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Syringe Exchange in the United States: A National Level Economic Evaluation of Hypothetical Increases in Investment

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Abstract

To examine whether increasing investment in needle/syringe exchange programs (NSPs) in the US would be cost-effective for HIV prevention, we modeled HIV incidence in hypothetical cases with higher NSP syringe supply than current levels, and estimated number of infections averted, cost per infection averted, treatment costs saved, and financial return on investment. We modified Pinkerton's model, which was an adaptation of Kaplan's simplified *needle circulation theory* model, to compare different syringe supply levels, account for syringes from non-NSP sources, and reflect reduction in syringe sharing and contamination. With an annual $10 to $50 million funding increase, 194–816 HIV infections would be averted (cost per infection averted $51,601–$61,302). Contrasted with HIV treatment cost savings alone, the rate of financial return on investment would be 7.58–6.38. Main and sensitivity analyses strongly suggest that it would be cost-saving for the US to invest in syringe exchange expansion.

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Keywords

Cost-effectiveness; Mathematical model; Syringe exchange; Injection drug use; HIV

Introduction

HIV infections cause significant human suffering and exact substantial financial costs, with each infection in the United States estimated to result in a loss of between 9 and 21.1 years of life [1-3], between 5.33 and 6.433 qualityadjusted life years [2, 3], and $379,668 (2010 dollars) in lifetime treatment costs [4]. The sharing of drug injection equipment is the second-most common route of HIV transmission—approximately 9.4 %of new HIV infections in the United States in 2009 occurred among persons who injected drugs (PWID) and 2.7 % occurred among men who had sex with men and injected drugs (MSM/PWID) [5].

Access to sterile needles and syringes (herein referred to as “syringes”) is a proven approach for reducing HIV transmission enumerated in the 2010 National HIV/AIDS Strategy for the United States [6]. The evidence in favor of needle/syringe exchange programs (NSP) is well-documented, with economic evaluations repeatedly showing that NSPs are cost-effective and cost-saving for the prevention of HIV [7-14]. The 2012 US President’s Emergency Plan for AIDS Relief (PEPFAR) Blueprint envisions an AIDS-free generation within our lifetime, calling for “smart investments based on sound science”, and establishing NSPs as one of the three central elements of the PEPFAR comprehensive prevention package for PWID, in addition to community-based outreach programs and drug treatment [15].

The 2010 National HIV/AIDS Strategy set the objective of reducing the annual number of new HIV infections by 25 % by year 2015 [6]. This objective was elaborated in the Centers for Disease Control and Prevention’s (CDC) Strategic Plan for 2011–2015 as reducing HIV infections in each of several vulnerable populations including PWID by at least 25 % [16]. Although NSPs may be an essential strategy for achieving this goal, none of the funds in the CDC HIV prevention budget (approximately $750 million for fiscal year 2013 [17]) could be used to support NSPs, as federal funding of NSPs has been banned since 1988 with the exception of a 2-years period from December 2009 to December 2011 [18, 19]. Private donors and state and local governments provided approximately $24 million in 2009 to support over 200 NSPs in the US [20]. Despite these local efforts to reduce injections with non-sterile syringes, NSP syringe coverage in the US remains low. Tempalski et al. [21] found that the number of sterile syringes from NSPs in 35 large metropolitan areas was equal to only about 3 % of the number of drug injections. Although new syringes are also obtained through pharmacies and other means, there is evidence to suggest that the vast majority of drug injections are with syringes that are not new [22, 23].

No single intervention will be sufficient for reaching the goal of an AIDS-free generation, but scaling up NSPs may be an important component for reducing HIV infections among PWID. What benefits might be realized through increased investment in NSPs? What would be the costsavings or cost-effectiveness of different levels of investment? The answers to

these questions are essential for informing national policy development and funding decisions, but to our knowledge no previous study has estimated the potential costs and benefits of increasing investment in NSPs in the US.

NSPs are diverse in the range of services they provide. The key component shared across programs is syringe exchange, which increases access to sterile syringes and speeds up removal of used and potentially HIV-contaminated syringes from circulation, thereby reducing HIV transmission through shared syringes. In addition to this key component, many NSPs provide additional services such as referrals to drug treatment programs, HIV testing and counseling, and condom distribution [24], which have other possible direct and indirect benefits: changing social norms among PWID towards safer injecting, facilitating entry into drug treatment and cessation of drug use, increasing condom use, increasing testing and treatment of HIV and other sexually transmitted infections (STI) leading to lower HIV viral load and infectivity, increasing testing, treatment and vaccination for hepatitis viruses, and reducing drug overdoses.

The present study aimed to estimate the impact on HIV transmission of hypothetical increases in syringe exchange investment. Its focus is the impact of the most essential component of NSPs: increasing access to sterile syringes and faster removal of used syringes. With this purpose, our analysis took into consideration the costs associated specifically with the supply and exchange of syringes, and its impact on syringe sharing and syringe contamination, and based on which estimated the number of HIV infections averted and HIV treatment costs avoided. The method was mathematical modeling using existing data. We applied with modification the model that Pinkerton [13] used to evaluate Vancouver's Insite program, which was an adaptation from Kaplan's simplified *needle circulation theory* model [25-27].

The impacts of the additional NSP services listed above are outside the scope of this paper. To evaluate their costeffectiveness, other modeling approaches would be needed, and additional research would be required to generate the data needed for modeling inputs.

Methods

From existing data, we derived estimates for the current situation in the US: the number of syringes supplied by NSPs in a year and the number of people who contract HIV due to drug injecting risk in a year. The key question is if NSP syringe supply were increased by a certain amount, what would happen to the number of people contracting HIV—it is expected to go down, but by how much. If we could answer this question, we could evaluate the costeffectiveness of such hypothetical increase in NSP syringe supply by costing it and estimating savings resulting from infections averted.

The Model

The strategy for answering this question is to start from an equation for the *number of new HIV infections* due to injection drug use over a 1-year period, and to relate parameters in this equation to *syringe supply*. Such equation would allow us to estimate how a hypothetical increase in syringe supply would affect the number of new infections.

The initial equation is based on the premise that the number of new infections in a year equals the number of uninfected (thus at risk) persons times the probability that an uninfected person becomes infected over the course of the year. It is:

$$I \approx N(1-\alpha)Bc\gamma.$$

I is the number of new HIV infections due to drug injecting risk in the US in a year. ***N*** is the number of PWID in the US and α is HIV prevalence among PWID, therefore $N(1-\alpha)$ is the number of uninfected PWID who are at risk of contracting HIV. The product $Bc\gamma$ is an approximation for the probability that an uninfected PWID becomes infected in the year, with ***B*** being the average number of times a PWID injects drugs with a receptively shared syringe (or number of "borrows") in a year, ***c*** being the proportion of shared syringes that are contaminated with HIV, and γ representing the probability of getting infected through one injection with an HIV-contaminated syringe. The probability γ averages risk over the heterogeneity of syringe contamination including variation in blood amount and variation in viral load in the blood—the latter being a mixture of low levels (from HIV-positive persons who have viral suppression as a result of antiretroviral treatment) and high levels (from those without viral suppression).

We use these notations to refer to parameters in the current situation, or the status quo, which we call the *base case*. In a *hypothetical case* with increased NSP syringe supply, the number of new HIV infections due to injection risk in a year is denoted by I'. The number of borrows and the contaminated proportion are expected to decrease as a result of increased syringe supply; we denote them with B' and c'. The other parameters ***N***, α and γ are conservatively assumed to stay the same. As such,

$$I' \approx N(1-\alpha)B'c'\gamma.$$

We are interested in estimating number of infections averted as a result of increasing syringe supply ($A = I - I'$). It is more tractable, however, to compare I' to ***I*** using the ratio:

$$\frac{I'}{I} = \frac{N(1-\alpha)B'c'\gamma}{N(1-\alpha)Bc\gamma} = \frac{B'}{B} \cdot \frac{c'}{c}.$$

Once I'/I has been worked out, the number of infections averted can be estimated:

$$A = I - I' = I\left(1 - \frac{I'}{I}\right).$$

To estimate the ratio of syringe contamination proportions (c'/c), we applied Kaplan's simplified *needle circulation theory* model [25-27], which was adapted and used by Pinkerton in his evaluation of Vancouver's InSite program [13]. Based on this model, the proportion of syringes that are contaminated is proportional to the rate at which syringes become contaminated, which in turn is proportional to the ratio of the number of injections

with a borrowed syringe to the number of injections with either a new or a borrowed syringe. Thus:

$$\frac{c'}{c}=\frac{B'/(B'+S')}{B/(B+S)}$$

where S and S' denote the number injections with brand new syringes per PWID per year, in the base case and in the hypothetical case.

Results from the *needle circulation theory* are based on an average 1-to-1 exchange assumption; greater exchange ratios (more dirty syringes for a new one) would result in greater reduction in contamination. While programs vary in exchange policies and may not rigorously enforce 1-to-1 exchange, the overall result is close to 1-to-1 exchange and the assumption holds for our calculations. Data on syringes distributed by and returned to NSPs (available from the North American Syringe Exchange Network [20]), and discounting for syringes being unused/lost and for NSP syringes replacing the use of syringes from other sources (see details about such discounting below), point to an effective ratio of 1 new syringe for 1.04 or 1.06 old syringes (for 2009 and 2008).

From the contamination ratio above, it follows that

$$\frac{I'}{I}=\frac{B'}{B}\cdot\frac{c'}{c}=\frac{B'}{B}\cdot\frac{B'/(B'+S')}{B/(B+S)}=\left(\frac{B'}{B}\right)^2\cdot\frac{B+S}{B'+S'}.$$

The infections ratio thus depends on base case and hypothetical case values of two parameters: (1) the number of injections with new syringes per PWID per year, which is also the average number of new syringes used by a PWID per year; and (2) the number of borrows per PWID per year. The question is how these two parameters would change as a result of an increase in NSP syringe supply.

First, the average number of new syringes a PWID uses in a year (S) is a combination of syringes from NSPs (S_{NSP}) and syringes from other sources (S_{nonNSP}). Of the total volume of syringes supplied by NSPs to PWID in the US over 1 year (V_{NSP}), we assume that a certain proportion (w) go unused, and the average number of new NSP syringes used by a PWID in a year is:

$$S_{NSP}=\frac{V_{NSP}(1-w)}{N}.$$

With an increase in NSP syringe supply of ΔV_{NSP}, the number of new NSP syringes used per PWID per year is increased by:

$$S'_{NSP}-S_{NSP}=\frac{\Delta V_{NSP}(1-w)}{N}.$$

We assume also that as NSP syringe supply increases, a proportion (***r***) of the additional NSP syringes would replace syringes that otherwise would have been obtained from non-NSP sources, such that:

$$\begin{aligned} S'_{nonNSP} - S_{nonNSP} &= -r\left(S'_{NSP} - S_{NSP}\right) \\ &= -\frac{\Delta V_{NSP}(1-w)r}{N}. \end{aligned}$$

Summing each side of the two equations above, we have:

$$S' - S = \frac{\Delta V_{NSP}}{N}(1-w)(1-r).$$

Let ***f*** denote (1 − ***w***) (1 − ***r***), representing a discount for both the NSP syringes that would go unused and the replacement of non-NSP syringes, and name it the "supply increase discount factor". The hypothetical case number of syringes used per PWID per year is:

$$S' = S + \frac{\Delta V_{NSP}}{N} f.$$

Second, how would an increase in NSP syringe supply affect the number of borrows (***B***)? While the number of injections per PWID per year (***M***) is expected to remain the same, the number of injections with a new syringe per PWID per year (***S***) would increase with increased NSP syringe supply. The number of injections with a syringe that is not new ("non-new" injections, for short), which is (***M*** − ***S***), would go down, and this number includes injections with borrowed syringes (***B***) and injections with reused syringes. To our knowledge, no previous study has examined the relationship between ***S*** and ***B***. Our own exploratory analysis of site level data from the NIDA Cooperative Research Evaluation Study indicated that proportions of non-new injections that occurred with borrowed syringes were independent of proportions of injections with new syringes. We assume that the proportion of non-new injections that occur with borrowed syringes (***B***/(***M*** − ***S***)) would remain constant:

$$\frac{B}{M-S} = \frac{B'}{M-S'}.$$

This implies a reduction in the number of borrows:

$$B' = B\left(\frac{M-S'}{M-S}\right).$$

Finally, by supplying estimates (based on existing data and assumptions) for the number of PWID in the US (***N***), annual number of new HIV infections due to injection risk (***I***), per-PWID per-year numbers of injections (***M***), injections with a new syringe (***S***), and injections with a borrowed syringe (***B***), and the supply increase discount factor (***f***), the number of HIV

infections averted with increased NSP syringe supply can be estimated. For a given increase in NSP syringe volume (($\Delta \boldsymbol{V_{NSP}}$)), the number of HIV infections averted is:

$$A = I\left(1 - \frac{I'}{I}\right) = I\left[1 - \left(\frac{B'}{B}\right)^2 \cdot \frac{B+S}{B'+S'}\right]$$

where

$$\boldsymbol{B'} = \boldsymbol{B}\left(\frac{\boldsymbol{M} - \boldsymbol{S'}}{\boldsymbol{M} - \boldsymbol{S}}\right) \text{ and } \boldsymbol{S'} = \boldsymbol{S} + \frac{\boldsymbol{\Delta} V_{NSP}}{\boldsymbol{N}}\boldsymbol{f}.$$

Computations

Calculations started with levels of hypothetical additional investment, which we set to range from zero to 50 million US dollars (in 2011 currency). Dividing the additional investment by the estimated cost per NSP syringe distributed (***U***) provided an estimate of the increase in US NSP syringe supply $\Delta \boldsymbol{V_{NSP}}$, from which the number of infections averted (***A***) was calculated. HIV treatment costs avoided as a result of averting those infections were derived by multiplying the number of infections averted by the estimated per person lifetime HIV treatment cost (***T***), which was represented in net present value (i.e., discounting future costs to present time), so that these savings could be compared to investment.

Parameter Values

The model requires the specification of several parameters, with values drawn from or estimated based on existing data. Where there was uncertainty about a value, a range of credible values was examined through sensitivity analysis. A worst-case scenario sensitivity analysis was also conducted, combining the least favorable values on all parameters. These parameter values, their basis/sources and the value ranges for sensitivity analysis are presented in Table 1. The reasoning behind the selection of such values is provided below.

Number of new HIV infections due to drug injection risk in the US per year in the base case ***(I)*** = 2,575 infections. HIV incidence estimates available for the most recent year (2009) served as the basis for our analysis, with 4,500 new HIV infections acquired by PWID and 1,300 by MSM/PWID [5]. For this analysis, only infections due to drug injection risk are of interest, and existing research suggests that HIV sexual transmission among PWID is common. Male PWID who engage in homosexual activity are more likely to become infected [28-30]. Female PWID who have a drug-injecting sex partner, have had an STI [30], or engage in prostitution [28] are more likely to become infected. Findings from studies comparing the sexual risk of PWID and people who use non-injecting drugs are mixed: one found less sexual risk among PWID [30], another found comparable risk [31].

A recent study with 337 PWID in New York City [32] found a significant association between HSV-2 and HIV infection and no association between HCV and HIV infection, and thus concluded that most HIV infections in this sample occurred through sexual transmission. While New York City is one of the cities in the US most active in meeting

PWID's safe injection needs and therefore may have less parenteral transmission than in other areas, this finding suggests generally that in settings where interventions to reduce parenteral transmission are effective, sexual transmission may account for a large part of HIV infections among PWID.

Given the lack of precise estimates, we assumed that 50 % of the infections in the PWID category and 25 % of the infections in the MSM/PWID category were due to injection risk —a total of 2,575 infections in 2009—and used this as the *base case number of new HIV infections due to injection risk per year*. To address the uncertainty of these proportions, we conducted sensitivity analysis on the range of 2,060–3,090 infections (corresponding to 40–60 % of PWID category and 20–30 % of MSM/PWID category).

Number of persons who injected drugs in the past year in the US (***N***) = 1.55 million. Using anchor PWID population estimates of 1.75 million in 1992 [33] and 1.35 million in 1998 [34], Brady et al. estimated the size of the US PWID population for the period of 1992–2002 based on drug treatment, HIV testing and AIDS diagnosis data, and validated their estimates through correlations with unemployment rate, hepatitis C mortality and poisoning mortality [35]. Their analysis suggests that the PWID population was relatively stable between 1992 and 2002, and the average PWID population over this period was about 1.55 million. Since this is the most rigorous PWID population estimation to date, we used this estimate as a basis for our analysis. There is significant uncertainty around this population size, however. An analysis of selfreporting data from several household surveys—which were likely to miss people who are homeless, without stable housing, or in residential treatment, and to suffer from under-reporting due to the behavior's sensitivity—provided a much lower estimate of nearly 760 thousand PWID in 2009 [36]. On the other hand, a review of the global epidemiology of injection drug use and HIV listed for the US an PWID population of 1.86 million, calculated based on experts' reports [37]. Our sensitivity analyses thus examined a range of 0.76–1.86 million.

Number of injections per PWID per year (***M***) = 812.02 injections. This estimate assumed a mean of 2.8 injections per day, based on two main sources. Using data from the NIDA Cooperative Research Evaluation Study, Lurie et al. [38] estimated 2.8 injections per PWID per day for 1996. Based on a review of the literature and consultation with various experts, Tempalski et al. [21] arrived at the same estimate of 2.8 injections per PWID per day in 2000. This is equivalent to 1,022.7 injections over a year of 365.25 days. However, not every PWID injects for the whole year. Galai et al. [39] tracked how PWID in Baltimore moved in and out of drug injecting. Using data from their paper, we found that people in this sample were injecting drugs for only 79.4 % of the time they would be classified as past-year injectors. This means on average, each PWID had 1,022.7 injections * 79.4 % = 812.02 injections per year. Sensitivity analyses examined a range of 720–900 injections.

Number of borrows per PWID per year in the base case (***B***) = 81.20 borrows. This was based on an estimate of the proportion of injections that occur with borrowed syringes, out of all injections. Pinkerton estimated this proportion to be 0.083 in Vancouver, by multiplying the proportion of PWID who borrowed with the proportion of injections by those who borrowed that were with borrowed syringes [13]. To estimate this proportion for

the US, we used data from the NIDA Cooperative Research Evaluation Study, presented in an early paper by McCoy et al. [40]. Of 12,323 active PWID recruited from 19 sites, 31.9 % reported sharing both syringes and drug preparation tools in the past 30 days; another 8.6 % reported sharing syringes only. Those in the first group reported using syringes previously used by another PWID on average 29.4 times in the past 30 days; those in the second group reported 14.1 times. Combining this with the injection frequency of 2.8 times per PWID per day, we could estimate borrowing = (31.9 % * 29.4 times + 8.6 % * 14.1 times)/(30 days * 2.8 times) = 12.6 %. The NIDA study is dated, however. One could expect borrowing behavior to have declined over time as a result of HIV prevention efforts. To incorporate this expectation, instead of 12.6 %, we used 10 %, and arrived at number of borrows = 812.02 injections * 10 % = 81.20 borrows. Sensitivity analyses examined a range of 64.96–105.56 borrows (corresponding to 8–13 % of injections).

Number of brand new syringes used per PWID per year in the base case (***S***) = 146.16 syringes. Apart from injections that happen with borrowed syringes, the rest (***M*** − ***B*** = 730.82 injections) occur with syringes a PWID owns (or “own syringes”, for short). This number, divided by the number of injections per own syringe, would give the number of brand new syringes a PWID uses per year (***S***). Estimates of the number of injections per own syringe are available from several sources. Heimer et al. [41] studied the number of injections per syringe among NSP clients in four cities in the early and mid 1990s. With the implementation of NSP, they found that the mean number of injections per syringe in Chicago decreased from a mean of 6.83 (median 5) before the start of NSPs to a mean of 1.4 (median 1) after, and in Baltimore decreased from 12.4 (median 6) to 3.6 (median 2). In New Haven, the number of injections per syringe decreased from 7.14 to 3.97 when individuals began using an NSP. Using data collected between 1997 and 2000 in Chicago, Huo and Oullet found that the median number of injections per own syringe among PWID who reused their syringes was 3 for NSP users and 5 for non-users [22]; including PWID who did not reuse any syringes in their analyses would have resulted in medians that were lower. Given the range of available values above, we assumed that on average a PWID in the US uses a syringe he/she owns for five injections. Thus the number of brand new syringes a PWID uses in a year is 730.82 injections/5 injections per syringe = 146.16 syringes. Sensitivity analyses examined a range of 104.40–182.71 syringes (corresponding to 7–4 injections per own syringe).

Supply increase discount factor(***f***) = 0.855. This was based on an assumption of 5 % NSP syringes going unused, and 10 % of the increased NSP syringe supply replacing non-NSP syringes. As no data are currently available to suggest what these proportions should be, these estimates were based on author consensus. Sensitivity analyses examined an ***f*** range of 0.8–0.9.

NSP unit cost (***U***) = $0.48 per syringe. The Beth Israel Medical Center/North American Syringe Exchange Network (NASEN) Survey provides information on the budgets of and number of syringes distributed by NSPs in the US. However, these programs provide a number of services beyond syringe distribution, while our analysis focused on the costs and benefits of increased syringe supply. For this purpose we estimated programmatic costs for a minimal set of services including syringe exchange, referrals to off-site services and no

more than one additional on-site service such as HIV testing or condom distribution. Analysis of costs data reported to the NASEN survey by programs that provide such level of service gives an average cost of $0.48 per syringe (in 2011 USD).

Lifetime HIV treatment cost per infected person (***T***) = $391,223 (in 2011 USD). The CDC published that on average, the lifetime treatment cost of an HIV positive case, discounted to net present value, was $379,668 in 2010 USD [4]. Adjusted for inflation in medical care costs, this is equivalent to $391,223 in 2011 USD.

Results

In the base case scenario with no additional syringe exchange funding, an estimated 2,575 HIV infections occur in a year due to drug injection risk. Based on lifetime treatment costs of $391,223 in 2011 USD per infection, the total treatment costs for these infections is $1.01 billion.

Figure 1 displays the estimated effects of hypothetical increases in syringe exchange funding, including number of HIV infections averted and savings in lifetime HIV treatment costs that result from averting them. Table 2 presents the same estimates plus cost per infection averted, net savings (i.e., treatment cost savings minus investment increase), and average and marginal rates of financial return on investment.

Based on the model and parameter estimates, an additional $10 million investment for NSPs providing a minimal set of services in a year would avert 194 HIV infections and result in treatment cost savings of $75.8 million. A $50 million increase in funding would avert 816 infections and save $319.1 million in treatment costs. The cost per infection averted would range from $51,601 (in case of $10 million additional investment) to $61,302 (in case of $50 million additional investment). This corresponds to a rate financial return of investment of 7.58 to 1 in the former case and 6.38 to 1 in the latter case.

The US National HIV/AIDS Strategy specified a goal of 25 % HIV incidence reduction. Based on our model, to reduce by 25 % the number of HIV infections among PWID attributable to injection risk that occur in a year, an increase in annual NSP funding of slightly less than $40 million would be needed.

Figure 2 presents the findings of sensitivity analyses with two outputs, the number of infections averted (top panel) and net savings (bottom panel). The uncertainty in three parameters, ***B*** (injections with a borrowed syringe), ***S*** (injections with a new syringe) and ***f*** (discount factor for syringe supply increase) caused minimal change in modeling results. Variations in ***M*** (injections per PWID per year) and ***U*** (cost per syringe distributed) corresponded to slightly bigger changes, and variations in ***I*** (HIV incidence) caused the most substantial change. The low value for ***N*** (number of PWID) resulted in very high estimates of infections averted. Over all these sensitivity analyses, the conclusion that additional investment in syringe exchange would be highly cost-saving does not change.

In the worst-case scenario sensitivity analysis, the least favorable values of all the seven parameters were combined (Fig. 2). Under this scenario, an investment increase of $10

million would avert 99 infections, save $38.76 million in HIV treatment costs, and represent a rate of financial return on investment of 3.88–1. An investment increase of $50 million would avert 445 infections, save $173.97 million in HIV treatment costs, and represent a rate of return on investment of 3.48 to 1. Even in this worst-case scenario, additional investment in syringe exchange would be highly cost-saving.

Discussion

These analyses indicate that it would be highly cost-saving to invest additional funds to expand syringe exchange services in the US. Over the course of 1 year an additional investment of only $10 million would avert an estimated 194 HIV infections and avoid $75.8 million in lifetime HIV treatment costs (saving $65.8 million net), representing a rate of financial return on investment of 7.58. If the investment increase were $50 million, it would also be highly cost-saving: approximately 816 HIV infections would be averted, equivalent to nearly one-third (32 %) of the annual number of new HIV infections due to drug injection risk; $319.1 million of lifetime HIV treatment costs would be avoided (net savings $269.1 million), representing a 6.38 rate of financial return on investment. Sensitivity analyses showed that when uncertainties about parameter values were accounted for, investment increase remained highly cost-saving.

Our analyses were conservative in scope, focusing on the effects of increased NSP syringe supply in terms of reducing number of injections with borrowed syringes and reducing HIV contamination of syringes in circulation. We did not account for the impacts of other services provided by NSPs on HIV transmission, such as referrals for drug treatment which may reduce the number of PWID at risk for HIV, HIV testing and counseling which may reduce risk behavior and lead to earlier initiation of HIV treatment and reduced infectivity, condom distribution which may reduce sexual transmission among PWID and their sex partners, etc.; and did not account for reductions in secondary HIV infections. We also did not estimate benefits of increased NSP syringe supply on hepatitis C infections. In calculating return on investment, our study was also conservative in including only savings in HIV treatment costs, without estimating the additional social and economic costs avoided, or assigning a monetary value to the lives and life years saved.

As the scope of our study was restricted to the costeffectiveness of increased syringe supply (the most essential component of NSPs), we estimated programmatic costs associated with a minimal set of services. This level of cost ($0.48 per syringe) allows for what is offered by the leanest programs: the exchange of syringes plus referrals to off-site services and no more than one additional on-site service. As such, our study did not estimate the benefits of services beyond syringe exchange. If instead of this $0.48 per syringe we used the average cost from all NSPs surveyed by NASEN including programs with more comprehensive services (which if divided by the syringe volume would be about $0.72), even without accounting for the additional benefits of the broader range of services, this would still lead to the conclusion that increased investment would be highly cost-saving.

That is not to say that the other effects of NSP services should be neglected. They represent a gap in the syringe exchange literature, so their magnitudes are not known. No study has

estimated, for example, NSPs' potential effect on the HIV treatment cascade, from increased counseling and testing, to earlier treatment initiation, to viral suppression, to reduced infectivity, even though it has been established that early treatment [42] and viral suppression [43] reduces infectivity and sexual transmission. To estimate such effect requires data that causally link NSP attendance to earlier initiation of HIV treatment, which currently do not exist. As more data become available on the various effects of NSPs, cost-effectiveness analyses should incorporate them so that the impacts of NSPs could be captured fully and the package of NSP-related services could be tailored to optimize the cost-benefit tradeoff.

Two parameters in our model—HIV prevalence and the average infectivity of an HIV-contaminated syringe—were conservatively assumed to be the same in the hypothetical case as well as the base case, while theoretically, they could go down over time in the hypothetical case, relative to the base case. Higher syringe supply means fewer new infections, which could make prevalence in the hypothetical case lower than in the base case. NSP attendance could lead to earlier HIV testing and treatment initiation, which would reduce the amount of virus contaminating syringes, lowering the overall infectivity of syringes. Since the short (1-year) time frame being considered means these effects would likely be very small, and due to lack of estimates for them, we excluded them from this analysis. These effects, however, could not be ignored in studies that project HIV incidence over several or more years into the future.

One unconservative aspect of our model is that it does not address the competing risk of sexual transmission. The individuals who avoided injection-related infections in the hypothetical case would remain in the pool of people at risk for infection through sex. If we applied the population average sexual transmission rate among PWID (based on the data on new infections and PWID population size used in this study), out of the 194 persons who avoid injectionrelated infections in the $10-million-investment-increase scenario, we would expect 0.21 persons to become infected sexually; out of the 816 persons in the $50-millioninvestment-increase scenario, we would expect 0.88 persons to become infected sexually; both of these are small numbers. This, however, assumes no correlation between sexual and parenteral transmission risks, but it is difficult to estimate the correlation of these risks and the relevant sexual transmission incidence rate for these individuals. We have thus excluded this detail from our analysis. When more data are available on risk correlation, this issue should be revisited. On the other hand, NSPs typically provide HIV testing and condoms, both of which may be associated with reduction of sexual risk behavior. Thus, expansion of NSPs may actually be associated with reduced sexual transmission. As we believe that this effect would be small within a 1-year time frame, and do not have the data needed to estimate this effect, we have not included it in the model.

It should be mentioned that the model we used in this analysis is a relatively simple model that requires a small number of parameters. This was deemed suited for a national level analysis, because of limited data availability and our hesitation to make too many assumptions. In other words, the gain in big picture comes with a certain loss in resolution. In local level analyses, other researchers have used more complex models. For example, Vickerman et al. incorporated estimates of PWID who do not share syringes or have

different levels of sharing and injection network characteristics [44, 45]. Bobashev et al. [46] proposed agent-based models that allow simulating HIV transmission under different NSP syringe coverage scenarios. For our purpose of national level analysis, data were too sparse to allow reasonable assumptions about individual PWID behaviors and their injection networks to use any of these complex models.

The quality of a cost-effectiveness analysis depends on the quality of the data that inform the values of modeling parameters. As our analysis was at the national level, we were able to draw from data from different national and local studies for different parameters. Many of the parameters, however, were estimated from either older data from national studies or more contemporaneous data from localized studies, which may or may not accurately reflect contemporary national epidemiology of HIV and injection practices among PWID. There was uncertainty about quite a few parameters, such as the size of the PWID population, HIV incidence due to injection drug use, sharing/borrowing practices, number of injections per syringe, and the quantity of non-NSP syringes.

To address these issues, we relied on multiple data sources to reduce bias and conducted sensitivity analyses covering ranges of plausible parameter values to account for the uncertainty in each parameter. Even when the least favorable values of all these parameters were combined, the results indicated substantial cost savings, making it clear that the conclusion about increased syringe exchange funding being highly cost-saving is robust to uncertainties in parameter values. When more precise data for the parameters in this model become available, updating the analysis may provide more accurate estimation of the degree of effectiveness of syringe exchange expansion.

A feature of the model that should be mentioned is that it is an average model that assumes parameter values are similar across different geographical locations in the United States. To be precise, it assumes that the ratio of new infections in the hypothetical case to the base case (I'/I) is the same (or similar), which means B, c (and B', c') are similar, in different parts of the country. This is an inaccurate assumption but was necessary for the model to be estimated, because data on B (number of borrows) were not widely available. While we produced one estimate of costeffectiveness for the country based on this average model, for funding decisions, we would like to highlight that if investment increase were to be targeted, it would be more cost-effective and cost-saving in areas where syringe coverage is lower and borrowing is more prevalent (higher B than average, which means increased syringe supply will displace more borrows, leading to a smaller I'/I ratio), and where HIV incidence is high (higher I for PWID population than average), as these conditions combined give rise to a larger number of infections averted ($I - I'$). Local NSP cost is also an important factor —in areas where NSP operating costs are lower, investment increase would be more cost-effective.

To inform local funding decisions, it would be even better to have local analyses, especially in areas where injecting drug use, HIV among PWID, and syringe exchange have been extensively researched, and local data are thus available for model parameters (for an example about how such data could be used for local analysis, see the spreadsheet available

online as supplemental material). Data availability may even allow the consideration of one or more of the more complex models mentioned above.

Conclusions

With an estimated total syringe coverage of about 18 % of drug injections (including 2.8 % coverage by NSPs), there is tremendous unmet need for clean syringes among PWID in the US. From a public health perspective, more investment is needed for syringe exchange, to avert infections and save lives. From a financial management perspective, in a time of difficult economic conditions constricting resources for public spending, it is especially important to invest in interventions that are effective and cost-effective. Investment in syringe exchange not only meets these two criteria but also would save more resources than what needs to be spent. Given that about three-fourths of HIV treatment costs in the US are borne by the public sector [47], expanding syringe exchange could contribute to reducing the country's public budget deficit in the long run. These are important factors that US policy makers should consider in deciding whether or not to support expansion of syringe exchange.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Harrison KM, Song R, Zhang X. Life expectancy after HIV diagnosis based on national HIV surveillance data from 25 states, United States. JAIDS J Acquir Immune Defic Syndr. 2010; 53:124–30.
2. Holtgrave DR, Wolitski RJ, Pals SL, Aidala A, Kidder DP, Vos D, et al. Cost–utility analysis of the housing and health intervention for homeless and unstably housed persons living with HIV. AIDS Behav. 2013; 17:1626–31. [PubMed: 22588529]
3. Hutchinson AB, Patel P, Sansom SL, Farnham PG, Sullivan TJ, Bennett B, et al. Cost-effectiveness of pooled nucleic acid amplification testing for acute HIV infection after third-generation HIV antibody screening and rapid testing in the United States: a comparison of three public health settings. PLoS Med. 2010; 7:e1000342. [PubMed: 20927354]
4. Centers for Disease Control and Prevention. HIV cost-effectiveness. 2014. http://www.cdc.gov/hiv/prevention/ongoing/costeffectiveness. Retrieved Apr 19
5. Prejean J, Song R, Hernandez A, Ziebell R, Green T, Walker F, et al. Estimated HIV incidence in the United States, 2006–2009. PLoS One. 2011; 6:e17502. [PubMed: 21826193]
6. Office of National AIDS Policy. National HIV/AIDS Strategy for the United States. 2010. http://www.whitehouse.gov/sites/default/files/uploads/NHAS.pdf
7. Gold M, Gafni A, Nelligan P, Millson P. Needle exchange programs: an economic evaluation of a local experience. Can Med Assoc J. 1997; 157:255–62. [PubMed: 9269195]

8. Jacobs P, Calder P, Taylor M, Houston S, Saunders LD, Albert T. Cost effectiveness of Streetworks' needle exchange program of Edmonton. Can J Public Health. 1999; 90:168–71. [PubMed: 10401166]
9. Laufer FN. Cost-effectiveness of syringe exchange as an HIV prevention strategy. JAIDS J Acquir Immune Defic Syndr. 2001; 28:273–8.
10. Cabasés JM, Sánchez E. Costs and effectiveness of a syringe distribution and needle exchange program for HIV prevention in a regional setting. Eur J Health Econ. 2003; 4:203–8. [PubMed: 15609186]
11. Kumaranayake L, Vickerman P, Walker D, Samoshkin S, Romantzov V, Emelyanova Z, et al. The cost-effectiveness of HIV preventive measures among injecting drug users in Svetlogorsk, Belarus. Addiction. 2004; 99:1565–76. [PubMed: 15585048]
12. Bayoumi AM, Zaric GS. The cost-effectiveness of Vancouver's supervised injection facility. Can Med Assoc J. 2008; 179:1143–51. [PubMed: 19015565]
13. Pinkerton SD. Is Vancouver Canada's supervised injection facility cost-saving? Addiction. 2010; 105:1429–36. [PubMed: 20653622]
14. Wodak A, Cooney A. Effectiveness of sterile needle and syringe programmes. Int J Drug Policy. 2005; 16S:S31–44.
15. The Office of the Global AIDS Coordinator. PEPFAR blueprint: creating an AIDS-free generation. 2012. http://www.pepfar.gov/documents/organization/201386.pdf
16. National Center for HIV/AIDS, Viral Hepatitis S and TP. Strategic Plan: Division of HIV/AIDS Prevention: 2011 through 2015. 2011. http://www.cdc.gov/hiv/pdf/policies_DHAP-strategic-plan.pdf
17. Centers for Disease Control and Prevention. FY 2013 Full Year CR Operating Plan. http://www.cdc.gov/fmo/topic/BudgetInformation/appropriations_budget_form_pdf/FY2013_CDC_Full-Year_CR_Operating_Plan.pdf
18. Health Omnibus Program Extensions of 1988 Act. http://history.nih.gov/research/downloads/PL100-607.pdf
19. Barr, S. Needle-exchange programs face new federal funding ban. Kaiser health news. 2011 Dec 21. http://www.kaiserhealthnews.org/stories/2011/December/21/needle-exchange-federal-funding.aspx
20. Des Jarlais, DC.; Guardino, V.; Arasteh, K.; Mcknight, C.; Milliken, J.; Purchase, D. Current state of syringe exchange in the known universe. Presentation at the National Syringe exchange Conference; 2010 Nov 17.
21. Tempalski B, Cooper HLF, Friedman SR, Des Jarlais DC, Brady JE, Gostnell K. Correlates of syringe coverage for heroin injection in 35 large metropolitan areas in the US in which heroin is the dominant injected drug. Int J Drug Policy. 2008; 19(Suppl 1):S47–58. [PubMed: 18295468]
22. Huo D, Ouellet LJ. Needle exchange and injection-related risk behaviors in Chicago: A longitudinal study. JAIDS J Acquir Immune Defic Syndr. 2007; 45:108–14.
23. Office of Applied Studies SA and MHSA. Injection drug use and related risk behaviors. The NSDUH Report. 2009 Oct 29. http://www.samhsa.gov/data/2k9/139/139IDU.htm
24. Des Jarlais DC, Pinkerton SD, Hagan H, Guardino V, Feelemyer J, Cooper HLF, et al. 30 Years on selected issues in the prevention of HIV among persons who inject drugs. Adv Prev Med. 2013; 2013 346372.
25. Kahn, JG. Are NEPs cost-effective in preventing HIV infection?. In: Lurie, P.; Reingold, AL.; Bowser, B.; Chen, D.; Foley, J.; Guydish, J., et al., editors. The public health impact of needle exchange programs in the United States and abroad. San Francisco: University of California; 1993. p. 477-511.
26. Kaplan EH, Brandeau ML. AIDS policy modeling by example. AIDS. 1994; 8(Suppl 1):S333–40.
27. Kaplan EH. Economic analysis of needle exchange. AIDS. 1995; 9:1113–9. [PubMed: 8519446]
28. Kral AH, Bluthenthal RN, Lorvick J, Gee L, Bacchetti P, Edlin BR. Sexual transmission of HIV-1 among injection drug users in San Francisco, USA: risk-factor analysis. Lancet. 2001; 357:1397–401. [PubMed: 11356437]

29. Shafer KP, Hahn JA, Lum PJ, Ocha K, Graves A, Moss A. Prevalence and correlates of HIV infection among young injection drug users in San Francisco. JAIDS J Acquir Immune Defic Syndr. 2002; 31:422–31.

30. Strathdee SA, Sherman SG. The role of sexual transmission of HIV infection among injection and non-injection drug users. J Urban Health. 2003; 80:iii7–14. [PubMed: 14713667]

31. Poulin C, Alary M, Bernier F, Carbonneau D, Boily M-C, Joly JR. Prevalence of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* among at-risk women, young sex workers, and street youth attending community organizations in Quebec City, Canada. Sex Transm Dis. 2001; 28:437–43. [PubMed: 11473214]

32. Des Jarlais DC, Arasteh K, McKnight C, Hagan H, Perlman DC, Friedman SR. Using hepatitis C virus and herpes simplex virus-2 to track HIV among injecting drug users in New York City. Drug Alcohol Depend. 2009; 101:88–91. [PubMed: 19108958]

33. Holmberg SD. The estimated prevalence and incidence of HIV in 96 large US metropolitan areas. Am J Public Health. 1996; 86:642–54. [PubMed: 8629714]

34. Friedman SR, Tempalski B, Cooper HLF, Perlis TE, Keem M, Friedman R, et al. Estimating numbers of injecting drug users in metropolitan areas for structural analyses of community vulnerability and for assessing relative degrees of service provision for injecting drug users. J Urban Health. 2004; 81:377–400. [PubMed: 15273263]

35. Brady JE, Friedman SR, Cooper HLF, Flom PL, Tempalski B, Gostnell K. Estimating the prevalence of injection drug users in the U.S. and in large U.S. metropolitan areas from to 2002. J Urban Health. 1992; 2008(85):323–51.

36. Lansky, A.; Finlayson, T.; Johnson, C.; Holtzman, D.; Wejnert, C.; Mitsch, A., et al. Estimating the number of injection drug users in the United States to calculate National Rates of HIV Infection. Poster presentation at the 2012 National Summit on HIV Diagnosis, Prevention and Access to Care; 2012. http://www.hivforum.org/storage/hivforum/documents/_2012NationalSummit_Posting/c_115_lansky.pdf

37. Mathers BM, Degenhardt L, Phillips B, Wiessing L, Hickman M, Strathdee SA, et al. Global epidemiology of injecting drug use and HIV among people who inject drugs: a systematic review. Lancet. 2008; 372:1733–45. [PubMed: 18817968]

38. Lurie P, Gorsky R, Jones TS, Shomphe L. An economic analysis of needle exchange and pharmacy-based programs to increase sterile syringe availability for injection drug users. J Acquir Immune Defic Syndr Hum Retrovirol. 1998; 18:S126–32. [PubMed: 9663635]

39. Galai N, Safaeian M, Vlahov D, Bolotin A, Celentano DD. Longitudinal patterns of drug injection behavior in the ALIVE study cohort 1988–2000: description and determinants. Am J Epidemiol. 2003; 158:695–704. [PubMed: 14507606]

40. McCoy CB, Metsch LR, Chitwood DD, Shapshak P, Comerford ST. Parenteral transmission of HIV among injection drug users: assessing the frequency of multiperson use of needles, syringes, cookers, cotton, and water. J Acquir Immune Defic Syndr Hum Retrovirol. 1998; 18:S25–9. [PubMed: 9663620]

41. Heimer R, Khoshnood K, Bigg D, Guydish J, Junge B. Syringe use and reuse: effects of syringe exchange programs in four cities. J Acquir Immune Defic Syndr Hum Retrovirol. 1998; 18:S37–44. [PubMed: 9663622]

42. Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, et al. Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med. 2011; 365:493–505. [PubMed: 21767103]

43. Tovanabutra S, Robison V, Wongtrakul J, Sennum S, Suriyanon V, Kingkeow D, et al. Male viral load and heterosexual transmission of HIV-1 subtype E in northern Thailand. JAIDS J Acquir Immune Defic Syndr. 2002; 29:275–83.

44. Vickerman P, Hickman M, Rhodes T, Watts C. Model projections on the required coverage of syringe distribution to prevent HIV epidemics among injecting drug users. JAIDS J Acquir Immune Defic Syndr. 2006; 42:355–61.

45. Vickerman, P.; Miners, A.; Williams, J. Assessing the cost-effectiveness of interventions linked to needle and syringe programmes for injecting drug users: an economic modelling report Authors.

2008. http://www.nice.org.uk/nicemedia/pdf/NSPEconomicmodellingFullreportJune08.pdf. Retrieved 2012 Apr 3

46. Bobashev, GV.; Zule, WA.; Morris, RJ. Projecting sexual and injecting risks into future HIV outcomes with agent-based modeling. Poster presentation at the International AIDS Conference; Vienna, Austria. 2010. http://www.rti.org/pubs/bobashev_aids2010_poster.pdf

47. National Research Council. Public financing and delivery of HIV/AIDS Care: securing the legacy of Ryan White. Washington, DC: The National Academies Press; 2005. http://www.iom.edu/Reports/2004/Public-Financing-and-Delivery-of-HIVAIDS-Care-Securing-the-Legacy-of-Ryan-White.aspx

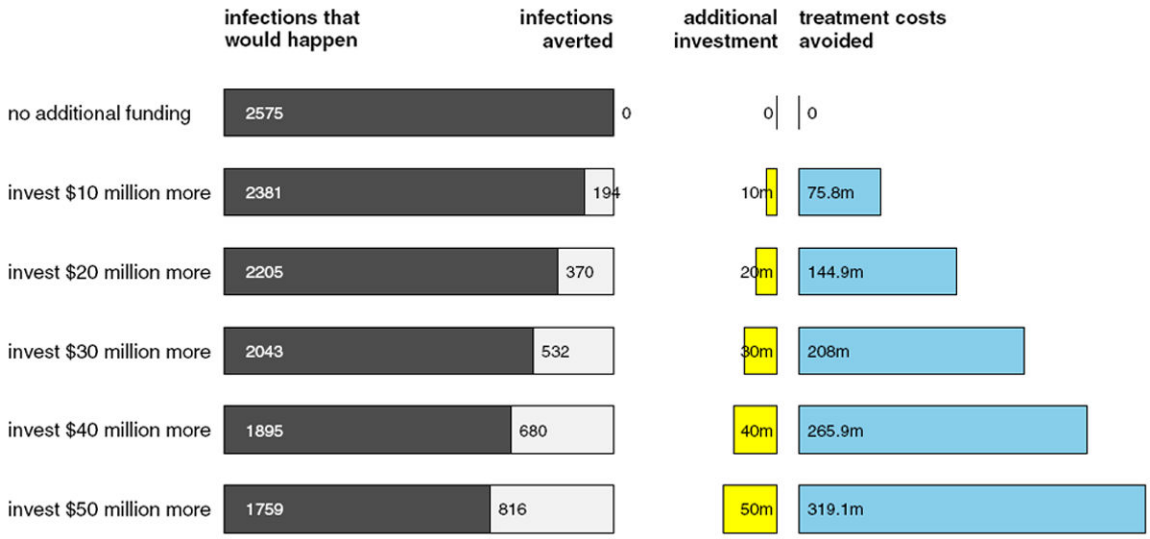

Fig. 1.

Modeled effects of hypothetical increases in syringe exchange funding: HIV infections averted in a 1 year time frame, and resulting savings in lifetime HIV treatment costs (net present value, in 2011 USD)

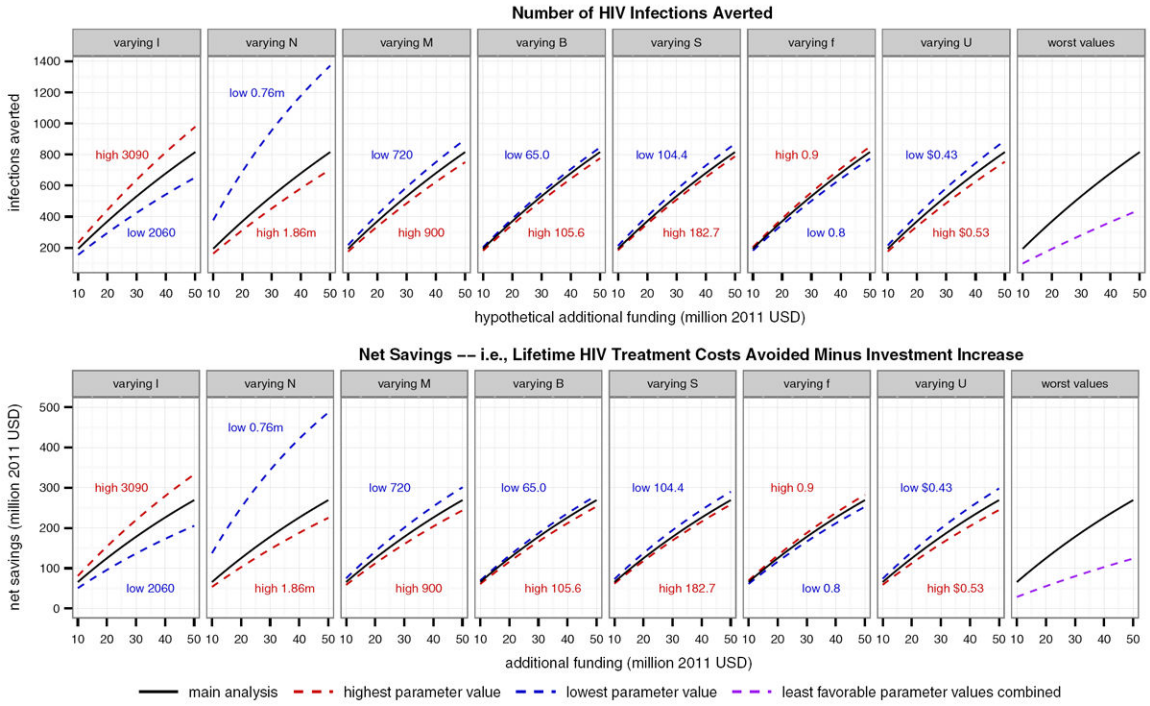

Fig. 2.

Sensitivity analyses with higher/lower values on each parameter + combining all least favorable values

Table 1

Parameter values and sources

Parameter	Main value	Sources/basis	Sensitivity analysis value range
I: number of new HIV infections due to drug injection risk in the US per year in the base case	2,575	Based on CDC's 2009 HIV incidence estimates [5], assuming 50 % of infections in PWID category and 25 % in MSM/PWID category are due to injection risk	2,060–3,090 infections (corresponding to 40 % to 60 % of PWID category and 20 % to 30 % of MSM/PWID category)
N: number of persons who injected drug in the past year in the US	1.55 m	Based on PWID population size estimation by Brady et al. [35]	0.76–1.85 million PWID
M: number of drug injections per PWID per year	812.02	= 365.25 days * 2.8 injections per day * 0.794 Number of injections per day is from Lurie et al. [38]; Tempalski et al. [21]. The factor 0.794 adjusted for the cycling in and out of injection, based on data in Galai et al. [39]	720–900 injections
B: number of injections with a borrowed syringe (or number of borrows) per PWID per year in the base case	81.20	= ***M*** * 10% 10 % (proportion of all injections) was based on calculation using data from NIDA Cooperative Research Evaluation Study presented in by McCoy et al. [40], with down adjustment to account for reduction in borrowing over time	64.96–105.56 borrows (corresponding to 8 % to 13 % of all injections)
S: average number of brand new syringes a PWID uses per year in the base case	146.16	= (***M*** − ***B***)/5 On average, a PWID uses a syringe he/she owns five times, based on Heimer et al. [41] and Huo and Ouellet [22]	104.40–182.71 syringes (corresponding to 7–4 uses per own syringe)
f: supply increase discount factor	0.855	= (1 - ***w***)(1 - ***r***) Assuming that ***w*** (proportion of NSP syringes that go unused) = 5 % and that ***r*** (proportion of NSP syringes that replace non-NSP syringes which would have been used otherwise) = 10 %	0.8–0.9
U: syringe exchange unit cost	$0.48 per syringe	Based on cost data reported in NASEN survey	$0.43–$0.53
T: lifetime HIV treatment cost per person (net present value)	$391.2 k	CDC published cost in 2010 dollars [4] converted into 2011 dollars using CPI for medical costs in US cities	

Table 2

Estimated effects of hypothetical increases in syringe exchange funding: HIV infections, HIV infections averted, cost per infection averted, HIV treatment costs avoided, net savings, and rate of return on investment

Additional investment	Infections	Infections averted	Cost per infection averted	HIV treatment costs avoided	Net savings	Rate of return on investment	
						Average	Marginal
$0	2575	0	–	$0	$0	–	–
$10 million	2381	194	$51,601	$75.8 million	$65.8 million	7.58	7.58
$20 million	2205	370	$53,999	$144.9 million	$124.9 million	7.25	6.91
$30 million	2043	532	$56,414	$208.0 million	$178.0 million	6.93	6.31
$40 million	1895	680	$58,849	$265.9 million	$225.9 million	6.65	5.79
$50 million	1759	816	$61,302	$319.1 million	$269.1 million	6.38	5.32

All currency values are in 2011 US dollars. Future treatment costs savings are discounted and presented in net present value