Effectiveness of sterile needle and syringe programmes
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Abstract
This is the first comprehensive international review of the evidence for needle syringe programmes. The major, and now overwhelmingly strong, finding is that needle syringe programmes reduce HIV transmission effectively, safely and cost effectively. The size of the benefit is substantial. There is compelling evidence that needle syringe programmes reduce HIV incidence and HIV prevalence by reducing HIV risk behaviour. The Bradford Hill criteria, generally regarded as the most robust method of assessing public health interventions, were used for the evaluation framework: Conservatively, six of the nine Bradford Hill criteria were fulfilled (strength of association, replication of findings, temporal sequence, biological plausibility, coherence of evidence, and reasoning by analogy). Three of the Bradford Hill criteria were not fulfilled (specificity of association, biological gradient and experimental evidence). Five additional criteria were clearly fulfilled (cost-effectiveness, absence of negative consequences, feasibility of implementation, expansion and coverage, unanticipated benefits, and application to special populations). The findings in this review are consistent with seven published national reviews conducted by, or on behalf of, United States government agencies, which had previously found that needle syringe programmes were effective in reducing HIV infection among injecting drug users and did not increase illicit or injecting drug use. Countries affected or threatened by HIV infection among injecting drug users should carefully consider the convincing evidence now available for the effectiveness and safety of needle syringe programs with a view to establishing or expanding needle syringe programs to scale. Although some research questions still remain unanswered, and areas exist where improved research methodology is needed, the failure to implement needle syringe programmes in time and on a sufficient scale cannot be justified by a lack of available evidence.

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Introduction
HIV/AIDS is probably the most serious global public health threat since the plague. Injecting drug use is the major or second major risk factor for HIV in seven of the ten UNAIDS regions, accounting for 90% of the world’s population.
The establishment of needle and syringe programmes (NSPs) can be traced to an epidemic of hepatitis B and hepatitis C (and HIV as discovered later) among injecting drug users (IDUs) in Edinburgh, Scotland between 1982 and 1984. A local pharmacist began providing sterile injecting equipment but was soon stopped by authorities (Burns, Brettele, Gore, Peutherer, & Robertson, 1996). It was not until 1983 in Amsterdam, the Netherlands, that the first official NSP was established also in response to a hepatitis B outbreak. HIV/AIDS soon became the rationale for this NSP and similar programmes were rapidly established in many parts of the world. NSPs, which are services dedicated to providing needles and syringes, including exchange of used for sterile needles and syringes, now operate officially in over 65 countries (Aceijas, 2004). Evaluation of the effectiveness and safety of these programmes began soon after their establishment and there exists a vast literature supporting their effectiveness.

Providing access to and encouraging utilisation of sterile needles and syringes for IDUs is now considered a fundamental component of any comprehensive and effective HIV prevention programme (WHO, 2003). A wide variety of measures have been developed to improve access to and utilisation of sterile injecting equipment such as NSPs,
strategies for disinfecting needles and syringes in settings where they are reused or shared, pharmacy based distribution, sale or exchange schemes, vending machines and other distribution programmes, policies and programmes to encourage more appropriate disposal of used needles and syringes and liberal injecting paraphernalia legislation.

Much effort has been expended on improving knowledge, changing attitudes and reducing risk behaviour, but unless the means for behaviour change also become more readily available, improved knowledge and attitudes do not result in reduced risk. Likewise, unless efforts to increase access to sterile injecting equipment are buttressed by other efforts to support behaviour change, risk reduction will remain unaffected. Interventions to improve access to sterile injecting equipment have been implemented in many countries throughout the developed world and to a lesser extent in transitional and developing countries. In the absence of an effective vaccine against HIV, measures to improve access to sterile needles and syringes will remain the most effective tool available to reduce HIV transmission among and from IDUs.

This review examines whether NSPs have been demonstrated scientifically to reduce the spread of HIV among IDUs.

Methodology

This review should be considered in the light of several limitations. The only literature reviewed was in English. Most of this literature originated from developed countries, which although peer reviewed, may still be subject to one or more forms of publication bias. The overwhelming majority of studies were quantitative and there were limited qualitative data to illuminate them. The literature regarding the effectiveness of NSPs is so vast that there is little need to review the grey literature.

Research findings not supported by randomised controlled trials are often questioned by clinical medicine and public health specialists. However, conducting a strictly randomised controlled trial to evaluate a NSP is impossible due to insurmountable ethical and logistical impediments. In the absence of randomisation other methodological problems arise including the accurate measurement of needle sharing and injecting frequency. In addition, evaluation studies are generally conducted at different stages of HIV epidemics with wide variations in seroprevalence and seroincidence.

In addressing such methodological concerns, a USA National Academy of Sciences’ Institute of Medicine report concluded that to reject NSPs, based on limitations of the design of single studies, ignores both the preponderance and pattern of the evidence and ‘is both poor scientific judgment and bad public health policy’ (Normand, Vlahov, & Moses, 1995), citing in support Bradford Hill who has argued that if certain criteria are met in a number of evaluations of observational studies, then there is an increased probability that a statistical association is causal.

The Bradford Hill criteria to infer causality have increasingly been used to assess evidence from studies evaluating interventions. These original criteria and five additional criteria have been applied to this evaluation of NSPs. The null hypothesis used for this study is that measures to increase the availability and utilisation of sterile injecting equipment do not reduce HIV risk behaviour, HIV seroprevalence or the HIV seroincidence among IDUs. The criteria discussed below have been categorised as either Bradford Hill Causal Criteria or Additional Feasibility and Implementation Criteria.

Bradford Hill Causal Criteria

Strength of association

The strength of a supposed association between an exposure factor and an outcome is gauged by the relative risk or odds ratio with associated confidence intervals used to measure the protective effect of an intervention.

Replication of findings

Also referred to as “consistency”, this criterion examines whether different studies conducted in different locations by different investigators have reported similar findings.

Specificity of association

Specificity is said to be present when the alleged exposure factor (or intervention) is exclusive to the outcome and when the outcome has no other known cause or associated risk factors.

Temporal sequence

For a cause-and-effect relationship to be supported, the introduction of an intervention must be followed by a reduction in the outcome factor.

Biological plausibility

This criterion refers to the presence or absence of a likely biological mechanism linking the risk exposure or intervention to the observed findings.

Biological gradient

Evidence that increasing exposure to an intervention or risk factor results in a commensurate positive or negative change in an outcome.
Experimental evidence

This criterion often provides the strongest support for causation and measures the effect of an action.

Reasoning by analogy

Causality is supported by analogy if there are similar associations or causal relationships in other clinical or epidemiological areas of relevance.

Coherence

When the evidence from different disciplines and different sources "hangs well together", this criterion is considered to be fulfilled.

Additional feasibility and implementation criteria

Cost-effectiveness

Although estimated in a number of different ways, authorities pay increasing attention to the magnitude of benefit achieved from the allocation of public resources.

Absence of negative consequences

Consideration of possible inadvertent adverse consequences has a major impact on adoption or expansion of interventions.

Feasibility of implementation, expansion and coverage

Is it feasible to implement in diverse settings, including resource-poor settings, and to expand these interventions to a scale commensurate with public health need?

Unanticipated benefits

Does the intervention lead to other unintended and welcome benefits?

Special populations

How successful are interventions in reaching special populations that are particularly at risk or of considerable public health significance?

Results: the effectiveness of needle syringe programmes

Strength of association

Forty-five studies from 1989 to 2002 with NSP implementation as an intervention and HIV seroconversion, HIV seroprevalence or HIV risk behaviours among IDUs as outcome variables were examined. Some studies assessed multiple outcomes. Six out of ten studies, which evaluated HIV seroconversion or seropositivity as outcomes, found that NSP use was protective (Des Jarlais et al., 1996; Health Outcomes International, 2002; Heimer, Kaplan, Khoshnood, Jariwala, & Cadman, 1993; Hurley, Jolley, & Kaldor, 1997; Ljungberg et al., 1991; Monterosso et al., 2000); outcomes in two studies were negatively associated with NSP use (Bruneau, Lamothe, & Franco, 1997; Strathdee et al., 1997) and two studies showed no effect (Patrick, Strathdee, & Archibald, 1997; Schechter, Strathdee, & Cornlisse, 1999).

HIV risk behaviour outcomes were examined in 33 studies with the majority focused on syringe sharing, borrowing, lending or reuse: 23 were positive (Bluthenthal, Kral, Erringer, & Edlin, 1998; Bluthenthal, Kral, Gee, Erringer, & Edlin, 2000; Cox, Lawless, Cassin, & Geoghegan, 2000; Donoghoe, Stimson, & Dolan, 1989; Des Jarlais et al., 1994; Frischer, Elliot, & Taylor, 1993; Gibson & Flynn, 2001; Gleghorn, Wright-De Aguero, & Flynn, 1998; Guydish, Bucardo, Clark, & Bernheim, 1998; Guydish, Clark, Garcia, & Bucardo, 1995; Hartgers, Buning, van Santen, Verster, & Coutinho, 1989; Heimer, Khoshnood, Bigg, Guydish, & Junge, 1998; Kaplan, 1991; Kaplan & Heimer, 1995; Kaplan, Khoshnood, & Heimer, 1994; Keene, Stimson, Jones, & Parry-Langdon, 1993; Monterosso et al., 2000; Oliver, Maynard, & Friedman, 1994; Paone et al., 1994; Peak, Rana, Maharanj, Jolley, & Crofts, 1995; Power & Natalya, 2002; Schoenbaum, Hartel, & Gourevitch, 1996; Singer, Himmelgreen, Weeks, Radda, & Martinez, 1997; Vlahov, Junge, & Brookmeyer, 1997; Watters, Estilo, Clark, & Lorvick, 1994), one negative (Klee, Faugier, Hayes, & Morris, 1991) and five were indeterminate (Donoghoe, Dolan, & Stimson, 1992; Hartgers, Van Ameijden, van den Hoek, & Coutinho, 1992; Klee & Morris, 1995; Van Ameijden, van den Hoek, van Haastrecht, & Coutinho, 1992; Van Ameijden et al., 1994; Van Ameijden & Coutinho, 1998; Van Haastrecht et al., 1996); while six studies examined diverse outcomes including 'injecting frequency' – one positive (Watters et al., 1994), 'proportion of syringes exchanged' – one indeterminate (Van Ameijden & Coutinho, 1998), 'syringe return rate or exchange rate' – three positive (Kaplan, 1991; Kaplan et al., 1994; Kaplan & Heimer, 1995) and 'mortality among NSP users versus non-users' – one indeterminate (Van Haastrecht et al., 1996).

Overall, these studies provide strong evidence to reject the null hypothesis that attendance at NSP does not confer protection against HIV. However, it is not possible to exclude the possibility that selection bias may account for the findings in studies comparing IDUs who attend NSPs with those who do not.

Several authors have offered explanations for findings in some studies that HIV was more prevalent in attenders compared with non-attenders (Bastos & Strathdee, 2000; Coutinho, 2000; Lurie & Drucker, 1997; Schechter et al.,...
1999; Strathdee & Vlahov, 2001). It is well known that NSPs in many settings attract high risk IDUs, who may therefore have a higher risk of HIV seroconversion before ever attending the programme. This self-selection factor may explain why cities such as Montreal and Vancouver, Canada, have observed higher HIV seroconversion rates among NSP attenders compared to non-attenders (Lowndes & Alary, 1998; Schechter et al., 1999).

Bastos and Strathdee (2000) notes that evaluations of NSPs typically employ dichotomous categorisations (such as NSP attenders versus non-attenders, frequent versus infrequent attenders). This simplistic approach overlooks the fact that non-attenders may have only used sterile injecting equipment. For example, in an analysis of NSP attenders in Amsterdam, the Netherlands, a city where sterile syringes are readily available through pharmacies, irregular NSP attenders, but not non- or frequent attenders, were at highest risk of HIV seroconversion (Van Ameijden & Coutinho, 1998). The authors concluded that irregular NSP attenders had the least exposure to sterile injecting equipment and consistent prevention messages, which placed them at highest risk of infection.

Studies examining NSP effectiveness have generally relied on self-reported outcome measures. At least one study compared self-reported risk behaviour with actual programme data and concluded that self-reported risk behaviour data underestimated the protective association of NSP attendance by 18% (Safaeian et al., 2002).

Strong as the evidence is for NSP effectiveness, these data are confounded by the presence or absence of alternative availability of sterile injecting equipment through pharmacies. A systematic review (Gibson, Flynn, & Perales, 2001) identified 42 studies evaluating NSP effectiveness. The potential confounding of pharmacy access to syringes was examined. Twenty-eight studies concluded that NSP use had positive effects (reduced risk behaviour or seroconversion), 12 showed no effectiveness and two found negative effects. Thirteen of the 14 studies with no effect or negative effects compared clients with non-clients of NSPs. When these 13 studies were examined carefully and an additional 12 studies that compared users with non-users of NSPs were considered, all 13 studies with negative or null findings were found to have been conducted in settings where IDUs had legal access to syringes from pharmacies as well as NSPs. By way of contrast, in settings with NSPs but without additional legal access to sterile injecting equipment, there were no negative or null findings. Five studies found positive effects (reduced risk behaviour and/or seroconversion) despite legal access through NSPs and pharmacies. Nevertheless, the relationship between pharmacy access (yes/no) and positive versus negative findings was significant at the $P = 0.002$ level. Finally, when studies in settings where legal pharmacy access was available were excluded, 23 of the remaining 24 studies showed positive effects for NSP use.

There is sufficient evidence to consider that the criterion of strength of association has been fulfilled.

Replication of findings

The above findings strongly support the effectiveness of NSPs as interventions that reduce risk behaviour such as syringe sharing among IDUs and HIV infection. The number of studies showing protective effects far outweighs those with ambiguous or negative effects. The preponderance of positive findings is strengthened by their replication by different authors, at different stages of the HIV epidemic, at different times and geographical locations and with diverse study designs. Furthermore, in instances where NSP use has been statistically associated with increased HIV incidence or higher risk behaviours, convincing arguments for possible sources of confounding have been presented.

The efficacy of individual NSPs has been reported in at least 10 different countries, including several resource-poor countries. In addition, ecological studies have found strong associations between NSP and lower HIV incidence and prevalence in comparisons involving diverse countries. Most notably, the Return on Investment study (Health Outcomes International, 2002) compared HIV prevalence in 103 cities in 24 countries of which 16 countries had NSPs. HIV seroprevalence declined by a mean annual 18.6% for 36 cities with NSPs compared to an 8.1% increase in 67 cities without NSPs. Hurley et al. (1997) compared HIV seroprevalence among IDUs in 52 cities without NSPs and 29 cities with NSPs in Asia, Europe, North America, South America and the South Pacific. On average, seroprevalence increased by 5.9% per year in the 52 cities without NSPs and decreased by 5.8% per year in the 29 cities with NSPs.

In a recent systematic review, results favouring the efficacy of NSP use were recorded from six studies with longitudinal/prospective designs, four studies with multiple cross-sectional designs, eight observational studies, five ecological studies and several modelling studies (Gibson et al., 2001).

There is sufficient evidence to consider that the criterion of replication of findings has been fulfilled.

Specificity of association

Many studies have demonstrated other health and social benefits of NSPs apart from a reduction in HIV infection, though these benefits are less well documented and do not seem to be as powerful as the impact on HIV infection. Additional benefits include improved entry to primary health care and drug treatment, prevention of other blood-borne viral infections, reduced proximal bacterial infection (e.g. abscess and cellulitis) and reduced distal bacterial infection (e.g. subacute bacterial endocarditis, brain abscess), reduced frequency of injecting and improved quality of life.

NSPs offer a ‘package’ of different services including education about protection against other blood-borne viruses and sexually acquired HIV, education about cleaning injecting equipment and information about drug treatment. However,
reduce risk and adopt safer behaviors. 

Temporary sequence

While NSPs are not the only intervention credited with achieving reduced risk behavior, in the large majority of settings where NSPs exist, there was a subsequent reduction in risk behavior and, where measured, HIV seroconversion. As discussed above (see Strength of association), in settings where NSP implementation has been followed by increased risk behavior and/or seroconversion among actual NSP users, the availability of pharmacy access to clean syringes obtained from shooting galleries in Miami, United States, had detectable amounts of HIV-1 RNA with 94% of the sample containing antibodies to HIV-1 polypeptides.

Earlier studies found HIV-1 in 3% of blood-contaminated needle and syringes collected from exchange programmes in Sydney, Australia (Wodak et al., 1987), 10% of needle and syringes from shooting galleries in South Florida, United States (Chitwood et al., 1990), 50% of used needles and syringes obtained from shooting galleries in Miami, United States (McCoy et al., 1995; Shah et al., 1996) and in New Haven, Connecticut, United States, HIV-1 was detected in 67.5% of used “street” syringes and in 91.7% of needles from a shooting gallery (Heimer et al., 1993). Further evidence of a link between the use of shared injecting equipment and HIV seroconversion is provided by field studies of the biological mechanisms of HIV transmission among IDUs. Practices such as registering, “booting” and “backloading” have been shown to increase the risk of HIV-1 transmission by directly placing blood within the needle and syringe (Inciardi et al., 1994). Chitwood et al. (1995) used logistic regression analysis adjusted for age, gender and race to determine risk factors associated with HIV-1 seroconversion among IDUs and found that sharing needles and syringes in the year prior to conversion was the primary independent risk factor. Other studies have broadened the definition of sharing to include injecting paraphernalia such as cookers, cottons and rinse water, as well as to the practice of “frontloading.”

IDUs with a history of diabetes have a significantly lower HIV seroprevalence rate (9.8%) compared with non-diabetic IDUs (24.3%; P = 0.03). This result highlighted that increased access to sterile syringes and less use of contaminated equipment were important factors contributing to lower HIV infection rates (Nelson et al., 1991).

Biological plausibility

Although the minimum quantity of HIV necessary for infection is not known, viable HIV has been detected in syringes stored at room temperature for up to 4 weeks (Abdala, Stephens, Griffith, & Heimer, 1999). Field studies confirm that HIV can be detected in blood-contaminated syringes for some weeks. The presence of HIV-1 RNA in needles and syringes indicates the risk associated with sharing of needles and syringes, and also paraphernalia and wash waters. Shapshak et al. (2000) found 39% of rinses from 36 needles and syringes containing visible blood collected from shooting galleries in Miami, United States, contained HIV-1 RNA with 94% of the sample containing antibodies to HIV-1 polypeptides. 

In the absence of NSPs, interventions to reduce risk and seroconversion were implemented. 

Heimer et al. (1993) in their evaluation of the New Haven, United States, needle exchange, demonstrated that the prevalence of HIV in syringes decreased following an increase in the exchange rate. In a multiple cross-sectional study of 1304 untreated IDUs in Oakland, United States, needle and syringe sharing declined over time concurrent with an increase in NSP use and distribution of supplies (Bluthenthal et al., 1998). There are no published studies reporting an unexpected temporal sequence.

There is sufficient evidence to consider that the criterion of temporal sequence has been fulfilled.
consider that the criterion of biological plausibility has been fulfilled.

**Biological gradient**

Heimer et al. (1993) found in their syringe tracking study in New Haven, United States, that HIV prevalence in syringes decreased as the exchange rate increased. However, no studies were found measuring a possible relationship between an increase in NSPs and reduced HIV infections. There is insufficient evidence to consider that the criterion of biological gradient has been fulfilled.

**Coherence of the evidence**

The arguments for coherence of the evidence span several of the Bradford Hill criteria including biological plausibility, strength of association and replication. To minimise repetition, material which has already been presented will not be repeated in this section.

There is strong evidence that HIV can be transmitted when contaminated injecting equipment is shared and such sharing is the strongest risk factor predicting HIV seroconversion among IDUs. Evidence that a reversal to the status quo occurs after an intervention is withdrawn adds further to the coherence of the evidence. Studies of IDUs risk behaviour in settings without NSPs show that most engaged in needle sharing and other unsafe injecting practices. For example, Gleghorn, Jones, Doherty, Celentano, and Vlahov (1995) found that in a cross-sectional survey of IDUs in Baltimore, United States, almost 50% of respondents said their usual source for needles and syringes was street dealers while a further 4.1% reported friends/neighbours or shooting galleries. A number of studies investigating the main risk factors for HIV seroconversion found syringe borrowing to be an independent determinant (Van Ameijden, Langendam, Notenboom, & Coutinho, 1999) while some studies found backloading and frontloading to be independent predictors.

Modelling studies have demonstrated that obtaining clean needles from NSPs reduces the circulation time of each syringe, whether for reuse or for sharing. Evaluations of numerous NSPs in many countries have concluded that IDUs who attend NSPs reduce their HIV risk behaviours compared with those who do not attend, and that the evidence is particularly consistent in areas where non-attenders cannot obtain clean needles from any other sources. Even in areas where pharmacy and other sources exist, the large majority of studies show that NSP use is significantly associated with a decline in risk behaviour (Gibson et al., 2003). Evidence that a reversal to the status quo occurs after an intervention is withdrawn adds further to the coherence of arguments for causality (Broadhead et al., 1999). Some large ecological studies show a clear association with NSP implementation and declining HIV incidence and prevalence over time.

Evidence for the efficacy of NSPs in stemming the spread of HIV has been questioned because of an apparent lack of reduction in HCV transmission. HIV entered drug-injecting populations in New York, United States, during the mid-1970s and in Australia in the early 1980s while hepatitis C first spread among IDUs in the 1960s and therefore had a comparatively higher baseline prevalence when NSPs were established in the early 1980s (Crofts, Aitken, & Kaldor, 1999). Furthermore, hepatitis C is about an order of magnitude more infectious by blood–blood contact than HIV (Coutinho et al., 1997; Crofts et al., 1999). Despite reported disparities there is increasing evidence that NSPs have led to significant reductions in both hepatitis B and C (Hagan, Des Jarlais, Friedman, Purchase, & Alter, 1995). There is sufficient evidence to consider that the criterion of coherence of the evidence has been fulfilled.

**Experimental evidence**

An appropriate experiment could theoretically be provided by a randomised controlled trial whereby IDUs were randomly allocated to an experimental group who would be issued with an adequate supply of sterile syringes at an exchange and a control group who would not be provided with sterile syringes. The experiment would need to take place in a controlled setting isolated from access to pharmacy or vending machines.

Other factors would need to be measured and controlled such as rate of incarceration, availability and quality of drug treatment (especially methadone treatment for heroin dependence), utilisation of strategies to reduce sexual transmission (such as condoms and treatment of sexually transmitted infections) and overlap with special populations such as men who have sex with men and sex workers. As discussed, there are strong logistical and ethical arguments against conducting such experiments. There is insufficient evidence to consider that the criterion of experimental evidence has been fulfilled.

**Reasoning by analogy**

The provision of sterile injecting equipment to reduce HIV infection among IDUs is analogous to the provision of condoms to reduce the sexual transmission of HIV as both may be controversial in most countries, there are myths surrounding both, yet both have high biological plausibility.

Condom provision is well accepted to have strong support from empirical evidence of effectiveness (Weaver, Smith, & Kippax, 2005). It could be argued that both are implemented less vigorously than would be justified by the evidence of effectiveness, safety and cost-effectiveness. Concern has often been expressed that condom provision might increase the frequency of sexual activity, especially among unmarried partners and result in an earlier sexual initiation. There is no
convincing evidence to support these concerns (Weaver et al., 2005).

Drug use and sexual activity are sensitive issues in virtually all countries, especially when these occur among teenagers. Like NSPs the benefits of condom provision go beyond protection from HIV to reducing the incidence of sexually transmitted infections and unwanted pregnancies. Condom provision and NSPs are both cost-effective interventions.

There is sufficient evidence to consider that the criterion of reasoning by analogy has been fulfilled.

Cost-effectiveness

Many studies have demonstrated that NSPs are cost-effective and cost-saving. In a retrospective analysis, Lurie and Drucker (1997) estimated that the number of HIV infections that could have been prevented in the United States had NSPs been implemented in the early stages of the HIV/AIDS epidemic was between 4394 (with a 15% incidence reduction due to NSPs) and 9666 (with a 33% incidence reduction) with the cost of treatment calculated at between US $244 million and US $358 million, respectively.

Furthermore, Lurie, Gorsky, Jones, and Shompe (1998) estimated the cost per syringe distributed through five syringe distribution strategies (a NSP, a pharmacy-based NSP, free pharmacy distribution of pharmacy kits, sale of such pharmacy kits to IDUs and sale of syringes in pharmacies), finding that when NSPs were the most expensive and syringe sales the cheapest. At an annual sero-incidence exceeding 2.1%, all strategies were estimated to be cost-saving.

Others have used mathematical modelling to estimate the cost per HIV infection averted by NSPs. Holtgrave, Pinkerton, Jones, Lurie, and Vlahov (1998) estimated that 100% coverage of a previously unmet need for sterile syringes in the USA would require 954.8 million syringes at a cost of US $423 million. This would prevent 12,350 cases of HIV infection at a cost of US $277 million, with subsequent HIV treatment costing approximately US $442, still notably cost-effective. This study confirms the absence of negative consequences.

A variety of HIV prevention strategies was compared for cost-effectiveness in an East coast city of the United States. Cost per HIV infection prevented was equal lowest for needle exchange and counselling/education (about US $4000; Kahn, Washington, & Showstack, 1992). In New York City, United States, the cost per HIV infection averted for a year by a NSP was estimated to be US $2067. This is far below the estimated cost of lifetime treatment (prior to protease inhibitors) of US $56,000 to US $80,000 (Kahn & Sanstad, 1997). Another analysis of New York State-approved NSPs also concluded that syringe exchange is a cost-effective and cost-saving strategy with an estimated 87 HIV infections averted across seven programmes at a total cost of US $1.8 million, resulting in a cost-savings of almost US $20,947 per HIV infection averted (Laufer, 2001).

A cost effectiveness analysis applied a simplified Yale Needle Circulation Model to four hypothetical NSPs in four United States cities with differing HIV prevalence and incidence rates. Reductions in HIV incidence rates varied across cities from 17% to 70% across the four settings. Higher reductions were associated with more needles per client-year and greater efficiency was associated with lower cost per needle exchanged. The estimated cost savings per HIV infection averted ranged from US $12,000 to US $99,000 (Kahn, 1998).

Most cost effectiveness studies have been conducted in developed countries with far fewer conducted in resource poor settings. However, a cost-effectiveness study of NSPs in Svetlogorsk, Belarus, evaluated a comprehensive strategy that included NSPs, safe sex counselling, condom promotion, bleach distribution and referral to STD services. The average cost per HIV infection averted was estimated at about US $68 (estimated range: US $54–US $100; Kumarasayake et al., 2000). If the cost of the mass-media campaign was included, the cost per HIV infection averted rose between US $240 and US $442, still notably cost-effective. This study confirms the cost-effectiveness of NSPs as an HIV prevention measure in a resource poor setting.

There is sufficient evidence to consider that the criterion of cost effectiveness has been fulfilled.

Absence of negative consequences

Studies have searched for and found no convincing evidence of the following unintended complications associated with NSPs: greater injecting frequency (Hartgers et al., 1998; Watters et al., 1994); increased illicit drug use (Guydish, Bucardo, Young, Woods, & Grinsdale, 1993; Wolk, Wodak, Guinan, Macaskill, & Simpson, 1990); a rise in syringe lending to other IDUs (Hartgers et al., 1989; Schechter et al., 1999); recruitment of new IDUs (Heimer et al., 1993; Van Ameijden & Costinoutsos, 2001; Watters et al., 1994); social network formation (Junge, Valente, Laskin, Riley, & Vlahov, 2000); greater numbers of discarded used needles (Broadhead et al., 1999; Doherty et al., 2000; Oliver, Friedman, Maynard,
Feasibility of implementation, expansion and coverage

NSPs have been shown to be successful in a variety of settings but their expansion remains a challenge. In Germany, establishing NSPs in larger cities was easier than in smaller cities and more conservative states, while establishing NSPs in prisons was considered desirable but only possible as limited pilot projects (Weber et al., 1999).

An evaluation of a Hawaiian NSP showed that the following characteristics were required to achieve sustainable high coverage: broad based political support; allocation of public funds; progressive expansion and removal of counter-productive aspects; peer-educators; links to other services, especially drug treatment; and periodic formal evaluation (Vogt, Breda, Des Jarlais, Gates, & Whiticar, 1998).

NSPs have been successfully established in a few resource-poor settings, such as Brazil, Iran, Kathmandu in Nepal (Peak et al., 1995), northern Thailand (Gray, 1995), Hanoi, Vietnam (Quan, Chung, & Abdul-Quader, 1998) and Ukraine. A report on NSPs in northern Thailand mentioned co-operation from government agencies and non-government agencies in addition to the local communities as key factors for successful implementation (Gray, 1995). The Hanoi NSP gained local acceptance by holding workshops with key community people including the local police, using outreach services to distribute needles and syringes rather than established exchange sites, collecting used injecting equipment, and recruiting and training ex-IDUs as outreach workers (Quan et al., 1998).

Successful implementation has also been achieved in some transitional countries such as in Sverlogorsk, Belarus, (Kumarnanyake et al., 2000), Vickerman & Watts, 2002) and in Sverdlovsk Oblast, Russia (Power & Natalya, 2002). The latter was achieved through a process of “many months of negotiation and discussion with all relevant agencies” including the Ministry for Internal Affairs, educating officials at seminars at which international best practices were presented, a study tour to harm reduction programmes in Britain, training workshops at the pilot sites and an early evaluation report to satisfy politicians and health care providers. A number of international organisations were also involved in encouraging policy-makers and health practitioners to implement harm reduction strategies (Power & Natalya, 2002).

In a number of countries, implementation of NSP in the early stages of an HIV epidemic, combined with multiple prevention initiatives including community outreach, has been shown to have maximum impact (Des Jarlais et al., 1995). In Australia, the first NSP was established in 1986 and within a couple of years, a national network of programmes had been implemented distributing 30 million needles and syringes for a population of less than 20 million in 2000 (Health Outcomes International, 2002).

However, in many countries implementation has been delayed and the scale has been inadequate. This is especially true in developing and transitional countries, as well as those countries, which have responded to illicit drugs through a predominantly supply control perspective (Bastos & Strathdee, 2000).

There is sufficient evidence to consider that the criterion of feasibility of implementation, expansion and coverage has been fulfilled.

Unanticipated benefits

A number of studies have demonstrated additional benefits resulting from NSP use, apart from a reduction in injecting risk behaviour and HIV infection. At the New Haven and Seattle exchanges, United States, increased enrolment in drug treatment and higher treatment retention rates compared with non-users of NSPs were reported (Gibson, 2000; Hagan et al., 2000; Heimer et al., 1998). An evaluation study in Baltimore, United States, found that NSP attendance was independently associated with entry into drug treatment for HIV-infected IDUs (Strathdee et al., 1999). In San Francisco, United States, Bluthenthal et al. (2001) found that NSP clients’ attitudes and motivation to change their drug using patterns was positive, concluding that NSPs have a possible link to drug treatment.

Gibson (2000) found NSP use to be associated with substantial reduction or cessation of injecting compared to IDUs who had never attended a NSP.

During a 1-year pilot NSP conducted in a Swiss women’s prison, no abscesses were observed and there were no instances of aggressive or threatening behaviour among inmates using syringes (Nelles & Harding, 1995).

Despite some reported disparities there is increasing evidence that use of syringe NSPs have led to significant reductions in both hepatitis B and C (Hagan et al., 1995).

There is sufficient evidence to consider that the criterion of unanticipated benefits has been fulfilled.

Special populations

Prisons

Mathematical modelling has been proposed as a useful technique for estimating HIV transmission through sharing in prisons (Dolan, Wodak, Hall, & Kaplan, 1998). Using conservative assumptions, where measurement of relevant variables for the model was unavailable, a relatively large number of HIV infections was estimated to occur in prisons, even though...
these observations were made in a country with a low HIV prevalence among IDUs. A pilot intervention project, which distributed 5335 syringes at a rate of 0.2 syringes/day per inmate, was carried out in a Bern prison, Switzerland, accommodating up to 110 women, of whom a high proportion injected with nearly half of these reporting sharing injecting material regularly. Sterile injecting equipment was made available from a one-to-one automatic dispenser and sharing virtually ceased during the trial (Nelles & Harding, 1995).

By December 2000, 19 prisons in three countries had syringe exchange programmes. All evaluations of these programmes have been favourable and without any reported unintended negative consequences (Dolan, Rutter, & Wodak, 2003). More recent data on NSPs in 53 prisons in six countries (Belarus, Germany, Kyrgyzstan, Moldova, Spain and Switzerland) has been recently published (Lines, Jürgens, Stöver, Laticevschi, & Nelles, 2004).

Young IDU

Young IDUs have been found to be at higher risk of acquiring HIV. Multivariate analysis in one study showed recent onset of injecting to be an independent predictor for seroconversion (Fennema, Van Ameijden, Van Den Hoek, & Coutinho, 1997). A study of IDUs in Rio de Janeiro, Brazil, found that younger age was the principal factor associated with high risk injecting behaviour (Telles et al., 1997). In most countries, young people appear to be under-represented among IDUs attending NSPs, which may be because attendance at a NSP amounts to a relatively public identification as an IDU.

Sears, Guydish, Weltzien, and Lum (2001) investigated an HIV prevention programme for homeless young adult IDUs in San Francisco, United States, finding significant differences between IDUs who frequented a secondary NSP intervention site and a comparison group who did not. The latter were more at risk of sharing syringes (AOR = 3.748; 95% CI, 1.406–9.988) and reusing syringes (AOR = 2.769; 95% CI, 1.120–6.847).

Other populations

Several studies have observed that women who attend NSPs and engage in sex work typically report greater HIV risk behaviours than non-sex worker women attending NSPs. A study comparing sex workers with non-sex workers in five United States cities found that sex workers were significantly more likely to inject more frequently ($P < 0.005$), to reuse syringes more than twice ($P < 0.005$), to engage in “back-loading” syringes ($P < 0.005$) and to obtain syringes from non-NSP sources ($P < 0.05$; Paone, Clark, Shi, Purchase, & Des Jarlais, 1999; Paone, Cooper, Alperen, Shi, & Des Jarlais, 1999).

Sex workers in a Vancouver study, Canada, engaged in heavier drug use, reported a greater variety of injecting and non-injecting drugs, injected substantially more frequently and engaged more frequently in unsafe injecting practices such as renting, buying or borrowing used syringes and using shooting galleries than both sexually active and non-sexually active women (Schechter et al., 1999). In some countries, extensive HIV infection has occurred among sex workers before a generalised epidemic, e.g. Thailand (Nelson et al., 1996; Paone, Clark, et al., 1999; Paone, Cooper, et al., 1999).

Male IDUs who have sex with men may be a population who transmit HIV between groups. Lima et al. (1994) looked at determining risk factors for HIV-1 among IDUs ($n = 123$) in Rio de Janeiro, Brazil, and found that being a male IDU who has had sex with other men in the previous 5 years was a significant independent risk factor for HIV infection. The authors concluded that men who have sex with men and IDUs may be a group through which HIV entered drug-injecting networks in that city.

Developing countries

Successful NSP interventions have been set up either as pilot programmes or ongoing services in a number of developing countries, including three remote villages in northern Thailand (Gray, 1995), Hanoi, Vietnam (Quan et al., 1998) and Dhaka and Rajshahi, Bangladesh (Jenkins, Rahman, Saidel, Jana, & Hussain, 2001). Evaluation results for these studies were reported above under Strength of association and Feasibility of implementation, Expansion and coverage. There is sufficient evidence to consider that the criterion of special populations has been fulfilled.

Discussion

In many countries, HIV epidemics started among IDUs, spreading rapidly to general populations. The evidence for the effectiveness and safety of some HIV prevention strategies in this population has accumulated. Beginning in some developed countries, NSPs were rapidly identified as a valuable strategy for keeping HIV under control among IDUs. Although a wide variety of different activities and operational methods are now subsumed by the term ‘NSP’, there is sufficient commonality to allow evaluation of this large and growing literature. Large numbers of research studies with widely differing designs in diverse countries have been reported. An increasing number of countries commenced NSPs and then began to expand them to scale. Although evidence supporting the effectiveness and safety of NSPs grew, HIV has continued to spread more rapidly among and from IDUs than the adoption and expansion of NSPs. Some excellent and comprehensive reviews of the evidence for NSPs have appeared (General Accounting Office, 1993; Institute of Medicine for the National Academy of Science, 2001; Lurie et al., 1993; National Commission on Acquired Immune Deficiency Syndrome, 1991; National
Institutes of Health Consensus Panel, 1997; Normand et al., 1995; Office of Technology Assessment of the US Congress, 1995; Satcher, 2000). All have confirmed the effectiveness of NSPs in reducing HIV transmission. This conclusion was drawn with increasing confidence in more recent reviews as more and better quality data have become available.

This study is the first systematic review to consider the extent to which evidence for NSPs fulfils the Bradford Hill criteria. These criteria, originally devised to assess infer-
ences of causality drawn from observational studies, have been used increasingly in recent years to assess intervention studies. This review has attempted to rigorously and con-
servatively apply the Bradford Hill criteria but in so doing has often encountered the problem of 'double negatives' in drawing conclusions. Accordingly, readers are encouraged to carefully review the wording of all conclusions relating to Bradford Hill criteria. Each of these refers specifically to a null hypothesis.

The overwhelming majority of studies evaluating the effectiveness and safety of NSPs are highly supportive. But in spite of the impressive volume and quality of this sup-
porting evidence, some still question the efficacy and safety of NSPs. A somewhat tendentious interpretation of a handful of negative studies from Montreal (Bruneau et al., 1997) and Vancouver (Strathdee et al., 1997), Canada, is relied upon by critics of the proposition that NSPs are effective and safe, despite subsequent papers providing plausible alternative explanations for these negative findings (Bastos & Strathdee, 2000; Coutinho, 2000; Lurie & Drucker, 1997; Schechter et al., 1999; Strathdee & Vlahov, 2001).

This review was also inevitably limited by inherent defi-
ciences in the quality of the existing literature. For example, much of the literature classifies IDUs as persons who either attend or do not attend NSPs, whereas in reality this phe-
nomenon is dimensional rather than categorical. In addition, outcome measures are usually categorical; although again the phenomenon is usually dimensional. For example, sharing is usually measured as either present or absent during a partic-
ular period, rather than estimated on a continuum (Bastos & Strathdee, 2000).

Conclusions

There is compelling evidence that increasing the avail-
ability and utilisation of sterile injecting equipment by IDUs reduces HIV infection substantially.

Overall, there is convincing evidence that NSPs, assessed conservatively, fulfil six of the nine Bradford Hill criteria and all of the five additional criteria. Measured against any objec-
tive standards, published studies support the conclusion that NSPs are effective in substantially reducing HIV transmis-
sion.

Carefully evaluated pilot programmes of NSPs have their place in allowing the introduction of this invaluable pro-
tection of public health but they also have some risks. The case for NSPs is already so compelling and the international experience so impressive that there is no longer any real jus-
tification for pilot programmes as they may further delay the much needed expansion phase.

NSPs are only one way of increasing the availabil-
ity of sterile injecting equipment and these exist in many forms around the world with some cities requiring ‘one-for-
one’ exchange, others attempting to achieve high levels of exchange but accepting less than 100%; while authorities in other jurisdiction provide sale or free distribution without attempting to remove used injecting equipment from circu-
lation. There is no evidence that any one method is notably more efficacious or cost effective.

Attempts to increase the availability of sterile inject-
ing equipment should be accompanied by endeavours to increase its utilisation, reduce the utilisation and availability of non-sterile injecting equipment and improve the disposal of used injecting equipment. These objectives are best met through education of IDUs through peer based, explicit campaigns, which generally have been found to be highly effective.

Many jurisdictions have found that a diversity of approaches is optimal with some methods working best in certain locations and conditions and other approaches better suited in other places and conditions. The aim is to reduce the circulation time of needles and syringes.

There is no convincing evidence of any major, unintended negative consequences. After almost two decades of exten-
sive research, there is still no persuasive evidence that NSPs affect the initiation, or increase the duration or frequency of illicit drug use or drug injecting.

The studies reviewed in this report present a compelling case that NSPs substantially and cost effectively reduce the spread of HIV among IDUs and do so without exacerbat-
ing injecting drug use at either the individual or societal level. This suggests that authorities responsible for areas threatened by, or experiencing, a HIV epidemic among IDUs should adopt measures urgently to increase the available-
ity and utilisation of sterile injecting equipment and expand implementation to scale as soon as possible. As an approxi-
mation it is reasonable to assume that providing 200 sterile needles and syringes per injecting drug user per year is a fig-
ture which is achievable and likely to control HIV infection in this population. It may take several years, starting from scratch, to reach this figure. Higher targets may be needed where seroprevalence has already reached unacceptable lev-
els. The precise quantity of injecting equipment required is not known. Cocaine injectors require more needles and syringes than heroin injectors. Needle syringe programmes are cost-effective.

It is more difficult to generalise from studies of cost effec-
tiveness of NSPs in one country to other similar countries, let alone from developed countries to resource poor settings. However, a number of careful studies in several developed countries and some transitional countries have demonstrated convincingly that NSPs are cost-effective.
Needle syringe programmes have additional and worthwhile benefits apart from reducing HIV infection among IDUs. There is reasonable evidence that needle syringe programmes can increase recruitment into drug treatment. Pharmacies and vending machines increase the availability and probably the utilisation of sterile injecting equipment by IDUs.

There is reasonable evidence that pharmacy availability of sterile injecting equipment does provide specific benefit in addition to the benefits of NSPs. The population attending pharmacies tends to be less disadvantaged than those attending community based NSPs, although there is often a considerable degree of overlap. Pharmacy schemes complement the benefits of NSPs, although some jurisdictions have relied entirely on pharmacy-based outlets. Vending machines increase access in some geographical locations to some special populations and/or at times of the day that are otherwise difficult to provide for.

Pharmacy based NSPs appear to complement community based schemes and may provide access to a somewhat different population of IDUs. Vending machines increase coverage geographically and across time zones but have the disadvantage of not providing information, counselling or referral.

NSP should be expanded to cover special populations. Special populations of IDUs are of great public health significance in HIV control, especially populations such as sex workers and male IDUs who also have sex with men, as these groups may transmit HIV between population groups. In most countries, a large proportion of IDUs spend a considerable proportion of their drug injecting careers behind bars; while a large proportion of prison inmates have a history of injecting drug use. Many inmates of correctional facilities continue to inject while they are incarcerated. The limited evidence available from evaluation of the few existing prison NSPs suggests that their benefits are similar to community programmes; while there is no evidence to date that these programmes are inherently unsafe or counter-productive. On the available evidence, there is a strong case for establishing and expanding NSPs in correctional facilities.

Needle syringe programmes on their own are not enough to control HIV infection among IDUs. There is no evidence of a protective effect for single interventions strong enough to guarantee HIV control but the aggregate effect of several harm reduction interventions appears to be generally successful in controlling HIV. However, worthwhile it may be to increase the availability and utilisation of sterile injecting equipment with the aim of controlling HIV infection among IDUs, this appears to be a necessary rather than a sufficient intervention. Other activities that complement the benefits of sterile injecting equipment programmes include education of IDUs, increasing the capacity, range and quality of drug treatment (especially substitution treatment), and community development of IDUs.

Further study and research are required. This review has demonstrated significant gaps in studies and research. The quantity and quality of research needs to be improved in phar-macy and vending machine evaluation, measures to reduce inappropriate disposal and the reform of restrictive injecting paraphernalia legislation in countries other than the United States. More and better qualitative research would illuminate the findings of the numerous quantitative studies. Researchers should make more use of continuous measures of baseline characteristics, interventions and outcome variables. However, it is important to recognise that the limited implementation of NSPs is not fundamentally due to a lack of adequate research data. Therefore, it is unlikely that increasing the quantity of the same kind of research as exists already will increase the implementation of NSPs.

References


Further readings

