coverage to the 60% target recommended by WHO/UNAIDS resulted in reductions in both HIV incidence and prevalence and that the additional resources required to achieve this level of coverage represented a 'worthwhile use of resources'. One CEA that sought to determine the optimal allocation of resources within a multi-site needle exchange programme found that cost-effective allocation within a multi-site NSP required that sites were located where the density of IDUs was highest and that the number of syringes exchanged per client was equal across sites. By way of an example, the author reported that a multi-site programme in Philadelphia, USA, could spend the same budget more effectively by equalising the number of syringes exchanged per client, which could be achieved by increasing operating hours across the sites, in particular at sites in areas of the city with a high density of IDUs.

Further modelling undertaken by Vickerman et al (2006b) suggests that there are critical coverage thresholds for syringe distribution that need to be reached to substantially reduce HIV prevalence among IDU populations, for example, to reduce the HIV prevalence in London to less than 1%, the coverage of syringe distribution would need to increase to 27%.

8.3 What types of NSPs are effective and cost-effective?

Few studies examined how different types of approaches to the distribution of injecting equipment impact on effectiveness. However, based on the literature identified we were able to examine effectiveness across the following areas: 1) accessibility of NSPs based on studies of geographical proximity; 2) distribution of injecting equipment in different settings including community sites, pharmacies, mobile vans, hospitals, vending machines, and prisons; and 3) different polices on the return and distribution of needles and syringes (e.g. one-for-one exchange).

Two cross-sectional studies that examined the impact of geographical proximity to NSPs found that IDUs living in close proximity to NSPs were more likely to utilise NSP services and report lower levels of injection risk behaviours.

Eight studies were identified which examined a variety of outcomes among IDUs depending on their main source of needles. Two RCTs, one that compared pharmacy sales only with NSP exchange plus pharmacy sales and one that compared a hospital and a community-based NSP reported no effect of setting on injection risk behaviours. However, participants who attended a hospital-based NSP had improved access to inpatient and outpatient services compared to those attending a community-based NSP. Findings from six observational studies were inconsistent and difficult to interpret, but three studies demonstrated that mobile van sites and vending machines attracted younger IDU and IDUs with higher risk profiles. Two uncontrolled before and after studies were identified that examined the role of needle exchange in prisons. The needle exchange intervention consisted of a vending machine in two evaluations and in a third evaluation social workers from an non-governmental organisation exchanged sterile syringes and equipment. Reductions in syringe sharing and HIV incidence were found.

Three cross-sectional studies examined the impact of different syringe dispensation policies on injection risk behaviours among IDUs. These studies found that syringe dispensation policies had a limited impact on behavioural outcomes such as sharing but had some impact on syringe re-use.

None of the economic evaluation studies identified examined the cost-effectiveness of different types of NSPs.

8.4 Which additional harm-reduction services offered by NSPs are effective and cost-effective?

Few studies were identified that directly examined the effectiveness of additional harm reduction services offered by NSPs. However, it was clear from the literature that few NSP services only distributed sterile needles and syringes, in fact the large majority were linked into wider HIV prevention services including outreach, distribution of harm reduction materials and counselling and testing for BBVs.

Seven studies were identified that addressed the provision of additional services offered by NSPs beyond needle and syringe exchange, two RCTs examined interventions to encourage IDUs into drug treatment, and one cohort study compared users and non-users of NSP-based health care services. Strength-based case management was found to support drug treatment entry among IDUs who were seeking treatment. However, the primary outcome reported was based on IDUs entering into treatment within 7 days, and therefore the impact of the intervention on treatment retention was not clear. A second RCT found that MI had no impact on the

treatment interest and enrolment of NSP participants. A cohort study that examined the provision of a range of health care services delivered alongside an NSP found that the intervention reduced emergency department use among IDUs who utilised these services compared to those who did not.

Four studies examined secondary distribution of needles and syringes to IDUs. Two studies found that IDUs who exclusively obtained their needles from NSPs were less likely to engage in high risk injection behaviours than those who obtained them via secondary distribution. However these studies also found that IDUs who obtained needles via secondary distribution engaged in high risk injection behaviours less than IDU who obtained no needles directly or indirectly from NSPs.

None of the economic evaluation studies identified examined the cost-effectiveness of additional harm reduction services offered by NSPs.

8.5 Are NSPs delivered in parallel with, or alongside, opiate substitution therapy (OST) effective?

Two studies were identified that examined needle and syringe distribution delivered in parallel to, or alongside OST. One study assessed the effects of enrolment in two low-threshold MMT programmes delivered via NSPs. At 6-months follow-up, the proportion of participants injecting drugs, sharing needles, sharing drug equipment and indirectly sharing had declined significantly over the whole cohort. However, within a subgroup of participants who continued to inject during follow-up, only the sharing of injection equipment declined significantly. The second study examined the impact of different levels of harm reduction on HIV and HCV incidence in a cohort of drug users in Amsterdam. A comprehensive programme of adequate methadone therapy (≥60mg) and full participation in NSP contributed substantially to the reduction of the incidence of HIV and HCV among drug users in Amsterdam. However, a statistically significant effect was not seen when either intervention was considered separately.

None of the economic evaluation studies identified examined the cost-effectiveness of NSPs delivered in parallel with, or alongside OST.

8.6 Limitations of the review

8.6.1 Review of effectiveness

Despite a large literature on the impacts of NSPs on risk behaviours and HIV incidence, few studies have addressed the question of how NSPs operate best. It

was clear from the literature that few of the NSP services examined only distributed sterile needles and syringes but few of these 'additional services' have been subject to research. In particular no studies originating from the UK were identified that addressed the key research questions for the review. From the studies reviewed in the first phase of full text screening it is apparent that large-scale evaluations assessing the effectiveness of NSPs have not been undertaken in the UK since the early to mid-1990s.

None of the studies identified for inclusion examined how the diversity of populations attending NSPs may impact on effectiveness and cost-effectiveness. In particular, steroid users who represent a small but significant proportion of NSP users are underrepresented in the literature and further research is required to determine how services can be tailored or targeted to meet their needs.

Quality of the included studies

Studies that have examined the effectiveness of NSPs have largely used observational research designs. Twenty of the 24 studies included in the review were observational, and 14 studies were based on cross-sectional designs. Observational studies are particularly vulnerable to selection bias and some studies have identified a tendency for NSP users to report different levels of risk than other IDUs (e.g. Hagan et al 2000). Although statistical adjustments may be made to account for confounding in observational studies, it is not possible to adjust for unknown and unmeasured confounding (CRD report 4 2001). Four experimental studies, all RCTs, were identified for inclusion and on the whole these were good quality studies and suggest that further experimental research is feasible with IDU populations.

There was a lack of standardised outcomes across the studies examined. The majority of the studies examined self-reported sharing behaviours, in particular sharing of needles and syringes. Fewer studies examined sharing of other types of injecting equipment, despite the role that this behaviour plays in the transmission of HCV. There is a reliance on self-reported data in studies of NSPs which may introduce bias, although self-reports of drug users have been found to be sufficiently reliable and valid (Darke 1998). However, none of the studies included in the review reported on reliability or validity of their data collection methods. There was also a wide variety in the 'types' of sharing examined. For example, some studies distinguished between receptive and distributive sharing, whilst other did not. Some examined sharing of other types of injection equipment grouped together, whilst others examined types of equipment individually. The literature has largely examined

the impact of NSPs in terms of their role in prevention of the transmission of BBVs. However, IDUs are also at an increased risk from wound site infections and overdose; yet none of the included studies examined these outcomes.

Applicability

The majority of the published research we identified for inclusion originated from the USA. Providing access to sterile syringes for IDUs is politically controversial in the US and a ban on federal funding for NSPs was enacted in 1988 (Burris et al 2003). Therefore, US-based research has tended to focus on whether NSPs are effective per se. As Burris et al (2003) commented in their review of syringe access policy in the USA, 'the United States continues to debate whether and how to make syringes available to injection drug users'. This is in contrast to the UK where NSPs have played a central role in harm reduction services since the 1980s and continue to receive funding and support from the Government.

8.6.2 Review of published economic evaluations

We identified 13 full economic evaluations that examined the costs and benefits of NSPs. As with the review of the effectiveness evidence, none of the studies identified originated from the UK and the majority of the studies were from the US. In addition, only three of the included economic evaluations were directly applicable to the key research questions for the review. However, data from all of the articles identified were presented as they provide a useful overview of the economic literature for NSPs.

Quality of the included economic evaluations

All the economic evaluations were subject to limitations. A variety of interventions comprising needle exchange and other harm reduction interventions (e.g. outreach) were examined and compared to the absence of the intervention. Effectiveness estimates were largely drawn from cross-sectional surveys, ecological studies, or mathematical modelling studies and with the exception of one evaluation these estimates were not identified from a systematic search of the literature. Therefore, the validity of the effectiveness estimates used in the included economic evaluations was questionable and the effectiveness of NSPs was largely not established. The analysis of costs was poorly reported in a number of studies and only one study included out of pocket costs to IDUs in their analysis. This was despite the requirement for IDUs to purchase the intervention in some of the studies. Models were developed in all of the evaluations reviewed and all of these models required a variety of assumptions to be made. A large number of studies used lifetime treatment

costs for HIV/AIDS as a threshold to determine cost-effectiveness of NSPs, however sources of cost data and costs considered varied considerably across these studies resulting in a wide range of cost saving estimates.

Applicability

The studies identified for inclusion are, on the whole, of limited generalisbility to a UK setting. Cost and benefit estimates were either based on locally derived data or from studies conducted in North America, and a range of assumptions were made often limiting the applicability of the findings beyond individual studies.

8.7 Conclusions and recommendations for further research

There is a paucity of evidence with regards to the optimal provision of NSPs and it is therefore difficult to draw conclusions on 'what works best' within the range of harm reduction services available to IDUs. However, it is apparent from the literature that there is consensus among researchers that the distribution of sterile needles and syringes alone is not sufficient to reduce the transmission of BBVs, among IDUs, especially the transmission of HCV. Programmes that deliver a comprehensive range of harm reduction services and which are accessible to IDUs may prove to be the best strategy but further research is needed.

This review has identified a number of gaps in the evidence, in particular with regards to the paucity of evidence regarding the optimal provision of NSPs in England. The gaps are large and wide-ranging in this respect and the research recommendations listed are not exhaustive.

- Research to determine the effectiveness and cost-effectiveness of NSPs services in England and the rest of the UK.
- Comparison of the different types of NSPs and an evaluation of the additional services that these programmes deliver.
- Research to determine how NSP services can be tailored to meet the needs of, or better targeted towards, specialist groups such as steroid injectors and recent initiates into injectors.
- There is a need for the standardisation of outcomes in relation to injection risk behaviours and examination of other health outcomes such as overdose and wound infection.

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Appendix 1. Search strategies

The following strategy was developed for Medline and then adapted for searching other databases:

1. ((incidence or prevalence or low$ or reduc$ or prevent$ or decreas$) adj5 (HIV or hepatitis or HCV or HBV or blood-borne or blood borne or BBV or transmission or infection$ or virus$ or bacteria$ or viral or morbidity or mortality or death$ or overdose$ or seroconversion or seroprevalence)).tw.
2. HIV/
3. Hepatitis C/ or Hepatitis B/
4. Morbidity/
5. Mortality/
6. Blood-Borne Pathogens/
7. Infection/
8. HIV infections/ep, pc
9. Bacterial infections/
10. virus diseases/
11. ((low$ or reduc$ or prevent$ or decreas$ or chang$) adj5 inject$).tw.
12. ((high$ or increas$ or improve$ or encourag$ or promot$) adj5 safe$ inject$).tw.
13. "Risk Reduction Behavior"/
14. (risk reduction behaviour$ or risk reduction behavior$).tw.
15. ((needle$ or syringe$ or inject$ or paraphernalia or equipment) adj3 (behaviour$ or behavior$ or practic$ or pattern$)).tw.
16. Risk-Taking/
17. Needle Sharing/
18. ((needle$ or syringe$ or inject$) adj3 (frequenc$ or cessation)).tw.
19. ((needle$ or syringe$ or inject$ or paraphernalia or equipment) adj3 (sharing or share$1)).tw.
20. ((needle$ or syringe$ or inject$ or paraphernalia or equipment) adj3 (reusing or reuse$ or return$)).tw.
21. ((needle$ or syringe$ or inject$ or paraphernalia or equipment) adj3 (exchange$ or suppl$ or provide$ or distrib$ or provision or access$ or dispens$) adj3 (less or more or incidence$ or prevalence$ or low$ or increase$ or decreas$ or number$1 or percentage$ or proportion$ or frequency$ or rate$)).tw.
22. inject$ others.tw.
23. (rate adj2 (relapse$ or stop$ or cessation)).tw.
24. ((utilisation or utilization or attendence$ or attending or visit$) adj5 (service$ or program$ or facility or facilities or centre$ or center$ or site$ or number$ or frequenc$ or percentage$ or proportion$ or low$ or more$ or increase$ or decrease$)).tw.
25. or/1-24
26. Needle-Exchange Programs/
27. (NSP or NEP or NSEP or NSPs or NEPs or NSEPs).tw.
28. ((needle$ or syringe$ or inject$ or paraphernalia or equipment) adj3 exchang$).tw.
29. ((needle$ or syringe$ or inject$ or paraphernalia or equipment) adj3 (supply$ or access$ or provision or provid$ or distribut$ or dispens$ or program$ or service$ or centre$ or scheme$ or center$ or site$1 or facilities or facility or scheme$ or area$ or prison$ or pharmacy or pharmacies or unit or units)).tw.
30. ((needle$ or syringe$ or inject$ or paraphernalia or equipment) adj3 (steril$ or equipment or bleach$ or disinfectant$ or disinfect$1 or citric acid$)).tw.
31. ((needle$ or syringe$ or injection$ or paraphernalia or equipment) adj3 pack$1).tw.
32. dispensing machine$.tw.
33. vending machine$.tw.
34. Substance Abuse Treatment Centers/
35. (drug consumption adj5 (room$ or facility or facilities or centre$ or center$ or service$ or area$ or site$)).tw.
36. (drug-use adj5 (room$ or facility or facilities or centre$ or center$ or service$ or program$ or scheme$ or site$ or area$)).tw.
37. ((needle$ or syringe$ or inject$ or paraphernalia or equipment) adj3 (safe$ or steril$)).tw.
38. shooting galler$.tw.
39. harm reduc$.tw.
40. harm reduction/
41. or/26-40
42. Substance Abuse, Intravenous/
43. ((substance$1 or drug$1 or stimulant$) adj3 (abuse or misuse or dependen$ or use$2 or usage or addict$ or inject$ or intravenous$)).tw.
44. ((opiod$ or morphine or heroin or opiate or cocaine or steroid$ or PIED$ or methadone) adj3 (abuse or misuse or dependen$ or use$2 or usage or addict$ or inject$ or intravenous$)).tw.

45. Heroin Dependence/
46. Morphine Dependence/
47. Substance-Related Disorders/
48. Street Drugs/
49. Opioid-Related Disorders/
50. Cocaine-Related Disorders/
51. anabolic agents/
52. steroids/
53. ((needle$ or syringe$ or inject$ or paraphernalia or equipment) adj3 sharer$1).tw.
54. or/42-53
55. 54 and 25 and 41
56. limit 55 to (english language and humans and yr="1990-2008")

Appendix 2. Reference to included studies

Systematic reviews and meta-analyses

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Appendix 3. Review of effectiveness: data extraction tables for primary studies

<table>
<tr><th>Study details</th><th>Intervention and population details</th><th>Intervention</th><th>Results</th></tr>
<tr>
<td>Bluthenthal R, Malik M, Grau L, Singer M, Marshall P, Heimer R (2004)

Country: USA

Cross-sectional -

Objectives: To compare syringe re-use and receptive syringe sharing among IDUs with NSPs and legal over-the-counter pharmacy access with limits of syringes that can be purchased, exchanged or possessed to IDUs with no pharmacy sales but unlimited syringe access through NSPs.

Funding source: NIDA, Office of AIDS Research at National Institutions of Health, National Institute of Mental Health, CDCP</td>
<td>Entry criteria: 18+ years old, injected illegal drugs at least once in previous 30 days

Participant characteristics
<table>
<tr><th></th><th>Oakland</th><th>Chicago</th><th>Hartford</th></tr>
<tr><td>Number of pts:</td><td>148</td><td>289</td><td>147</td></tr>
<tr><td>Gender (% male)</td><td>52</td><td>58</td><td>63</td></tr>
<tr><td>Ethnicity</td><td></td><td></td><td></td></tr>
<tr><td>White:</td><td>27%</td><td>17%</td><td>10%</td></tr>
<tr><td>African</td><td>31%</td><td>54%</td><td>27%</td></tr>
<tr><td>American:</td><td>35%</td><td>28%</td><td>61%</td></tr>
<tr><td>Hispanic:</td><td>7%</td><td><1%</td><td>1%</td></tr>
<tr><td>Other</td><td></td><td></td><td></td></tr>
<tr><td>Mean age (SD)</td><td>44.68 (8.95)</td><td>41.02 (8.49)</td><td>37.19 (8.06)</td></tr>
<tr><td>Homeless</td><td>NR</td><td>NR</td><td>NR</td></tr>
<tr><td>Mean injection duration (SD)</td><td>23.54 (10.67)</td><td>17.64 (11.13)</td><td>15.40 (10.52)</td></tr>
</table>
Analysis
Outcomes measured: Injection risk behaviours; Other
How measured: Semi structured survey
Length of follow-up: NA
Number of participants lost to follow-up: NA</td>
<td>Programme description
Hartford, CT: IDUs could legally carry a limited number of syringes (30 from Sept 99; 10 prior to this), could purchase up to 10 syringes from pharmacies per visit and/or make use of a 'small volume' NSP (<55,000 syringe exchanged per year) with a legally mandated cap of 10 syringes exchanged per visit prior to Sept 99 and 30 syringes thereafter.
Chicago, IL: No pharmacy access to syringe, but access to 'very large', legal NSP (exchanging >1m syringes per year) that provided syringes on a one-for-two basis. IDUs with a client ID card from the NSP could legally carry syringes.
Oakland, CA: Both syringe prescription and drug paraphernalia laws were in place and IDUs could not legally carry syringes. However, 'very large' NSP (>500,000 syringes exchanged per year) operated and provided syringe on a one-for-one plus five basis.
Operating hours: Not reported

Services
No further details reported.</td>
<td>Injection risk behaviours
In multivariate analysis, Chicago and Oakland IDUs were both less likely to report syringe re-use than IDUs in Hartford (Chicago vs. Hartford: AOR 0.09; 95% CI 0.03, 0.25; p<0.01/ Oakland vs. Hartford: AOR 0.10; 95% CI 0.03, 0.30; p<0.01). No significant differences in receptive syringe sharing were observed by city (Chicago vs. Hartford: AOR 0.29; 95% CI 0.08, 1.05/ Oakland vs. Hartford: AOR 0.49; 95% CI 0.15, 1.62).

Mean and median syringes received at last NSP visit varied; Chicago NSP users reported receiving a mean 119 syringes (median 40), Oakland NSP users reported a mean of 99 syringes (median 20) and Hartford NSP users reported a mean of 27 syringes (median 10).</td>
</tr>
</table>

Study details	Intervention and population details	Intervention	Results
Bluthenthal R, Anderson R, Flynn N, Kral A (2007) **Country**: USA (California) Cross-sectional - **Objectives**: To determine if adequate syringe coverage - "one shot for one syringe" - among NSP clients is associated with injection-related HIV risk behaviours and syringe disposal **Funding source**: CDCP, NIDA, University-wide AIDS Research Program	**Entry criteria:** Not reported **Participant characteristics** Number of pts: <50% 537; 50-99% 295; 100-149% 191; 150%+ 547 Gender (% male): 34% / 20% / 12% / 34% Ethnicity White: 34% / 19% / 12% / 35% African American: 29% / 19% / 14% / 39% Hispanic: 41% / 16% / 11% / 32% North American: 39% / 26% / 15% / 19% Other: 25% / 23% / 12% / 40% Age: NR / NR / NR / NR Homeless: 40% / 20% / 12% / 28% Injection duration (<10 yrs): 41% / 18% / 13% / 28% **Analysis** **Outcomes measured:** Injection risk behaviours **How measured:** Interviewer-administered HIV risk behaviour assessment using computer-assisted-personal-interview **Length of follow-up:** NA **Number of participants lost to follow-up:** NA	**Programme description** Setting: 24 of 25 NSPs in San Francisco area Policy: NR Operating hours: NR **Services** No details reported about NSPs. Syringe coverage % was calculated as follows: monthly NSP visits multiplied by the number of syringes retained from last NSP visit divided by number of illicit drug injections in the last 30 days (result multiplied by 100 to obtain a %).	**Injection risk behaviours** Compared to NSP clients with 100-149% coverage, clients with <50% coverage had significantly higher odds of reporting syringe re-use, receptive syringe sharing and distributive syringe sharing, but not sharing cookers <50% vs. 100-149%: OR (95% CI) Syringe re-use: 2.64 (1.76, 3.95) Receptive syringe sharing: 2.29 (1.44, 3.63) Distributive syringe sharing: 1.63 (1.07, 2.49) Sharing cookers : 1.14 (0.77, 1.68) No statistically significant differences in risk behaviours were observed between clients with 50-99% and 100-149% coverage levels. 50-99% vs. 100-149%: OR (95% CI) Syringe re-use: 1.31 (0.86, 2.01) Receptive syringe sharing: 1.48 (0.89, 2.44) Distributive syringe sharing: 0.90 (0.56, 1.44) Sharing cookers: 1.15 (0.75, 1.76) NSP clients with coverage >150% reported significantly lower odds of syringe re-use and receptive and distributive syringe sharing compared to clients with 100-149% coverage. For sharing cookers, only clients with coverage >150% reported significantly different odds of sharing cookers (i.e. lower) compared to clients with 100-149% coverage. 150% plus vs. 100-149%: OR (95% CI) Syringe re-use: 0.49 (0.33, 0.72) Receptive syringe sharing: 0.47 (0.28, 0.80) Distributive syringe sharing: 0.46 (0.29, 0.72) Sharing cookers: 0.61 (0.41, 0.89) Other In a multivariate logistic regression model controlling for potential confounders the authors found no statistically significant differences in safe syringe disposal by level of syringe coverage.

Study details	Intervention and population details	Intervention	Results
Fisher D, Fenaughty A, Cagle H, Wells R (2003) **Country**: USA (Alaska) RCT + **Objectives**: To determine whether the opportunity to use an NSP was associated with an increase in the number of injections of illicit drugs over time compared with those who did not have the opportunity to use the NSP directly **Funding source**: NIDA, Alaska Science and Technology Foundation	**Entry criteria:** 18+ years old; test positive for morphine, coke or amphetamine using ONTRAK system; present visible signs of injection **Participant characteristics** N= NSP 296, Pharmacy 304 Gender (% male) 79, 73 Ethnicity White: 54%, 58% African American: 20%, 18% Native American: 21%, 19% Other: 5%, 5% Age NR, NR Homeless Shelter: 22%, 27% Other: 13%, 13% Injection duration NR, NR **Analysis** **Outcomes measured:** Injection risk behaviours **How measured:** Urine analysis; questionnaire **Length of follow-up:** 6 and 12 months **Number of participants lost to follow-up:** 100 (18%)	**Programme description** Setting: NSP vs. pharmacy sales Policy: NR Operating hours: NR **Services** NSP distributed needles and syringes and additional harm reduction equipment (dental dams, alcohol wipes, lubricants, bleach, condoms, lubricant) Individuals assigned to the pharmacy sales condition were instructed in optimal methods for purchasing needles/syringes at pharmacies. Individuals assigned to the NSP condition were given a bar-coded ID card to gain access to the NSP. NB They could also make purchases at pharmacies.	**Injection risk behaviours** Neither NSP or pharmacy sales groups modified the association between time and injection frequency (i.e. did not reduce or increase injection frequency over 12 month course of study) based on complete case only data. Including all data, there was an association between time and injection frequency, but group assignment did not modify this and participants in both arms reduced their injecting drug use over time (Data only presented graphically).

<table>
<tr><th>Study details</th><th>Intervention and population details</th><th>Intervention</th><th>Results</th></tr>
<tr>
<td>Huo D, Bailey S, Hershow R, Ouellet L (2005)

Country: USA (Chicago)

Cross-sectional -

Objectives: To examine HIV risk practices associated with secondary needle exchange.

Funding source: NIDA</td>
<td>Entry criteria: Injected within past six months, speak English or Spanish, 18 years or older. NSP users to have used NSP twice ever and registered 30 or more days ago. IDUs who had participated in the National AIDS Demonstration Project (NADP) were excluded because of low levels of risk behaviour following that intervention

Participants were classified as follows: 1) ‘Primary only users’ were those who reported always getting needles from an NSP personally; 2) ‘Mixed/secondary users’ were those who obtained at least some needles indirectly from an NSP through other people; and 3) ‘NSP non-users’ were those who obtained no needles, directly or indirectly, from NSPs.

Participant characteristics
<table>
<tr><th></th><th>Primary Only NSP User</th><th>Mixed/ Secondary NSP User</th><th>Non-user</th></tr>
<tr><td>Number of pts:</td><td>490</td><td>224</td><td>172</td></tr>
<tr><td>Gender (% male)</td><td>73.3</td><td>67.0%</td><td>73.8%</td></tr>
<tr><td>Ethnicity
African American:
White:
Hispanic:
Other:</td><td>
46.7%
31.2%
21.2%
0.8%</td><td>
42.0%
37.5%
20.1%
0.4%</td><td>
44.8%
39.5%
14.5%
1.2%</td></tr>
<tr><td>Mean age (SD)</td><td>40.4 (10.5)</td><td>38.7 (10.7)</td><td>42.8 (7.4)</td></tr>
<tr><td>Homeless (past 6 months)</td><td>35.3%</td><td>34.4%</td><td>44.8%</td></tr>
<tr><td>Injection duration</td><td>NR</td><td>NR</td><td>NR</td></tr>
</table>
Analysis
Outcomes measured: Injection risk behaviours
How measured: Standardised questionnaire and venous blood samples (HIV) ELISA test
Length of follow-up: NA
Number of participants lost to follow-up: NA</td>
<td>Programme description
Setting: 3 storefront locations, 1 van
Policy: Two-for-one for first 5 needles/syringes, then one-for-one. No upper limit.
Operating hours: Some services were available 5 days/week for 7 hours/day; others operated for 4 days/week for 2 hours/day.

Services
Programme distributed sterile needles and syringes and additional injection equipment including cookers, bleach, water, cotton filters, and alcohol pads. The service was also able to provide referrals (e.g. drug treatment programmes), individual risk assessments and drug abuse counselling.</td>
<td>Injection risk behaviours
Proportion of study participants who reported receptive needle sharing was significantly lower among primary-only NSP users than mixed/secondary and nonusers. Among IDUs who shared needles, both primary-only and mixed/secondary NSP users were more likely than non-users to clean their needles with bleach. Primary–only NEP users had significantly lower proportions of backloading, sharing injection paraphernalia other than needles (cookers, cotton filters, and water), and lending used needles compared with the other two groups. A lower proportion of NEP users, both primary–only and mixed/secondary, reused their needles than did nonusers. The likelihood of having shared injection paraphernalia other than needles was not significantly different between mixed/secondary NEP users and nonusers.
<table>
<tr><th></th><th>OR (95% CI)
Primary vs. non-users</th><th>Mixed/secondary vs. non-users</th></tr>
<tr><td>Receptive Needle Sharing</td><td>0.40 (0.28-0.57)</td><td>0.69 (0.46-1.02)</td></tr>
<tr><td>Backloading</td><td>0.34 (0.23-0.50)</td><td>0.77 (0.51-1.16)</td></tr>
<tr><td>Lent needle use</td><td>0.54 (0.38-0.76)</td><td>0.93 (0.62-1.38)</td></tr>
<tr><td>Share injection equipment</td><td>0.49 (0.33-73)</td><td>1.18 (0.73-1.90)</td></tr>
<tr><td>Share cooker</td><td>0.47 (0.32–0.70)</td><td>1.02 (0.64–1.62)</td></tr>
<tr><td>Share cotton</td><td>0.52 (0.36–0.74)</td><td>1.04 (0.69–1.58)</td></tr>
<tr><td>Share water</td><td>0.51 (0.36–0.73)</td><td>0.98 (0.66–1.46)</td></tr>
<tr><td>Always bleach used needles</td><td>2.48 (1.39-1.44)</td><td>2.31 (1.23-4.34)</td></tr>
<tr><td>Needle reuse*</td><td>0.19 (0.11-0.34)</td><td>0.23 (0.13-0.43)</td></tr>
</table>
</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Intervention and population details</th><th>Intervention</th><th>Results</th></tr>
<tr>
<td>Khoshnood K, Blankenship K, Pollack H, Roan C, Altice F (2000)

Country: USA (Connecticut)

Cross-sectional -

Objectives: Examined the relationship among syringe source, use and discard by IDUs in New Haven, CT, where syringes were available through pharmacies and one NSP.

Funding source: NIDA</td>
<td>Entry criteria: Active IDU (injected within the last six months) in New Haven

Participant characteristics
<table>
<tr><th></th><th>Pharmacy</th><th>NSP</th><th>Both</th><th>Neither</th></tr>
<tr><td>Number of pts:</td><td>111</td><td>36</td><td>90</td><td>27</td></tr>
<tr><td>Gender (% male)</td><td>70%</td><td>67%</td><td>71%</td><td>48%</td></tr>
<tr><td>Ethnicity</td><td></td><td></td><td></td><td></td></tr>
<tr><td>White:</td><td>44%</td><td>32%</td><td>22%</td><td>12%</td></tr>
<tr><td>African American:</td><td>36%</td><td>50%</td><td>66%</td><td>46%</td></tr>
<tr><td>Latino:</td><td>20%</td><td>18%</td><td>13%</td><td>42%</td></tr>
<tr><td>Age</td><td>NR</td><td>NR</td><td>NR</td><td>NR</td></tr>
<tr><td>Homeless</td><td>NR</td><td>NR</td><td>NR</td><td>NR</td></tr>
<tr><td>Injection duration</td><td>NR</td><td>NR</td><td>NR</td><td>NR</td></tr>
</table>
Analysis
Outcomes measured: Injection risk behaviours
How measured: Self-report
Length of follow-up: NA
Number of participants lost to follow-up: NA</td>
<td>Programme description
Setting: NSP v Pharmacy
Policy: NR
Operating hours: Restricted compared to pharmacy (no further details reported)

Services
Provided on-site vaccination for HBV and referrals to drug treatment, health and social services.</td>
<td>Injection risk behaviour
Injection risk behaviour use by usual source of syringe and pharmacy access
<table>
<tr><th>Characteristic</th><th>Pharmacy (n=111)</th><th>NSP (n=36)</th><th>Both (n=90)</th><th>Neither (n=27)</th></tr>
<tr><td>Shares syringes*</td><td>11 (10%)</td><td>5 (14%)</td><td>15 (17%)</td><td>1 (4%)</td></tr>
<tr><td>Re-uses**</td><td>96 (86%)</td><td>33 (92%)</td><td>74 (82%)</td><td>18 (67%)</td></tr>
</table>
*Injected with a syringe previously used by another IDU during the last 6 months
**Injected with a syringe two or more times before discard, p<0.05 for pharmacy or NSP vs. "neither" groups.

Other
IDUs who reported using the NSP or both the NSP and pharmacies were less likely to throw away used syringes compared to those who reported only using pharmacies.</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Intervention and population details</th><th>Intervention</th><th>Results</th></tr>
<tr>
<td>Kidorf M, Disney E, King V, Kolodner K, Beilenson P, Brooner R (2005)

Country: USA

RCT -

Objectives: To evaluate the effectiveness of motivational interviewing on the treatment interest and enrolment of NSP participants

Funding source: NIDA</td>
<td>Entry criteria: Opioid dependent, had not arranged treatment before study, were not too old or too young, completed the comprehensive assessment battery

Participant characteristics
<table>
<tr><th></th><th>MI</th><th>JR</th><th>SC</th></tr>
<tr><td>N=</td><td>98 (MI)</td><td>96 (JR)</td><td>108 (SC)</td></tr>
<tr><td>Gender (% male)</td><td>67</td><td>77</td><td>80 (p=n.s)</td></tr>
<tr><td>Ethnicity:</td><td>88% A-A</td><td>77% A-A</td><td>80% A-A</td></tr>
<tr><td>Age</td><td>38</td><td>40</td><td>39</td></tr>
<tr><td>Homeless</td><td>7</td><td>10</td><td>8</td></tr>
<tr><td>Injection duration</td><td>NR</td><td>NR</td><td>NR</td></tr>
</table>
MI Motivational Interviewing; JR Job Readiness; SC standard care (i.e. standard referral)

Analysis
Outcomes measured: Entry into drug treatment
How measured: Treatment uptake
Length of follow-up: 1 year
Number of participants lost to follow-up: 181 (38%)</td>
<td>Programme description
Setting: Mobile van
Policy: NR
Operating hours: NR

Services
Referrals to drug treatment</td>
<td>Other
33 participants (10.9%) enrolled in treatment; 28 of which enrolled in MMT. There was no group difference in treatment enrolment, and no effect of MI on treatment enrolment.
<table>
<tr><th></th><th>MI</th><th>JR</th><th>SC</th></tr>
<tr><td>Treatment enrolment</td><td></td><td></td><td></td></tr>
<tr><td>Any treatment</td><td>10%</td><td>13%</td><td>10%</td></tr>
<tr><td>MMT</td><td>8%</td><td>10%</td><td>9%</td></tr>
</table>
</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Intervention and population details</th><th>Intervention</th><th>Results</th></tr>
<tr>
<td>Kral A, Anderson R, Flynn N, Bluthenthal R (2004)

Country: USA (California)

Cross-sectional +

Objectives: To examine whether different syringe dispensations policies were associated with client-level injection-related HIV risk.

Funding source: DCDP and NIDA</td>
<td>Entry criteria: Had injected drugs and used NSP in previous 30 days

Participant characteristics
<table>
<tr><th></th><th>One-for-one</th><th>One-for-one plus</th><th>Dis-tribution</th></tr>
<tr><td>Number of pts:</td><td>161</td><td>282</td><td>88</td></tr>
<tr><td>Gender (% male)</td><td>74%</td><td>66%</td><td>57%</td></tr>
<tr><td>White:</td><td>42%</td><td>62%</td><td>65%</td></tr>
<tr><td>African American:</td><td>26%</td><td>10%</td><td>19%</td></tr>
<tr><td>Latino:</td><td>28%</td><td>18%</td><td>9%</td></tr>
<tr><td>Native American:</td><td>3%</td><td>7%</td><td>2%</td></tr>
<tr><td>Other:</td><td>1%</td><td>3%</td><td>5%</td></tr>
<tr><td>Age</td><td></td><td></td><td></td></tr>
<tr><td>< 30:</td><td>11%</td><td>25%</td><td>10%</td></tr>
<tr><td>30-49:</td><td>60%</td><td>56%</td><td>60%</td></tr>
<tr><td>>49:</td><td>29%</td><td>19%</td><td>30%</td></tr>
<tr><td>Homeless</td><td>48%</td><td>47%</td><td>19%</td></tr>
<tr><td>Injection duration</td><td>NR</td><td>NR</td><td>NR</td></tr>
</table>
Analysis
Outcomes measured: Injection risk behaviours; HIV
How measured: Interviews and HIV tests
Length of follow-up: NA
Number of participants lost to follow-up: NA</td>
<td>Programme description
Setting: Comparison of 23 of the 24 NSPs in San Francisco
<table>
<tr><th></th><th>One-for-one</th><th>One-for-one plus</th><th>Dis-tribution</th></tr>
<tr><td>Legal NSPs</td><td>50%</td><td>55%</td><td>50%</td></tr>
<tr><td>Mean #syringes exchanged</td><td>63,074</td><td>389,220</td><td>542,820</td></tr>
<tr><td>Mean client contacts</td><td>2,343</td><td>12,352</td><td>5,790</td></tr>
<tr><td>Mean syringes per client</td><td>26.9</td><td>31.5</td><td>93.8</td></tr>
</table>
Policy: Study examined three different NSP syringe dispensation policies: 1) One-for-one, NSPs had a stated policy of giving clients the same number of sterile syringes as were turned in by the client; 2) One-for-one plus, NSPs had a stated policy of giving clients a few more syringes as were turned in by the client (e.g. starter pack); and 3) Distribution, NSPs with a policy of giving clients the number of syringes that the clients request, regardless of the number turned in.
Operating hours
<table>
<tr><th></th><th>Mean hrs/wk</th><th>Days/wk</th></tr>
<tr><td>One-for-one</td><td>13.1</td><td>3.4</td></tr>
<tr><td>One-for-one plus</td><td>14.2</td><td>4.2</td></tr>
<tr><td>Distribution</td><td>35.8</td><td>6.0</td></tr>
</table>
Services
No further details reported</td>
<td>Injection risk behaviours
In bivariate analysis, no statistically significant differences in receptive or distributive sharing by policy. Participants of distribution programmes were less likely to reuse syringes (37%) than one-for-one (63%) and one-for-one plus (62%) ($p<0.05$). Participants of one-for-one programmes (33%) were less likely to share filters than one-for-one plus (50%) and distribution programme (52%) participants ($p<0.05$).
In multivariate analysis, participation in a distribution programme was not statistically significantly associated with receptive sharing (AOR 1.01; 95% CI: 0.56, 1.80), distributive syringe sharing (AOR 0.73; 95% CI: 0.41, 1.30) or sharing filters (AOR 1.50; 95% CI: 0.91, 2.50. Participants of distribution programmes ha lower odds of reusing syringes than other participants (AOR 0.43; 95% CI: 0.27, 0.71).</td>
</tr>
</table>

Study details	Intervention and population details	Intervention	Results
Masson CL, Soensen JL, Perlman DC, Shopshire MS, Delucchi KL, Chen TC, Sporer K, Des Jarlais D and Hall SM (2007) **Country**: USA (San Francisco) RCT ++ **Objectives**: To examine the effect of NSP setting on the injection practices, health status, and health service utilisation patterns of IDUs recruited from a public urban hospital. **Funding source**: NIDA	**Entry criteria:** (a) at least 18 years of ages; (b) DSM of Mental Disorders IV criteria for drug dependence disorder;(c) current injecting drug use; (d) not interested in receiving drug abuse treatment; and (e) residents of the Mission District in San Francisco (i.e. easy access to the hospital) **Participant characteristics** N= Community 83, Hospital 83 Gender (% male) 77% 77% Ethnicity White: 60% 55% African American: 20% 23% Latino: 16% 18% Other 4% 4% Mean age (SD) 41 yrs (8.99) 40 yrs (10.54) Homeless 66% 69% Injection duration NR NR **Analysis** **Outcomes measured:** Injection risk behaviours; Other **How measured:** Addiction Severity Index, Texas Christian University HIV/AIDS Risk Assessment and SF-36. **Length of follow-up:** 6- and 12-months from baseline **Number of participants lost to follow-up** 6 months: n=20 community participants and n=11 hospital participants 12 months: n=24 community participants and n=15 hospital participants	**Programme description** Setting: Community NSP (12 locations); Hospital NSP Policy Community: 10 starter and then one-for-one, no upper limit Hospital: NR Operating hours Community: Mon-Sat 10am-12pm & 7-9pm; Hospital: Sat 12-2pm **Services** Both sites distributed sterile needles and syringes, and the following additional equipment: bleach, distilled water, cotton, latex tourniquets, alcohol wipes, antibacterial cream, cookers and condoms The hospital site provided referrals to drug abuse treatment programmes, medical care and social service programmes. In addition, participants assigned to the hospital site received an HIV risk reduction education session and referrals to inpatient and outpatient services. The community site did not provide education classes or referrals to the hospital for inpatient and outpatient services.	**Injection risk behaviours** NSP condition did not influence risk behaviours, health status, or self-reported NSP programme use. Drug use risk behaviours decreased over time in both groups ($p<0.0001$). **Other** Self-reported frequency of NSP use did not differ between conditions. At the 6-month assessment, 59% of participants assigned to the hospital-based NSP reported using syringe exchange in the past 30 days, compared to 52% of those assigned to the community NSPs ($p=0.61$). The proportion of participants reporting NSP use did not differ between the hospital NSP and community NSP groups at the 12-month assessment (47% vs. 46%; $p=0.11$). SF-36 scores increased over time in both groups ($p<0.001$). Persons assigned to the hospital NSP had 83% (CI: 29% to 160%) more inpatient admissions and 22% (CI: 13% to 32%) more ambulatory care visits than those assigned to community NSPs.

<table>
<tr><th>Study details</th><th>Intervention and population details</th><th>Intervention</th><th>Results</th></tr>
<tr>
<td>Miller C, Tyndall M, Spittal P, Li K, Palpu A, Schechter M (2002)

Country: Canada (Vancouver)

Cross-sectional -

Objectives: To characterise risk-taking behaviour according to primary source of clean needles accessed by an open cohort study of IDUs.

Funding source: Michael Smith Foundation for Health Research, Canadian Institute for Health Research,</td>
<td>Entry criteria: Had ever accessed NSP, reported primarily accessing pharmacies or fixed/mobile NSP within the previous six months.

Participant characteristics
<table>
<tr><th></th><th>Pharmacy</th><th>Fixed</th><th>Van</th></tr>
<tr><td>Number of pts:</td><td>62</td><td>768</td><td>190</td></tr>
<tr><td>Gender (% male)</td><td>81</td><td>64</td><td>59</td></tr>
<tr><td>Ethnicity Aboriginal:</td><td>15%</td><td>27%</td><td>33%</td></tr>
<tr><td>Median age (IQR)</td><td>36 (29-41)</td><td>35 (28-41)</td><td>32 (26-39)</td></tr>
<tr><td>Homeless (unstable housing)</td><td>66%</td><td>72</td><td>69</td></tr>
<tr><td>Median injection duration (IQR)</td><td>16 (9.5-22)</td><td>13 (5-23)</td><td>10 (5-17)</td></tr>
</table>
Analysis
Outcomes measured: Injection risk behaviours; HIV; HCV
How measured: Questionnaire, blood test
Length of follow-up: NA
Number of participants lost to follow-up: NA</td>
<td>Programme description
Setting: Fixed site and mobile van
Policy: NR
Operating hours: 8am-8pm 7 days/week (fixed site); 5:30pm-8am (van)

Services
No details reported</td>
<td>Injection risk behaviours
There was no significant trend for needle borrowing or lending, although pharmacy users were more likely to report needle sharing behaviours.

Needle sharing behaviours
<table>
<tr><th></th><th>Pharmacy</th><th>Fixed</th><th>Van</th><th>P value</th></tr>
<tr><td>Borrow</td><td>29 (47%)</td><td>200 (26%)</td><td>59 (31%)</td><td>0.374</td></tr>
<tr><td>Lend</td><td>28 (45%)</td><td>276 (36%)</td><td>69 (36%)</td><td>0.432</td></tr>
</table>
BBVs
The authors reported that there was no significant trend for HIV or HCV prevalence, although HIV prevalence was lower among pharmacy users than participants who reported using the van or fixed sites NSPs.
<table>
<tr><th></th><th>Pharmacy</th><th>Fixed</th><th>Van</th><th>P value</th></tr>
<tr><td>HIV+</td><td>10 (16%)</td><td>194 (25%)</td><td>40 (21%)</td><td>0.158</td></tr>
<tr><td>HCV+</td><td>55 (89%)</td><td>634 (83%)</td><td>149 (78%)</td><td>0.157</td></tr>
</table>
</td>
</tr>
</table>

Study details	Intervention and population details	Intervention	Results
Millson P, Challacombe L, Villeneuve PJ, Strike CJ, Fischer B, Myers T et al. (2004) **Country**: Canada Uncontrolled before and after study - **Objectives:** To assess injection-related HIV risk behaviours among opioid users six months after enrolment in low-threshold methadone maintenance treatment (MMT) programmes. **Funding source:** National Health Research and Development Program, Canadian Institute for Health Research, Canadian Foundation for AIDS Research	**Entry criteria:** Opioid users (opioid dependent according to DSM-IV) recruited at the time of entry into one of two low-threshold MMT programmes. **Participant characteristics** All participants Number of pts: 183 Gender (% male) 62.8% Ethnicity White: 87.4% Aboriginal: 5.5% Other: 7.1% Median age (range): 33 years (18-54) Duration of injection <5 years: 22.8% 5-9 years: 27.5% 10 or more years: 49.7% **Analysis** **Outcomes measured:** Injection risk behaviours **How measured:** Questionnaire **Length of follow-up:** 6 months **Number of participants lost to follow-up:** 19 (9.4%) and one participant died.	**Programme description** Setting: Low-threshold MMT offered within NSP services. Policy: NR Operating hours: NR **Services** Medical and social support services; clients may be offered counselling, assistance with issues such as housing and social support programmes, testing for HIV and hepatitis C and referral to other services such as primary health care.	At 6 months follow-up, 75.4% were still enrolled in the original MMT programme, 11.5% were enrolled in a different MMT programme, 2.7% were in prison but still receiving methadone, 1.1% were in another form of treatment and 9.3% were no longer in any form of drug treatment. Average methadone dose for those still receiving MMT at 6-months follow-up was 88 mg (range 1-240 mg). **Injection risk behaviours** Overall proportion of participants injecting drugs decreased significantly between baseline and 6 months follow-up (from 83% at treatment entry to 66%). At baseline, 16% shared needles compared to 9% at 6 months follow-up (OR 0.43; 95% CI 0.20, 0.94). Among the injecting subgroup (participants who reported injecting drugs between baseline and follow-up), 22% reported sharing at baseline compared to 14% at follow-up (OR 0.50; 95% CI 0.23, 1.11). There were significant changes in sharing of injection equipment; 28% reported sharing injection equipment at baseline compared to 14% at 6 month follow-up. In the injecting subgroup, 21% reported sharing injection equipment at the 6-month follow-up compared to 37% at baseline. The prevalence of indirect sharing (e.g. backloading and frontloading) was low at treatment entry. There was a decline in this behaviour from 9% to 3% across the whole cohort and among the injecting subgroup although the corresponding OR was not significant; from 10% to 5% (OR 0.40; 0.13, 1.28)

Study details	Intervention and population details	Intervention	Results
Nelles J, Bernasconi S, Dobler-Mikola A, Kaufmann B (1997) **Country**: Switzerland Before and after (uncontrolled) - **Objectives**: Evaluation of efficacy of prevention programme, detect undesirably developments, elaborate general recommendations **Funding source**: NR	**Entry criteria:** NR **Participant characteristics** Number of pts: 86 Gender (% male) 100% female Ethnicity: 40% Swiss **Analysis** **Outcomes measured:** Injection risk behaviours **How measured:** Not reported **Length of follow-up:** Not clear **Number of participants lost to follow-up:** NA	**Programme description** Setting: Prison, vending machine Policy: One-for-one Operating hours: NA (vending machine) **Services** Sterile needles and syringes Counselling, condoms	**Injection risk behaviours** 8 participants reported exchanging syringes in prison before the project started. Only one participant reported that they continued to do so at the end of the project. The authors reported that the results of the pilot project carried out at Hindelbank prison did not provide arguments against the continuation of the distribution of sterile injecting equipment, as there was no increase in drug consumption and no syringe-related incidents were observed. No abscesses related to drug injection were observed, and there were no new cases of HIV or HCV/HBV.

Study details	Intervention and population details	Intervention	Results
Obadia Y, Feroni I, Perrin V, Vlahov D, Moatti J (1999) **Country**: France Cross-sectional - **Objectives**: To evaluate whether vending machines represent a useful adjunct to other approaches for promoting access to sterile syringes, especially among young IDUs. **Funding source**: City of Marseille (Mission SIDA-Toxicomanie), French Sickness Fund of Social Security (CPCAM-Bouches du Rhone), the French Minister for Social and Health Affiars (DDASS-Bouches du Rhone), NIDA	**Entry criteria:** NR **Participant characteristics** Number of pts: Primary users of vending machines 73; Primary users of other programmes 270 Gender (% male): 79.5; 76.3 Ethnicity: NR; NR Age 17-30: 53.4%; 37.1% >30: 46.6%; 62.9% Homeless (not living in own house in previous month): 68.5%; 49.6 Injection duration ≤10yrs: 56.3%; 45.8% >10yrs: 43.7%; 54.2% **Analysis** **Outcomes measured:** Injection risk behaviours **How measured:** Survey **Length of follow-up:** NA **Number of participants lost to follow-up:** NA	**Programme description** Setting: Sterile needles and syringes were available for purchase from pharmacies, from four NSPs and at seen vending machines Policy: NR Operating hours: NR **Services** Additional services available not described	There was no differences between vending machine users and users of other sources in terms of sharing needles in the previous six months (11.0% vs. 11.6%; OR 1.0, 95% CI 0.5, 2.4). However, vending machine users reported that they were significantly less likely to have shared cookers, cotton and water during the previous 6 months compared to non-users (12.3% vs. 29.8%; OR 0.3; 95% CI 0.2, 0.7).

Study details	Intervention and population details	Intervention	Results
Pollack HA, Knoshnood K, Blankenship KM & Altice FL (2002) **Country**: USA (New Haven) Cohort + **Objectives**: To examine the impact of the New Haven Community Health Care Van (CHCV) in reducing emergency department use among IDUs **Funding source**: NIDA	**Entry criteria:** Active IDU **Participant characteristics** Number of pts: 117 256 Gender (% male) 70% 62% Ethnicity African American: 47% 33% Hispanic: 21%; 13%; White: 32% 50% Mean age 39.8 40.1 Homeless NR NR Injection duration NR NR **Analysis** **Outcomes measured:** Emergency department visits **How measured:** Standardised questionnaire **Length of follow-up:** 3 years **Number of participants lost to follow-up:** NR	**Programme description** Health Care van travelled in tandem with New Haven NSP Setting: Mobile (4 locations) Policy: NR Operating hours: 5 days per week **Services** In addition to the distribution of sterile needles and syringes, condoms were distributed among users. Other services available included on-site testing for BBVs, pre- and post-diagnostic counselling, general health advice, acute medical care, minor wound care, prescription refills, diagnosis and treatment of TB and STDs, and vaccination programme for influenza, tetanus, and pneumococcal infections. Clinical care and donated medication were available free to uninsured clients for medically indicated reasons. In addition, staff were able to provide referrals to community medical treatment, drug treatment and social services	**Other** Over the study period, CHCV users made more frequent emergency department visits. CHCV use was significantly associated with a reduction in the rate of ED use (incidence rate ratio [IRR] 0.79; 0.66-0.95; p<0.05). Reductions were prominent at the largest local hospital, Yale-New Haven Hospital ED (IRR 0.57; 0.46-0.70; p<0.001).

Study details	Intervention and population details	Intervention	Results
Rhodes T, Judd A, Makhailova L, Sarang A, Khurtoskoy M, Platt L, Lowndes C, Renton A (2004) **Country**: Russia Cross-sectional - **Objectives**: To compare risk factors for injecting drug equipment sharing among IDUs in Togliatti City, Russia. **Funding source**: NR	**Entry criteria:** Reported injecting in the previous 4 weeks, provided informed consent **Participant characteristics** Number of pts: 426 Gender (% male) 64% Ethnicity: NR Age (<25 yrs) 47% Homeless NR Injection duration 20% <2 yrs: 27% 3-5 yrs: **Analysis** **Outcomes measured**: Injection risk behaviours **How measured:** Questionnaire and saliva sample (HIV) **Length of follow-up:** NA **Number of participants lost to follow-up:** NA	**Programme description** Setting: NR Policy: NR Operating hours: NR **Services** No further details reported	**Injection risk behaviours** IDUs reported NSPs or outreach workers as their main source of new needles and syringes in the last 4 weeks had 0.3 times the odds of sharing compared with those obtaining them from a pharmacy or shop (OR 0.3; 95% CI 0.1, 1.1; p<0.001). Participants whose main source was buying needles and syringes on the streets or obtaining them from a sex partner, friend, other drug user, or drug dealer had 12 times the odds of sharing needles and syringes in the last 4 weeks (OR 12.4; 95% CI: 2.6, 58.5).

<table>
<tr><th>Study details</th><th>Intervention and population details</th><th>Intervention</th><th>Results</th></tr>
<tr>
<td>Riley ED, Safaeian M, Strathdee SA, Marx MA, Huettner S, Beilenson P, Vlahov D (2000)

Country: Baltimore, USA

Cross-sectional -

Objectives: To compare characteristics of first-time needle exchange participants who enrolled at a mobile van-based exchange site versus a fixed pharmacy-based exchange site, in an area where both types of needle exchange programmes were available.

Funding source: NIDA and US Department of Health and Human Services.</td>
<td>Entry criteria: First time NSP participants at van-based site or at one of two pharmacy-based site.

Participant characteristics
<table>
<tr><th></th><th colspan="2">Site of enrollment</th></tr>
<tr><th></th><th>Van</th><th>Pharmacy</th></tr>
<tr><td>Number of pts:</td><td>124</td><td>162</td></tr>
<tr><td>Gender (% male)</td><td>67%</td><td>74%</td></tr>
<tr><td>Ethnicity African American:</td><td>88%</td><td>96%</td></tr>
<tr><td>Age <40</td><td>56%</td><td>50%</td></tr>
<tr><td>Homeless</td><td>NR</td><td>NR</td></tr>
<tr><td>Duration of Injection ≥18 years:</td><td>50%</td><td>54%</td></tr>
</table>
Analysis
Outcomes measured: Injection risk behaviours
How measured: Interviews and HIV tests
Length of follow-up: NA
Number of participants lost to follow-up: NA</td>
<td>Programme description
Setting: Mobile van-based NSP and fixed site pharmacy-based NSP.
Policy: One-for-one exchange.
Operating hours: Two vans visiting six sites, four days per week, exchanging syringes for two-hour shifts at each site; two pharmacies were open for a comparable number of hours.

Services
Not detailed, however some study participants attended NSP sites to access HIV tests and treatment referrals.</td>
<td>Injection risk behaviours
The different sites attracted first-time NSP users with different characteristics. Compared with pharmacy-based NSPs, van based sites attracted twice as many high-frequency injectors.</td>
</tr>
</table>

Study details	Intervention and population details	Intervention	Results
Rockwell R, Des Jarlais DC, Friedman SR, Perlis TE & Paone D (1999) **Country**: USA (New York City) Cross-sectional - **Objectives**: To examine the relationship between residential location of IDUs in New York City and their use of an NSP **Funding source**: NR	**Entry criteria:** Currently active IDUs **Participant characteristics** Number of pts: 776 Gender (% male) 72% Ethnicity Black: 35% Latino: 27% White: 34% Mean age 36 years Homeless NR Injection duration NR **Analysis** **Outcomes measured:** Injection risk behaviours, programme use **How measured:** Structured questionnaire **Length of follow-up:** NA **Number of participants lost to follow-up:** NA	**Programme description** Setting: NR Policy: Unlimited Operating hours: NR **Services** Additional services offered were not described.	48% of participants were classified as living within a 10 min walk of an NSP. **Injection risk behaviours** Injected with syringe used by someone else at last injection (No; Yes) </= 10 min walk: 356 (96%); 16 (4%) >10 min walk: 370 (92%); 34 (8%) OR = 0.48; 95% CI 0.26, 0.90 (p=0.02) Syringe exchangers: 517 (96%); 22 (4%) Non-exchangers: 209 (88%); 28 (12%) OR = 0.31; 95% CI 0.17, 0.0.56 (p=0.001) In multivariate logistic regression analysis, respondents who were </=10 min walk from an NSP were less likely to report injecting with a used syringe at last injection (AOR 0.45; 95% CI 0.24, 0.86; p=0.01). Respondents who reported use of an NSP in the previous 6 months were less likely than non-exchangers to reported injecting with a used syringe at last injection (AOR 0.30; 95% CI 0.16, 0.55; p=0.001) **Other** NSP use in prior 6 mths (No; Yes) </= 10 min walk: 70 (19%); 302 (81%) >10 min walk: 167 (41%); 237 (59%) OR = 3.04; 95% CI 2.19, 4.21 (p=0.001) In multivariate logistic regression analysis, </=10 min walk from an NSP was significantly associated with typical use of an NSP (AOR 2.89; 95% CI 2.06, 4.06; p=0.001)

Study details	Intervention and population details	Intervention	Results
Schilling R, Fortdevila J, Fernando D, El-Bassel N, Monterroso E (2004) **Country**: USA (Harlem, NY) Cross-sectional - **Objectives**: To determine whether proximity to NSP, irrespective of the use of such programmes, associated with lower levels of drug and sex related risk behaviour **Funding source**: Center for Disease Control and Prevention, Atlanta	**Entry criteria:** Injected within previous six months. Participants were recruited at: 1) the NSP; 2) within ten blocks of the NSP; and 3) beyond ten blocks of the NSP **Participant characteristics** NSP: Number of pts: 186; Gender (% male) 74.7; Hispanic: 46.8%; African American: 31.2%; White/Other: 22.2%; Mean age 38.9; Homeless* 21.5%; Injection duration NR ≤10 blocks: Number of pts: 203; Gender (% male) 74.9; Hispanic: 47.8%; African American: 39.4%; White/Other: 12.8%; Mean age 39.3; Homeless* 17.3%; Injection duration NR >10 blocks: Number of pts: 198; Gender (% male) 75.8; Hispanic: 46.5%; African American: 35.9%; White/Other: 17.7%; Mean age 37.0; Homeless* 30.3%; Injection duration NR * Shelter, 1/2 way house, street or squat **Analysis** **Outcomes measured:** Injection risk behaviours **How measured:** Self-report **Length of follow-up:** NA **Number of participants lost to follow-up:** NA	**Programme description** Setting: NEP Policy: NR Operating hours: NR **Services** The programme provided pre- and post-diagnostic counselling, safer sexual health advice and referrals to drug treatment, social services, and soup kitchens.	**Injection risk behaviours** Post-hoc analyses indicated that the NSP recruited participants engaged in HIV risk behaviours less frequently than street recruited participants. NSP sample were less likely to inject with a needle that someone else had squirted drugs into (p=0.000); less likely to use dirty needles by themselves (p=0.004); and less likely to share a cooker (p=0.031).

Study details	Intervention and population details	Intervention	Results
Sears C, Guydish J, Witzien E, Lum P (2001) **Country**: USA (San Francisco) Cross-sectional - **Objectives**: To investigate an HIV prevention programme for homeless young adult IDUs that combined secondary NSP with community-level activities **Funding source**: San Francisco AIDS Foundation	**Entry criteria:** Aged 15-25 yrs, injected in past 30 days, homeless* **Participant characteristics** Number of pts: NSP area 67, Non-NSP area 55 Gender (% male): 63%, 74% Ethnicity White: 77.6%, 83.0% Mean age (SD): 20.3 (2.4), 21.5 (3.1) Homeless*: 100%, 100% Mean injection duration (SD): 4.3 (3.2), 4.9 (3.5) *defined as having primarily stayed in park, squat, street, hotel, shelter or friend's apartment in past 30 days. **Analysis** **Outcomes measured:** Injection risk behaviours **How measured:** Structured Interview **Length of follow-up:** NA **Number of participants lost to follow-up:** NA	**Programme description** Setting: Street outreach Policy: NR Operating hours: aimed for 24 hrs, 7 days/week **Services** The outreach programme distributed sterile needles and syringes, and the following additional items: cookers, cotton, water bottles, alcohol wipes, and sharps containers. Distribution of media was also part of the programme.	**Injection risk behaviours** Compared with participants recruited from the non-NSP area, intervention site participants reported lower rates of sharing syringes (40.3% vs. 69.1%; p=0.002), syringe reuse (32.8% vs. 65.5%; p=0.001), and using someone else's cotton (27.3% vs. 49.1%; p=0.013). There was no difference between the two groups in terms of backloading (89.6% vs. 94.6%; p=0.317) or inconsistent skin cleaning (88.1% vs. 74.6%; p=0.053). Logistic regression analyses: Comparison site IDUs were more likely than intervention site IDU to report syringe sharing, syringe reuse, and inconsistent condom use with a casual partner. No independent association was found between intervention site and using someone else's cotton. Outcome variables: invention vs. comparison site Shared needle: AOR 3.748 (95% CI 1.406, 9.988) Syringe reuse: AOR 2.769 (95% CI 1.120, 6.847) Used someone else's cotton: NS (AOR not reported) Inconsistent condom use with casual partner: AOR 4.825 (95% CI 1.392, 16.721)

Study details	Intervention and population details	Intervention	Results
Singer M, Himmelgreen D, Weeks MR, Radda KE and Martinez R (1997) **Country**: USA (Hartford, CT) Cross-sectional - **Objectives**: To determine whether increased availability of sterile syringes and HIV education produce changes in HIV risk behaviour and seroprevalence over time **Funding source**: NIDA	**Entry criteria:** NR; participants were part of a NIDA funded study (Community Outreach Prevention Effort; COPE II) **Participant characteristics** Number of pts: 571 Gender (% male) 80.4% Ethnicity African American: 33% Latino: 56.6% White: 8.6% Other 1.9% Age >35 yrs 64.1% Homeless 35.4% Injection duration NR **Analysis** **Outcomes measured:** Injection risk behaviours, BBVs **How measured:** Questionnaire **Length of follow-up:** NA **Number of participants lost to follow-up:** NA Serial cross-sectional analysis of baseline entry data from a cohort study across three periods: 1) when non-prescription pharmacy syringe sales were permitted but there was no NSP; 2) an NSP with a five syringe limit; and 3) when the five syringe limit was increased to ten syringes.	**Programme description** Setting: Pharmacy sales and community NSP (mobile van) Policy: NR Operating hours: NR **Services** No details reported	**Injection risk behaviours** Steady and statistically significant decrease in the percentage of IDUs reporting to use: 1) preused syringes (from 41.6% to 28.3% to 23.3%; p<0.005); 2) previously used supplies (from 45.6% to 40.7% to 36.1%). There was a significant reduction in the proportion of injections that involved the use of previously used syringes (mean [SD]: 0.21 [0.28] to 0.11 [0.25]) and supplies (mean [SD]: 0.31 [0.35] to 0.12 [0.25]). There was a non-significant decrease in the proportion of injections that involved new syringes [mean (SD): 0.24 (0.27) to 0.21 (0.25)] % of IDUs that injected with pre-used syringes was lowest among those that used both the NSP and pharmacy (18.5%) and highest among those who accessed neither programme (39.5%; p<0.005). The % of IDUs who injected with pre-used syringe was 30.8% for those accessing needles from NSP alone and 32.1% for IDUs using the pharmacy alone. **BBVs** The authors reported that there was a significant drop in the number of IDUs who were HIV positive (based on testing or self-report) between the periods of legal syringe purchase and when up to 5 needles could be exchanged at the NSP (35% to 22%; p<0.05). HIV seroprevalence increased to 25% during the period when up to 10 needles could be exchanged. Chi-squared analysis showed a significant increase in the number of IDUs between 36-45 yrs who were HIV positive from the period when up to 5 syringes could be exchanges at the NSP through the time when 10 syringes could be exchanged (18% to 29%; p<0.0001). IDUs aged 26-35 yrs showed no change in HIV status.

Study details	Intervention and population details	Intervention	Results
Stark K, Herrmann U, Ehrhardt S & Bienzle U (2006) **Country**: Germany (Berlin) Before and after (uncontrolled) - **Objectives**: **Funding source**: Senate of Berlin (Department of Justice, Department of Health), Federal Ministry of Education and Research (Research Network on Viral Hepatitis, Hep-Net)	**Entry criteria:** All inmates who had ever used illicit drugs. **Participant characteristics** Number of pts: 166 Gender (% male) 32% Ethnicity: Median age (IQR): 31 (27-34) Homeless NR Injection duration >5 yrs 72% **Analysis** **Outcomes measured:** Injection risk behaviours; HIV; HCV; HBV **How measured:** Questionnaires and blood tests **Length of follow-up:** median 12 months **Number of participants lost to follow-up:** n=124 had FU data (81 females, 43 males)	**Programme description** Setting: Prison, vending machine Policy: Exchange for used syringe/dummy syringe Operating hours: **Services** In female prison, dispensers provided a pack containing a sterile syringe and needle, and a skin disinfection pad. In the male prison, social workers from an NGO exchanged sterile syringes and needles for used equipment three times a week.	**Injection risk behaviours** Two thirds of IDUs had ever injected with syringes already used by someone else and 17% had done so in the six months prior to imprisonment. 71% had shared syringes in prison during the previous four month period of imprisonment or during four month follow up periods. 11% of IDUs reported syringe sharing at FU. Injecting drug use was reported at follow-up by 67% of females and 90% of males; 95% used heroine and 26% cocaine. Median frequency of injecting was 8 (range 1-100) in females and 23 (range 4-200) in males in the most recent 4 month period. **BBVs** At baseline, seroprevalence rates were 18% for HIV, 53% for HBV, and 82% for HCV. In multivariate analysis, injecting drug use during previous imprisonment was found to be an independent predictor of HIV infection (AOR 2.3; 95% CI 1.2, 4.9) and HCV infection (AOR 2.0; 95% CI 1.1, 5.6). During follow-up, no HIV or HBV seroconversions were observed. However, 4/22 participants who were seronegative at baseline developed HCV antibodies (incidence rate 18/100 person yrs). All IDU who seroconverted denied sharing syringes while in prison, but three quarters reported 'frontloading' or sharing spoons.

Study details	Population details	Intervention	Results
Strathdee AS, Ricketts EP, Huettner S, Cornelius L, Bishai D, Havens JR, Beilenson P, Rapp C, Lloyd JJ and Latkin CA (2006) **Country**: USA (Baltimore) RCT - **Objectives**: To determine whether the addition of case management services at Baltimore NSP could increase the proportion of IDUs entering drug abuse treatment, by linking IDUs to available services. **Funding source**: NIDA	**Entry criteria:** Clients of the Baltimore NSP who sought drug abuse treatment between Jan 2002 and Jan 2004. **Participant characteristics** Intervention: N= 128; Gender (% male): 71%; Ethnicity: Other 20%, African American 80%; Mean age (SD) 42.1 (8.2); Homeless NR; Injection duration NR Control: N= 117; Gender (% male): 67%; Ethnicity: Other 27%, African American 73%; Mean age (SD) 42.4 (8.0); Homeless NR; Injection duration NR **Analysis** **Outcomes measured:** Entry into drug treatment, defined as having attended the intake appointment for opioid agonist therapy at one of six publicly funded drug treatment programmes within 7 days of the baseline interview. **How measured:** Interview (Addiction Severity Index, AUDIT, Stages of change) **Length of follow-up:** 7 days **Number of participants lost to follow-up:** NA	**Programme description** Setting: Two mobile vans serving 10 NSP sites Policy: NR Operating hours: NR **Services** No details reported Intervention examined was based on the Strengths-based Case Management model, case managers assisted clients in setting treatment goals and helped manage clients' needs to achieve these goals. Duration and frequency were client driven. Control participants were provided only with a voucher printed with the date and time of their intake appointment at the drug treatment programme.	**Other** Overall, 34% of participants entered treatment within 7 days of the referral from the NSP (intervention 40% vs. control 26%; p=0.03). Factors associated with a greater odds of entering treatment were having been randomised to receive case management (OR 1.84; 95% CI 1.07-3.16), having two or more contacts with a case manager prior to intake visit (OR 2.47; 95% CI 1.33-4.59), having received more with a case manager or being driven to treatment by a case manager (both p<0.01). In a multivariate "intention to treat" analysis, those randomised to case management were 87% more likely to enter treatment within 7 days after adjusting for farther travel, access to a car, and clustering by NSP site (AOR 1.87 95% CI 0.91-3.86, P=0.06). In an "as treated" model, having received more case management time was independently predictive of treatment entry. Participants who received 30 min or more of case management within 7 days were 33% more likely to enter treatment (AOR not reported). Further analyses suggested that the "active ingredient" of case management was the provision of transportation to the treatment programme. The median duration of case management time received within the 7-day period was 25 min (IQR 15-80) among a total of 201 contacts (median number of contacts per person 2, IQR 1-3).

Study details	Intervention and population details	Intervention	Results
Tyndall M, Bruneau J, Brogly S, Spittal P, O'Shaunessy M, Schechter M (2002) **Country**: Canada (Montreal and Vancouver) Cohort + **Objectives**: To compare sources of needles and trends in needle distribution in Montreal and Vancouver, which have different policies regarding secondary exchange, over time. **Funding source**: British Columbia Ministry of Health, Health Canada (National AIDS Research Scientist award), National Institutes of Health Grand ROI	**Entry criteria:** Active IDUs or had injected in past month (Vancouver) or past six months (Montreal); 14 years of age or older, residing in greater Montreal or Vancouver area, providing informed consent. **Participant characteristics** Vancouver: SND / No SND; Montreal: SND / No SND Number of pts: 262 / 303 / 195 / 196 Gender (% male): 59% / 58% / 80% / 88% Ethnicity French: NA / NA / 87% / 91% Aboriginal: 22 / 36% / NA / NA Mean age (range) 37 (18-60) / 37 (16-59) / 34 (15-56) / 37 (19-62) Homeless*: 14% / 18% / 12% / 17% Mean Injection duration (range): 14 (0.06-38.0) / 13 (0.08-40.0) / 12 (0.01-42.0) / 0.98 (0.96-1.00) *Unstable housing **Analysis** **Outcomes measured:** Injection risk behaviours **How measured:** Interview and blood test (HIV test) **Length of follow-up:** One or more follow up visit between 1997 and 2000 **Number of participants lost to follow-up:** NR	**Programme description** Setting: Fixed site and mobile (both sites) Policy: One-for-one unlimited Vancouver; unlimited Montreal. Bulk exchanges of >20 needles per visit were not permitted at the Vancouver exchange. Operating hours: NR **Services** No further details reported	**Injection risk behaviours** Satellite needle distribution (SND) was associated with borrowing used injection equipment/paraphernalia (AOR 2.62; 95% CI: 1.85, 3.71). Exclusively receiving clean needles through SND (n=95) was associated with borrowing used equipment (AOR 2.44; 95% CI: 1.41, 4.23). Only providing needles through SND (n=196) was also associated with borrowing used equipment (AOR 2.41; 95% CI: 1.56, 3.69) and borrowing used needles

<table>
<tr><th>Study details</th><th>Intervention and population details</th><th>Intervention</th><th>Results</th></tr>
<tr>
<td>Valente T, Foreman R, Junge B and Vlahov D (2001)

Country: USA

Cross-sectional -

Objectives: Evaluate impact of NSP use patterns and whether differentially effective for different users.

Funding source: NIDA</td>
<td>Entry criteria: NSP users who had visited NSP more than once and returned syringe from NSP. Study participants who visited the NSP only once (n=1,910), participants who did not return any programme needles issued at the NSP (n=873), and participants who were missing any demographic information (n=12) were excluded from the analysis.

Participant characteristics
<table>
<tr><th></th><th colspan="3">NSP user</th></tr>
<tr><th></th><th>Low</th><th>Medium</th><th>High</th></tr>
<tr><td>Number of pts:</td><td>770</td><td>941</td><td>863</td></tr>
<tr><td>Gender (% male)</td><td>71.3</td><td>73.7</td><td>70.8</td></tr>
<tr><td>Ethnicity</td><td></td><td></td><td></td></tr>
<tr><td>African American:</td><td>88.5</td><td>90.2</td><td>90.8</td></tr>
<tr><td>Age</td><td>40.4</td><td>41.1</td><td>43.0</td></tr>
<tr><td>Homeless</td><td>NR</td><td>NR</td><td>NR</td></tr>
<tr><td>Injection duration</td><td>NR</td><td>NR</td><td>NR</td></tr>
</table>
Analysis
Outcomes measured: Syringe relay (returning a syringe originally given to someone else); HIV
How measured: Syringe tracking
Length of follow-up: NA
Number of participants lost to follow-up: NA</td>
<td>Programme description
Setting: NEP
Policy: One-for-one
Operating hours: NR

Services
Programme distributed clean needles and syringes. No other service details were reported except that secondary exchange was not accepted.</td>
<td>Injection risk behaviours
Low users of the NSP were more likely to return syringes originally distributed to someone else, and those syringes circulated in the community about 4 days (14%) longer. Results of the multivariate analysis showed that participants who returned their own syringes (p<0.001) and who returned them more quickly (p<0.05) used the NSP more.

BBVS
NSP use was not associated with HIV seroconversion (OR 1.18; 95% CI 0.65, 2.15), nor was circulation time (OR 0.98; 95%CI 0.93, 1.02), indicating that more NSP use and more rapid return of syringes did not directly lower the individual likelihood of becoming HIV positive.</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Intervention and population details</th><th>Intervention</th><th>Results</th></tr>
<tr>
<td>Van Den Berg C, Smit C, Van Brussel G, Coutinho R and Prins M (2007)

Country: Netherlands

Cohort +

Objectives: To investigate the impact of harm-reduction programmes on HIV and HCV incidence among ever-injecting IDUs from Amsterdam Cohort Study

Funding source: Netherlands National Institute for Public Health and the Environment</td>
<td>Entry criteria: Analysis restricted to participants with at least two visits and HIV negative and/or HCV negative at study entry

Participant characteristics
<table>
<tr><th></th><th>HIV negative</th><th>HCV negative</th></tr>
<tr><td>Number of pts:</td><td>710</td><td>168</td></tr>
<tr><td>Gender (male)</td><td>61.4</td><td>65.7</td></tr>
<tr><td>Ethnicity</td><td></td><td></td></tr>
<tr><td>W European:</td><td>84.8</td><td>82.7</td></tr>
<tr><td>Median age (IQR)</td><td>30.0 (27.0-36.0)</td><td>29.0 (25.0-33.0)</td></tr>
<tr><td>Homeless</td><td>NR</td><td>NR</td></tr>
<tr><td>Median injection duration (IQR)</td><td>7.21 (3.04-12.1)</td><td>2.43 (0.06-7.16)</td></tr>
</table>
Analysis
Outcomes measured: HIV incidence; HCV incidence
How measured: Questionnaire and blood test
Length of follow-up: every 4-6 months, 20 yrs (so far)
Number of participants lost to follow-up: 1,640 enrolled, 1,276 had at least two visits</td>
<td>Programme description
Five levels of harm reduction evaluated:
1. No harm reduction: no methadone past 6 months, injecting drug use in past 6 months, no NSP use
2. Incomplete harm reduction: any methadone dose in past 6 months, injecting drug use in past 6 months and irregular* or no NSP use; OR 0-59mg methadone daily in past 6 months, injecting daily in the past 6 months and always (ie 100%) use NSP
3. Full harm reduction: equal to or more than 60mg methadone daily in the past 6 months and no injecting drug use in the past 6 months; OR equal to or greater than 60mg methadone daily, injecting drug use in the past six months, and always use NSP
4. Limited dependence on harm reduction: 1-59mg methadone daily in the past 6 months and no injecting drug use in the past 6 months
5. No dependence on harm reduction: no methadone in past 6 months and no injecting drug use in past 6 months

*1-99%of needles used in past 6 months obtained via NSP</td>
<td>BBVs
Any prescribed dose of methadone was associated with lower incidence rates of HIV and HCV infection (NS; p=0.084 and p=0.21, respectively). NSP use was associated with a higher risk of HIV and HCV seroconversion (although this finding was NS when restricted to participants who had injected in the preceding 6 months). When methadone dose and NSP use were combined, full participation in harm reduction programmes was associated with a significant reduction in HIV and HCV seroconversion (see below).

HIV
<table>
<tr><th></th><th>Incidence (/100 PY)</th><th>sc</th><th>PY</th><th>IRR</th><th>95% CI</th></tr>
<tr><td>No HR</td><td>3.80</td><td>18</td><td>473.6</td><td>1</td><td></td></tr>
<tr><td>Incomplete HR</td><td>2.80</td><td>46</td><td>1640.8</td><td>0.74</td><td>(0.43, 1.27)</td></tr>
<tr><td>Full HR</td><td>1.22</td><td>18</td><td>1475.9</td><td>0.32</td><td>(0.17, 0.62)</td></tr>
<tr><td>Limited dependence</td><td>0.13</td><td>1</td><td>758.1</td><td>0.035</td><td>(0.005, 0.26)</td></tr>
<tr><td>No dependence</td><td>0.57</td><td>6</td><td>1048.4</td><td>0.15</td><td>(0.060, 0.38)</td></tr>
</table>
sc = seroconversion; PY = person years; IRR = incidence rate ratio

HCV
<table>
<tr><th></th><th>Incidence (/100 PY)</th><th>sc</th><th>PY</th><th>IRR</th><th>95% CI</th></tr>
<tr><td>No HR</td><td>23.16</td><td>11</td><td>47.5</td><td>1</td><td></td></tr>
<tr><td>Incomplete HR</td><td>24.12</td><td>34</td><td>141.0</td><td>1.04</td><td>(0.53, 2.05)</td></tr>
<tr><td>Full HR</td><td>3.47</td><td>6</td><td>173.0</td><td>0.15</td><td>(0.056, 0.40)</td></tr>
<tr><td>Limited dependence</td><td>0.57</td><td>1</td><td>174.9</td><td>0.024</td><td>(0.003, 0.19)</td></tr>
<tr><td>No dependence</td><td>1.64</td><td>5</td><td>305.2</td><td>0.071</td><td>(0.025, 0.20)</td></tr>
</table>
sc = seroconversion; PY = person years; IRR = incidence rate ratio

In multivariate analysis (after correcting for having an HIV+ steady partner and a smaller number of years since starting injection) drug users fully participating in HRPs were at a decreased risk of HIV seroconversion compared to IDU not participating (IRR 0.43; 95% CI 0.21, 0.87). For HCV (after correcting for the time elapsed since start of injecting), drug users participating in full HR were at a non-significantly decreased risk of HCV seroconversion compared with DU not participating (IRR 0.36; 95% CI: 0.13, 1.03).</td>
</tr>
</table>

Appendix 4. Review of effectiveness: quality assessment tables

Table 18. Quality assessment for systematic reviews and meta-analyses

	Cross et al 1998	Dolan et al 2003	Gibson et al 2001	Kall et al 2007	Ksobiech 2003	Ksobiech 2006	Ritter & Cameron 2006	Tilson et al 2006	Wodak & Cooney 2004	Wright et al 2005
The study addresses an appropriate and clearly focused question.	✓✓✓	✓✓	✓✓✓	✓✓	✓✓✓	✓✓✓	✓✓✓	✓✓✓	✓✓✓	✓✓✓
A description of the methodology used is included.	✓✓	✓	✓✓	✓	✓✓	✓✓✓	✓✓	✓✓	✓✓✓	✓✓✓
The literature search is sufficiently rigorous to identify all relevant studies.	✓✓	✓✓✓	✓✓	✓	✓✓✓	✓✓✓	✓✓✓	✓✓✓	✓✓✓	✓✓✓
Study quality is assessed and taken into account	✓	X	✓✓	X	X	X	✓✓	✓✓	X	✓✓✓
There are enough similarities between the studies selected to make combining them reasonable	✓✓	NA	NA	NA	✓	✓	NA	NA	NA	NA
Overall assessment	+	+	+	-	+	+	+	++	+	++

✓ poorly addressed; ✓✓ adequately addressed; ✓✓✓ well covered

Table 19. Quality assessment for RCTs

	Fisher et al 2003	Kidorf et al 2005	Masson et al 2007	Strathdee et al 2006
The study addressed an appropriate and clearly focused question	✓✓	✓✓✓	✓✓✓	✓✓
The assignment of subjects to intervention groups is randomised	✓✓✓	✓	✓✓✓	NR
An adequate concealment method is used	✓	NR	✓✓	NR
Subjects and investigators are kept 'blind' about intervention allocation	NA	NR	NR	NA
The intervention and control groups are similar at the start of the trial	✓✓	✓✓✓	✓✓✓	✓✓
The only difference between groups if the intervention under investigation	✓	✓✓✓	✓✓	✓✓
All relevant outcomes are measured in a standard, valid and reliable way	✓✓✓	✓✓	✓✓✓	✓
What percentage of the participants or clusters recruited into each intervention arm of the study dropped out before the study was completed?	NSP: 8.2% Pharm: 10.2%	NR	24-13% at 6 mths and 29-18% by 12 mths	None (FU was 7 days)
All subjects are analysed in the groups to which they were randomly allocated? (ITT)	NR	✓✓	NR	✓✓
Where the study is carried out at more than one site, results are comparable for all sites	NA	NA	NR	NA
Overall assessment of the study	+	-	++	-

✓ poorly addressed; ✓✓ adequately addressed; ✓✓✓ well covered

Table 20. Quality assessment for cohort studies

	Pollack et al 2002	Tyndall et al 2002	Van Den Berg et al 2007
Are the objectives or hypotheses of the study stated?	✓	✓	✓
Is the target population defined?	✓	✓	✓
Is the sampling frame defined?	×	×	×
Is the study population defined?	✓	✓	×
Are the study setting (venues) and/or geographic location stated?	✓	✓	✓
Are the dates between which the study was conducted stated or implicit?	✓	✓	✓
Are eligibility criteria stated?	×	✓	×
Are issues of 'selection in' to the study mentioned?	×	×	NR
Is the number of participants justified?	×	×	NR
Are the numbers meeting and not meeting the eligibility criteria stated?	×	×	×
For those not eligible, are the reasons why stated?	×	×	×
Are the numbers of people who did/did not consent to participate stated?	×	×	×
Are the reasons that people refused to consent stated?	×	×	×
Were consenters compared with non-consenters?	×	×	×
Was the number of participants at the beginning of the study stated?	✓	✓	✓
Were the methods of data collection stated?	✓	✓	✓
Was the reliability (repeatability) of measurement methods mentioned?	×	×	✓
Was the validity (against a gold standard) of measurement methods mentioned?	×	×	×
Were any confounders mentioned?	✓	✓	✓
Was the number of participants at each wave/stage specified?	NR	×	×
Were the reasons for loss to follow-up quantified?	×	×	×
Was the 'missingness' of data items at each wave mentioned?	×	×	×
Was the type of analyses conducted stated?	✓	✓	✓
Were 'longitudinal' analysis methods stated?	✓	×	✓
Were absolute effect sizes reported?	✓	✓	✓
Were relative effect sizes reported?	✓	✓	✓
Was loss to follow-up taken into account in the analysis?	NR	×	NR
Were confounders accounted for in analyses?	✓	✓	✓
Were missing data accounted for in the analyses?	NR	×	NR
Was the impact of biases assessed qualitatively?	✓	×	✓
Was the impact of biases estimated qualitatively?	×	×	×
Did the authors relate results back to the target population?	✓	✓	✓
Was there any other discussion of generalisability?	✓	✓	×
Overall assessment of study	+	+	+

✓ Yes; × No; NR Not reported

Table 21. Quality assessment for other study designs

	A) Selection bias	B) Study design	C) Confounders	D) Blinding	E) Data collection methods	F) Withdrawals and dropouts	Overall assessment of study

Bluthenthal et al 2004	Cross-sectional	+	-	++	-	-	-	-
Bluthenthal et al 2007	Cross-sectional	-	-	++	-	-	-	-
Huo et al 2005	Cross-sectional	+	-	+	-	-	-	-
Khoshnood et al 2000	Cross-sectional	-	-	-	-	-	-	-
Kral et al 2004	Cross-sectional	+	-	++	-	++	-	+
Miller et al 2002	Cross-sectional	-	-	-	-	-	-	-
Millson et al 2007	Uncontrolled BA	+	-	-	-	-	++	-
Nelles et al 1997	Uncontrolled BA	++	-	-	-	-	-	-
Obadia et al 1999	Cross-sectional	+	-	+	-	-	-	-
Rhodes et al 2004	Cross-sectional	-	-	-	-	-	-	-
Riley et al 2000	Cross-sectional	-	-	++	-	-	-	-
Rockwell et al 1999	Cross-sectional	-	-	-	-	-	-	-
Schilling et al 2004	Cross-sectional	+	-	+	-	-	-	-
Sears et al 2001	Cross-sectional	+	-	+	-	-	-	-
Singer et al 1997	Cross-sectional	-	-	-	-	-	-	-
Stark et al 2006	Uncontrolled BA	+	-	+	-	-	-	-
Valente et al 2001	Cross-sectional	-	-	+	-	-	-	-

++ strong; + moderate; - weak; BA before and after study

Appendix 5. Review of cost-effectiveness: data extraction tables

HIV infections averted

Author (Year)	Type of analysis	Country	Overview	Summary of effectiveness data	Summary of resource utilisation and cost data	Summary of cost-effectiveness data
Cabases & Sanchez 2003	CEA +	Spain	Estimated the costs and effectiveness of distributing "anti-AIDS kits" via NSPs or pharmacy sales. The kits contained one syringe and needle, one condom, a paper towel and an ampoule of distilled water.	Effectiveness was expressed as a function of the level of coverage of the programme. Coverage was defined as the extent of substituting nonsterile syringes with sterile syringes provided to the IDU population as part of the programme. Data were drawn from a survey of IDUs in Navarra, Spain, government data and Holtgrave et al. (1998). The estimated total number of HIV infections averted between 1993 and 2000 was 34.	Production, management, distribution and disposal costs of the anti-AIDS kits and the programme running costs were estimated from accounts. Unit costs of production were valued at the health authority purchasing price and commercial costs were valued at the price of the kit for the user (€0.3 per unit). Other costs considered included programme management costs, coordination costs (valued in Year 2000 prices and deflated at the consumer price index for each year), NGO costs, and syringe disposal costs. Total programme costs ranged from €27,490 in 1993 through to €54,477 in 2000.	The authors describe a CEA with calculations of incremental costs of syringe distribution per HIV averted per year. Annual ICERs ranged from €8,331 (1994) to €44,287 (2000). The annual cost per HIV infection averted was lower than the cost of treating one infected person (estimated at €99,371) and the results showed the programme to be cost saving for each of the 8 years of the study period.
Cohen et al 2004	CEA +	US	Study examined 26 HIV prevention interventions across four broad categories (individual, community and social network, biomedical and structural). Structural interventions examined included needle exchange	For each intervention, the authors selected one study that demonstrated its effectiveness in changing HIV incidence, STD incidence or risk behaviour (unprotected sex or needle sharing). Estimates of effectiveness were drawn from two previously published studies that examined the numbers of needles exchanged over a 3 month period.	The final parameter used was the programme cost per person. For some interventions, the authors used published cost analyses or cost-benefit analyses. For other interventions, the authors estimated the cost of person-hours, supplies, and overheads needed to implement the intervention based on salary and subcontract figures supplied by HIV prevention staff at the Louisiana Office of Public Health and/or the LA County Department of Health.	US$13,000 per HIV infection averted (adjusted to 12 months) Only cost-effective when HIV prevalence was high among IDUs (~2%)

Author (Year)	Type of analysis	Country	Overview	Summary of effectiveness data	Summary of resource utilisation and cost data	Summary of cost-effectiveness data
Cohen et al 2006	CEA -	US	The study examined whether structural HIV prevention interventions (e.g. needle exchange, condom availability) are cost-effective in reducing HIV among women in the Southern US states.	The number that would be reached by the interventions (n=1,000) and intervention effectiveness (increase in proportion of needle exchanged from 34% to 63%) were drawn from previous evaluations.	Costs were taken from the literature or estimated. The cost of NSP was estimated at $10 per person for a 3-month period (Heimer et al 1998; Lurie et al 1998). The authors arbitrarily chose a one time cost of $100,000 for needle deregulation to cover the lobbying and education of pharmacists.	$9,000 per HIV injection averted (over 3 months)
Gold et al 1997	CEA -	Canada	Examined whether a mobile needle exchange programme was cost-effective. The programme operated across three sites; one mobile and two fixed. In addition to needle exchange, the programme provides related harm reduction services including substance abuse counselling and referral, HIV testing, HBV vaccination, safer-sex counselling and the provision of condoms and dental dams.	The authors undertook a literature review (no methods reported). Baseline HIV prevalence rates were drawn from several Canadian studies (estimated at 3%), HIV incidence without NSPs were drawn from two American studies (estimated at 4%) and the estimate of HIV incidence with NSPs was drawn from Kaplan and Heimer (1994) (the authors assumed an HIV incidence rate of 2%). For 275 programme users, it was estimated that 24 cases of HIV infection would be prevented over a 5-year period.	NSP costs were drawn from budgetary data. Estimates of health costs relating to HIV infection were based on data from a previously published study. Costs were discounted (5%) and the authors included both direct and indirect costs. Indirect costs were productivity losses associated with time spent by the volunteers. Over the 5 years, the discounted costs of the programme was CAN$349,012.	At 5% discount rate and assuming 275 IDUs participated in the programme, total cost savings associated with the programme were CAN$1,292,44. If HIV incidence in the absence of an NSP was higher (10.7%) this resulted in savings of CAN$5,943,236 and increasing the number of IDUs using the service (n=550) resulted in cost savings of CAN$2,865,605. Varying the discount rate from 1% to 10% resulted in cost savings across the range (CAN$1.8 million to CAN $800,000, respectively).
Harris 2006	CEA +	US	The study sought to determine the optimal allocation of resources within a multi-site needle exchange programme. Prevention Point Philadelphia operated across six sites and provided sterile needles and syringes and clean injection equipment supplies. It also provided HIV testing and counselling, referrals for drug treatment, medical care for HIV and social and legal services.	Data were drawn from 12 studies of NSPs. Model parameters were largely drawn from the evaluation of the New Haven NSP.	Data on total costs and costs directly related to the numbers of syringes distributed were obtained via personal communication with the executive director of the NSP, and based on unpublished budgetary data.	At the optimal allocation, the estimated cost per HIV infection averted was US$2,800 (range US$2,258 to US$4,229).

Author (Year)	Type of analysis	Country	Overview	Summary of effectiveness data	Summary of resource utilisation and cost data	Summary of cost-effectiveness data
Holtgrave et al 1998	CEA -	US	The authors estimated the costs and cost-effectiveness of a policy of increased availability of sterile syringes via NSPs and pharmacy sales. Coverage was defined as the percentage of unsterile injections by IDUs for which sterile syringes were made available by the programme.	Based on data obtained from NSPs in San Francisco and Baltimore, the authors estimated that 15% of IDU injections were made with sterile syringes.	Gross unit costs per syringe distributed and disposed were calculated based on data from a previous study. The authors assumed that 25% of syringes were provided via NSPs and that 75% were provided via pharmacy sales. Costs of syringe distribution and disposal were combined. Costs were converted into 1996 prices.	Marginal cost per HIV infection averted at 100% coverage was US$342,783. The programme was marginally cost saving up to 88.4% coverage.
Jacobs et al 1998	CEA -	Canada	The authors conducted a CEA of the Edmonton Streetworks NSP. The programme was based at two fixed site locations and included an outreach van.	The amount of needle sharing and HIV seroprevalence within the IDU population, with and without an NSP was determined from a survey of 100 IDUs who used the NSP. In the first year of the programme the authors estimated that 20.33 new HIV infections would have been averted.	Data on costs were obtained from the financial records for the NSP. Costs of unpaid volunteers and donated facilities were included. Total programme costs were estimated at CAN$161,087.	Cost per HIV infection averted was CAN$9,537. When the prevalence rate was adjusted to 13.9%, cost per HIV infection averted was CAN$4,829.
Kumaranayake et al 2004	CEA +	Belarus	The authors undertook a CEA of a harm reduction and HIV prevention project in Belarus. The project included an NSP through which syringes, condoms and information, education and communication materials were distributed.	The impact of the programme on injecting and sexual behaviours was determined through behavioural surveys. The first survey was conducted prior to the intervention and the second survey was conducted at the two NSPs.	Cost data were collected retrospectively and included capital (e.g. start-up costs, building and equipment) and recurrent costs (e.g. personnel, mass media). A discount rate of 3% was used to obtain the annualised cost for capital items. Total programme costs with and without a gap in funding were estimated at $63,210 and $71,436, respectively.	Cost per HIV infection averted was US$323 (95% CI $188 to $680) (modelled without the shortfall in funding).

Author (Year)	Type of analysis	Country	Overview	Summary of effectiveness data	Summary of resource utilisation and cost data	Summary of cost-effectiveness data
Laufer 2001	CEA +	US	The author analysed the cost-effectiveness of state-approved NSPs in New York.	The reduction in risk from NSP participation was drawn from a previously published study (Des Jarlais et al 1996). NSP participation rates were provided by the New York state Department of Health, AIDS institute.	Costs reported were for personal services (including fringe benefits) for the syringe exchange activities as well as for other activities required (e.g. condom and bleach distribution) and ancillary activities (e.g. counselling). Expenses relating to supplies, materials, travel, subcontracts and other nonpersonal services were also collected. Costs incurred by participants were not included in the analyses. Estimates of costs relating to treatment for HIV were drawn from a previously published study.	Cost-effectiveness was analysed using a simplified circulation model, which used the number of needles exchanged per client year and the number of shared injections per IDU per year to estimate the decrease in HIV incidence through NSP participation. The cost-effectiveness ratio for the base case scenario was US$20,947 per HIV infection averted across all reported programmes. On a programme specific basis, costs per HIV infection averted ranged from US$11,648 to US$129,008.
Lurie & Drucker 1997	CEA -	US	The authors attempted to estimate the number of HIV infections that could have been prevented and the costs to the US health care system, had NSPs been implemented during the early stages of the HIV epidemic in the USA.	Data to calculate the percentage decline in HIV incidence than might have occurred in the presence of NSPs were drawn from two studies. One study based on the needle circulation theory model estimated that NSP participants had a 33% lower HIV incidence than non-participants. In the second study, three different models were constructed which yielded broad estimates of effectiveness. The authors used 15% as a lower limit and 33% as an upper limit (assumed constant over time).		Costs savings of US$287 million to US$630 million were estimated to have been forgone.

Author (Year)	Type of analysis	Country	Overview	Summary of effectiveness data	Summary of resource utilisation and cost data	Summary of cost-effectiveness data
Vickerman et al 2006	CEA +	Ukraine	The authors estimated the cost-effectiveness of a harm reduction intervention for IDUs in Odessa, Ukraine. The intervention consisted of harm reduction and peer education across two stationary sites and one mobile site. Main activities were promotion of safe drug use practices and sexual behaviour through provision of condoms, syringes and information materials.	HIV prevalence in IDUs was estimated from the prevalence of HIV in syringes collected by the mobile outreach points. HIV incidence was estimated to be 20 infections per 100 susceptible IDU person-years in March 2000. Data were drawn from three cross-sectional behavioural surveys among IDUs in Odessa (Oct 99, Mar 00 and June 01). Intervention coverage (20% to 38%) was estimated by dividing high and low estimates for the number of IDU that were "effectively reached" by the intervention by high and low estimates for the size of Odessa IDU population. Over 1 year, 792 HIV infections were averted (95% CI 422-1019), compared with no intervention.	Cost data were collected retrospectively for Sept 99 to Aug 00. Direct costs were estimated from the provider perspective and did not include costs borne by IDUs attending the intervention. Costs were obtained from interviews with the project coordinator and from observations of the resources used. Full details of the cost analysis are reported in the paper. The authors were not able to estimate costs for mass media or the time spent by volunteer peer educators.	Over 1 year, costs per HIV infection averted were US$97 (ranging from US$71 to US$272). The model developed projected that HIV prevalence would increase by 1.1%. Coverage: Assuming the same pattern of behaviour change, increasing coverage to 60%, the intervention would have decreased HIV incidence by 42% (16 infections per 100 person-years) and prevalence by 0.7% after 1 year. Reducing behaviour change by 15% resulted in a decrease in incidence of 39% and prevalence by 3% after 5 years.

HIV and HCV

Author (Year)	Type of analysis	Country	Overview	Summary of effectiveness data	Summary of resource utilisation and cost data	Summary of cost-effectiveness data

Health Outcomes International PTY Ltd et al 2002	CBA +	Australia	An economic model was developed that compared the costs of operating NSPs during the 1990s to the anticipated savings that will accrue from the number of cases of HIV and HCV avoided as a result of NSPs.	Estimates of the number of HIV and HCV infections avoided through the introduction of NSPs were calculated according to stage of disease. NSPs were assumed to have reduced HIV and HCV prevalence among IDUs from 1988 onwards. The authors estimated that by the year 2000, approximately 25,000 HIV infections and 21,000 HCV infections had been prevented since the introduction of NSPs in 1988.	Only direct costs were included. Direct costs included the costs of operating NSPs themselves, the infrastructure associated with their development and operation, and the costs of safe disposal of used syringes and needles. Data on the expenditure on operating NSPs in Australia during the 1990s was sought from all State and Territory health authorities. Health care cost estimates for HIV and HCV were drawn from previously published studies.	The authors calculated return on investment by discounting future cashflows associated with the investment in the NSP program and treatment costs avoided by an agreed discount rate (5%, 3% and 0%). HIV: Discounting savings at 5% resulted in a Net Present Value (NPV) of Government investment of $2,277 million ($3,415 million at 3% discount rate). Considering total expenditure, the equivalent returns were $6,876 million (undiscounted), $2,262 million (discount rate of 5%) and $3,398 million (discount rate of 3%). Considering the return achieved to the end of the investment period, (2000), government had achieved net savings of $373 million (after deducting the value of their investment), the NPV of which at a discount rate of 5% is $242 million ($287 million at a discount rate of 3%). The equivalent returns on the total investment in NSPs over the same period were $353 million (undiscounted), $227 million (discount rate of 5%) and $270 million (discount rate of 3%). HIV and HCV: The net savings to government from its investment in NSPs over the lifetime of cases of HIV and HCV avoided (after deducting the value of the initial government investment) before discounting are $7,678 million. Discounting these savings at 5% results in a NPV of their investment of $2,402 million ($3,653 million at 3% discount rate). When considering total expenditure, the equivalent returns are $7,658 million (undiscounted), $2,386 million (discount rate of 5%) and $3,637 million (discount rate of 3%). In sensitivity analysis the outcomes presented were most sensitive to the impact of NSPs on HIV incidence. Halving the rate of effect of NSPs on HIV incidence had a proportionally greater effect on the number of cases avoided over time. However, even at the most conservative estimate of effect (1/4 of the original effect estimate) the ROI was positive.

HCV infections averted

Author (Year)	Type of analysis	Country	Overview	Summary of effectiveness data	Summary of resource utilisation and cost data	Summary of cost-effectiveness data
Pollack 2001	CEA +	US	The author explored the potential of NSPs to reduce HCV incidence and prevalence among IDUs. A susceptible-infected, random-mixing model of disease spread was developed to explore the effectiveness and cost-effectiveness of NSPs. Within the model NSPs reduced the infectivity (or frequency) associated with unsafe needle sharing, thereby reducing HCV incidence and prevalence.	Effectiveness data were drawn from a previously published study based on the circulation theory model (Kaplan & Heimer 1994). It was assumed that the NSP created a 1/3 proportional reduction short-term disease incidence.	The authors used a programme cost of $5 per client per day, but the source of these estimates was not clear.	At levels of the reproductive rate of infection equivalent to the range for HCV, NSPs only had a small impact on steady state prevalence. Costs per HCV infection averted were high and exceeded US$1 million within the range of observed HCV prevalence in high-risk populations. In sensitivity analyses, the reproductive rate of infection emerged as a critical variable in the analysis. For example, a reduction in the frequency of high-risk needle sharing that lowered the reproductive rate of infection would have a small impact on steady state prevalence but would reduce the costs per averted infection of an NSP from $400,000 to $320,000.

Appendix 6. Review of cost-effectiveness: quality assessment table

	Study identification include author, title, reference, year of publication	**Cabases & Sanchez 2003**	**Cohen et al 2004**	**Cohen et al 2006**	**Gold et al 1997**	**Harris 2006**	**Health Outcomes International PTY Ltd 2002**	**Holtgrave et al 1998**	**Jacobs et al 1998**	**Kumaranayake et al**	**Laufer 2001**	**Lurie & Drucker 1997**	**Pollack 2001**	**Vickerman et al 2006**
Evaluation criterion														
1	Was a well-defined question posed in answerable form?	Yes	Yes	Yes	Partially	Yes	Yes	Yes	Partially	Yes	Yes.	Yes	Partially	Yes
2	Was a comprehensive description of the competing alternatives given (that is, can you tell who? did what? to whom? where? and how often?)?	Partially	Partially.	Partially	Partially	No	No	Yes	No	Yes	No.	No	No.	Yes
3	Was the effectiveness of the programmes or services established?	Not clear	Yes	Not clear	No	Yes	Partially	No	No	No	Partially.	Yes	Not clear	No
4	Were all the important and relevant costs and consequences for each alternative identified?	Yes	Partially	Not clear	Not clear	Not clear	Yes	Not clear	Partially	Yes	Partially	Not clear	No.	Yes
5	Were costs and consequences measured accurately in appropriate physical units (for example, hours of nursing time, number of physician visits, lost work-days, gained life-years)?	NR	NR	Not clear	NR	Not clear	NR	Not clear	NR	NR	NR	Not clear	Not clear	Yes
6	Were costs and consequences valued credibly?	Yes	NR	Not clear	Partially	Not clear	NR	Not clear	Yes	Yes	Partially.	Not clear	NR	Yes

7	Were costs and consequences adjusted for differential timing?	Yes	No	Not clear	Yes	No	Yes	No	No	Yes	No	Yes	Not clear	Yes
8	Was an incremental analysis of costs and consequences of alternatives performed?	Yes	No	No	No	No	No	No	No	Yes	No	No	No	Yes
9	Was allowance made for uncertainty in the estimates of costs and consequences?	Yes	Yes	No	Partially	Yes	Yes	No	Partially	Yes	Yes.	Not clear	Partially	Yes
10	Did the presentation and discussion of study results include all issues of concern to users?	No	Yes	No	No	Partially	No	No	No	Yes	Partially.	No	Yes.	Yes
	OVERALL ASSESSMENT OF THE STUDY	+	+	-	-	+	+	-	-	+	+	-	+	+

Appendix 7. References to excluded studies

Review of effectiveness

Stage 1 (n=313)

- Did not meet study criteria or did not evaluate effectiveness (n=155)

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