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VARIOUS TOPICS

The Impact of Needle-Exchange Programs on the Spread of HIV Among Injection Drug Users: a Simulation Study

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ABSTRACT Objective. *To determine the impact of the implementation of a needle-exchange program (NEP) on the spread of human immunodeficiency virus (HIV) in an injection drug user (IDU) community. We conducted a Monte Carlo simulation study of a theoretical population of 10,000 IDUs. The population was followed monthly from 1984 to 2000. HIV was assumed to be transmitted only by needle sharing. The NEP was introduced in 1989 and evaluated over a period of 11 years. The impacts of the proportion of the population attending the NEP, the risk level of IDUs attending the NEP, the reduction in needle-sharing frequency, and the number of new needle-sharing partners acquired at the NEP on prevalence and incidence of HIV were determined. Increasing the proportion of the population who always attend the NEP and eliminating needle-sharing incidents among IDUs who always attended the NEP were the most effective ways of reducing the spread of HIV. Attracting high-risk users instead of lower risk users to the NEP also reduced the spread of HIV, but to a lesser extent. NEPs are effective at reducing the spread of HIV; even under the worst case scenario of low risk users more likely to attend the NEP, one additional partner per month as a result of attending the NEP, and poor NEP attendance, the estimated prevalence was still less than that from the scenario without an NEP. Under our model, NEPs were shown to reduce the spread of HIV significantly. Efforts should be focused on getting as many IDUs as possible to become regular NEP attenders and stop sharing needles rather than partially reducing the frequency of sharing by a larger number of IDUs.*

KEYWORDS *HIV transmission, Injection drug user, Monte Carlo simulation, Needle-exchange program.*

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INTRODUCTION

Needle-exchange programs (NEPs) have been introduced in many cities to attempt to reduce the impact of human immunodeficiency virus (HIV) on injection-drug-using (IDU) communities.[1,2] However, there has been much controversy surrounding their implementation.[3,4] In fact, before March 31, 1998, federal funding of NEPs was banned in the United States.[5] Some NEP critics believe that NEPs increase the incidence of HIV in the IDU population by facilitating the formation of new social networks. Results from a cohort study of IDUs in Montreal, Canada, showing that consistent NEP users are 10.5 times more likely (95% confidence interval [CI], 2.7–41.0) to seroconvert than IDUs who do not attend an NEP, added fuel to this argument.[6] Other evidence, however, has shown that NEP users are at higher risk of HIV infection than nonusers before they start attending the NEP, so that higher rates of seroincidence among NEP users are to be expected.[7–10]

While the effectiveness of NEPs can vary according to such factors as whether individuals exchange their own syringes,[11] proponents of NEPs have estimated[12] the number of HIV infections that could have been prevented in the United States between 1987 and 2000 to be between 4,000 and 10,000. Seroprevalence was shown to increase by 5.9% per year in 52 cities without NEPs and decrease by 5.8% per year in 29 cities with NEPs,[13] and cost-effectiveness analyses have shown that the cost per HIV infection averted is considerably less than the lifetime costs to treat HIV infection.[14] Such data have prompted some to push for governmental support of needle-exchange programs.[15]

The prevalence of HIV infection among injection drug users (IDUs) in Vancouver increased dramatically, from a fairly stable rate[16,17] of 3%–4% in the late 1980s and early 1990s to 23.2% in 1996 among the first 1,006 participants enrolled in the Vancouver Injection Drug Use Study (VIDUS).[18] Of 257 uninfected subjects who attended their first semiannual follow-up visit, 24 had seroconverted,[18] yielding an estimated annual HIV incidence of 18.6 per 100 person-years (95% CI, 11.1–26.0). This increase in the prevalence of HIV occurred despite the implementation of a needle-exchange program in 1989 that by 1996 exchanged 2.3 million needles per year.[7] Similar explosive increases in HIV prevalence among IDUs have been documented in other cities.[19–22]

Simulation studies have been used by others to model the spread of HIV infection among injecting drug users.[23–29] Early work modeled the spread of HIV infection through shared drug-injecting equipment by assuming a homogeneously mixing population of IDUs in which all needles were shared in randomly selected shooting galleries.[23]

An elaboration of this model considered behavior changes due to knowledge of HIV status and cleaning of injection equipment after use by some addicts.[24] A model of the spread of HIV infection in situations similar to a single high-volume shooting gallery with varying numbers of partners and frequency of injection showed[25] that, within each level of injecting frequency, a substantial reduction in the spread of HIV could be achieved by increasing the rate of needle cleaning from low (25%) to moderate (50%). Increasing to a high rate of needle cleaning (75%) had less impact.

Instituting a public health intervention program that reduced the sharing of equipment in the IDU population by half when the prevalence of HIV in the population was low (1%) early in the epidemic was demonstrated[26] to be much more effective than waiting until the prevalence was high (40%). A stochastic simulation model to study the spread of HIV in populations of IDUs with low prevalence but

continuing risk behaviors determined the maximum prevalence to be 90% when contacts were assumed to be random and short lived, as might occur in a shooting gallery, but 50% when partnerships were formed in the "buddy" model.[27] The authors concluded that reducing needle sharing with strangers was more effective than reducing the overall number of needle-sharing partners, and prevention that focused on new IDUs could greatly reduce HIV incidence.

A model of the spread of HIV among IDUs in Italy found strong support for the hypothesis of varying infectivity during the course of HIV disease, with infectiousness peaking soon after infection.[28] Models have also been developed to determine such factors as the optimal needle-exchange rate, when it is justifiable to implement an NEP, and the optimal program size of a NEP.[30]

In this article, we describe the results of a simulation study of the impact of needle-exchange programs on the course of HIV epidemics among IDUs. To determine which factors have an impact on the effectiveness of an NEP, the effect of a NEP was investigated under various conditions in regard to the proportions of the IDU population attending the NEP, the risk characteristics of the population attending the NEP, the reduction in needle-sharing frequency, and the number of additional needle-sharing partners acquired as a result of attending the NEP. As much as possible, we based the model on empiric data from the VIDUS study.[18] We focused our attention on the impact of the NEP on this population.

METHODS

Monte Carlo simulation was used to study the effectiveness of different NEP scenarios to slow the spread of HIV in a network of 10,000 IDUs representative of the VIDUS cohort in Vancouver, British Columbia, Canada, between 1984 and 2000. The network is defined by the formation and dissolution of needle-sharing partnerships in an open population. As illustrated by the flowchart in Fig. 1, the natural history of HIV infection was modeled by dividing the population into three groups: HIV-negative individuals, susceptible $X^k(t_i)$; HIV-positive individuals in the acute phase of infection, $Y^k_A(t_i)$; and HIV-positive individuals in the latent phase of infection, $Y^k_L(t_i)$, where the *latent phase* was defined as the period following the acute

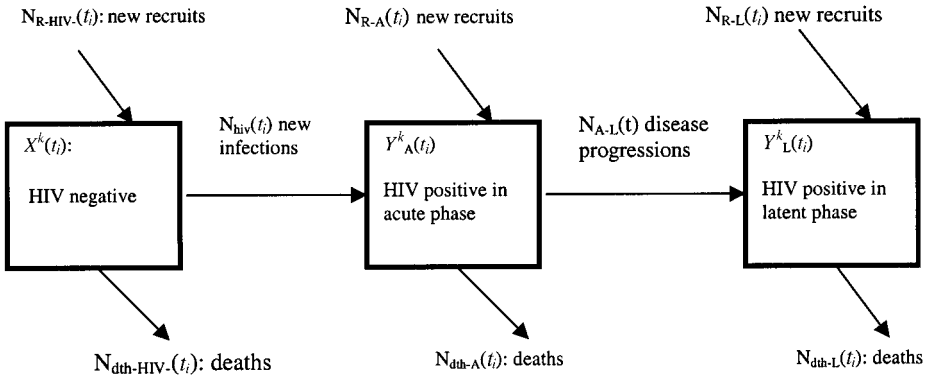

FIGURE 1. Flowchart of disease progression. Number of injecting drug users (IDUs) in risk group k at time $t_i = N^k(t_i) = X^k(t_i) + Y^k_A(t_i) + Y^k_L(t_i)$. Number of IDUs in total population at time $t_i = N(t_i) = \Sigma_k N^k(t_i)$.

phase. HIV-negative individuals became infected through needle sharing with HIV-positive individuals and passed from the acute stage of HIV infection to the latent phase at time T after infection. Sexual partnerships were not modeled because needle sharing was thought to be the cause of the majority of HIV transmissions in this population. The simulation process is summarized in the sequence of events that follows.

In the first step, the epidemic was seeded by randomly infecting 1% of the IDU population at the beginning of the simulation at time t_1, corresponding to a calendar time t_c of January 1984.

Second, the formation of the initial needle-sharing network occurred in the first time step:

1. The population of IDUs at time t_1, $N(t_1)$, was divided into seven groups representing different risks of being selected to form a partnership, according to a fixed distribution represented by f^k_{rg} ($k = 0, \ldots, 6$). We defined $N^k_p(t_i)$ [$= f^k_{rg}N(t_i)$] as the number of individuals in group k who were in p partnerships at the beginning of time interval t_i and RR^k_p as the relative risk of an individual in group k currently involved in p partnerships at time t_i to be selected to form a new partnership.
2. At t_1, $N(t_1)\mu(1984)/2$ unique partnerships were formed, so that the mean number of partnerships per person was $\mu(1984)$. Partnerships were formed by randomly selecting pairs of individuals with replacement from the population of individuals available for partnerships. The probability of individuals in risk group k being selected to be a member of a partnership was increased by a factor RR^k_p by proportionately weighting those individuals in the set of random numbers from which samples were drawn. Needle-sharing partnerships were generated in a proportionate mixing pattern with respect to risk weighting; that is, partnerships were formed randomly between individuals with different risk weighting depending on the availability of a type of partner. Therefore, the probability $P^{kk'}_{ij}(t_i)$ that a partnership is formed between any two individuals of risks k and k' is given by the product of the two probabilities $P^k(t_i)$ and $P^{k'}(t_i)$, where $P^k(t_i) = \Sigma_p(RR^k_p \cdot N^k_p(t_i))/\Sigma_k\Sigma_p(RR^k_p \cdot N^k_p(t_i))$ and $P^{k'}(t_i) = \Sigma_p(RR^{k'}_p \cdot N^{k'}_p(t_i))/\Sigma_{k'}\Sigma_p(RR^{k'}_p \cdot N^{k'}_p(t_i))$ if $k \neq k'$; $P^k(t_i) = \Sigma_p(RR^k_p \cdot N^k_p(t_i))/\Sigma_k\Sigma_p(RR^k_p \cdot N^k_p(t_i))$ and $P^{k'}(t_i) = \Sigma_p(RR^{k'}_p \cdot N^{k'}_p(t_i)) - RR^{k'}_p)/(\Sigma_{k'' \neq k}\Sigma_p(RR^{k''}_p \cdot N^{k''}_p(t_i)) - RR^{k'}_{p'}$ *if* $k = k'$.

Third, events occurred in discrete time thereafter. For each time interval t_i, $i = 1, \ldots, 193$, representing 1 month between calendar time $t_c = 1984$ and 2000, the following set of events occurred:

1. *Partnership dissolution.* $N_{pd}(t_i)$ existing needle-sharing partnerships were dissolved. The probability of a partnership dissolving $pd_{pp'}$ depended on the number of partners of each of the individuals in the pair, p and p', such that $pd_{pp'} = pd_p + pd_{p'}$. Partnerships were also dissolved as a result of the death of one member of the pair (see the event, Deaths).
2. *Frequency of needle-sharing incidents.* Each month, the number of needle-sharing incidents c_n was randomly assigned to each partnership according to a Poisson distribution with mean $\lambda_{nsi}(t_i)$.
3. *Transmission of HIV.* $N_{hiv}(t_i)$ new HIV infections occurred among partnerships discordant with respect to HIV status. Transmission occurred within

a discordant partnership with probability $p_{\text{hiv}} = (1 - (1 - \beta)^{C_n})$, where c_n is the number of needle-sharing incidents during the month t_i in that partnership, and β is the probability of HIV transmission for each needle-sharing incident for partnerships in which the HIV-positive individual is in the acute ($\beta = \beta_A$) or latent phase ($\beta = \beta_L$) of disease.

4. *Introduction of the NEP program.* The needle-exchange program was introduced at time t_{NEP}. After t_{NEP}, all IDUs in risk groups $k = 1, \ldots, 6$ were selected randomly to be never users of the NEP (N-NEP), sometimes users of the NEP (S-NEP), and always users of the NEP (A-NEP), with probabilities $f^k_{\text{N-NEP}}(t_c)$, $f^k_{\text{S-NEP}}(t_c)$, $f^k_{\text{A-NEP}}(t_c)$, respectively. Once selected to be a sometimes or always user of the NEP, an IDU maintained that behavior throughout his lifetime. Prior to $t_c = t_{\text{NEP}}$, the number of needle-sharing incidents for all partnerships followed a Poisson distribution with parameter $\lambda_{\text{nsi}}(t_i) = \lambda_{\text{N-NEP}}(t_c)$. After introduction of the NEP ($t_c = t_{\text{NEP}}$), $\lambda_{\text{nsi}}(t_i) = \lambda_{\text{N-NEP}}(t_c)$, $\lambda_{\text{S-NEP}}(t_c)$, or $\lambda_{\text{A-NEP}}(t_c)$ if both members of the partnership were never, sometimes, or always users of the NEP, respectively. Furthermore, $\lambda_{\text{nsi}}(t_i) = (\lambda_{\text{S-NEP}}(t_c) + \lambda_{\text{N-NEP}}(t_c))/2$ if one partner sometimes attended the NEP and the other never attended; $\lambda_{\text{nsi}}(t_i) = 0$ if at least one partner always attended the NEP.
5. *Progression from acute to latent phase.* All $N_{\text{A-L}}(t_i)(N_{\text{A-L}}(t_i) = \Sigma_k \Sigma_{\tau=60,90} Y_A^k(t_c - \tau))$ HIV-positive individuals who were infected at least two but not more than three time periods previously moved from the acute phase to the latent phase, where T, the duration of the acute phase, followed a normal distribution with mean μ_T and variance σ^2.
6. *Deaths.* $N_{\text{dth-HIV-}}(t_i)$, $N_{dth\text{-}A}(t_i)$, and $N_{\text{dth-L}}(t_i)$ deaths occur randomly, respectively, among HIV-negative IDUs, HIV-positive IDUs in the acute phase, and HIV-positive IDUs in the latent phase following monthly mortality rates of δ_0 and δ_1, respectively, for HIV-negative and HIV-positive individuals.
7. *Influx of individuals into population.* $N_{\text{R-HIV-}}(t_i)$ HIV-negative individuals, $N_{\text{R-A}}(t_i)$ HIV-positive individuals in the acute phase, and $N_{\text{R-L}}(t_i)$ HIV-positive individuals in the latent phase entered the population according to Poisson distributions with parameters τ_0, τ_1, and τ_2. The numbers of individuals entering the population were randomly distributed by risk groups according to f^k_{rg} so, for example, an average of $\tau^k_0 = f^k_{\text{rg}}\tau_0$ new HIV-negative recruits were assigned to risk group k.
8. *Formation of new partnerships.* $N_{\text{pf}}(t_i)$ new needle-sharing partnerships were formed in time interval t_i to (1) replace the $N_{\text{pd}}(t_i)$ partnerships that dissolved; (2) replace the partnerships in which one member had died; (3) generate partnerships for new members of the IDU population; and (4) increase the number of partnerships as a result of NEP attendance or the introduction of cocaine into the community, if necessary. Pairs of individuals were chosen to form the partnerships as described in frequency of needle-sharing incidents above. In any given time interval t_i, it was possible for some individuals to have several relationships dissolve and for others to have all of their relationships remain intact. Correspondingly, some individuals may have acquired several new needle-sharing partners, while others did not acquire any. The number of needle-sharing partners for an individual was allowed to vary during an individual's lifetime. Both concurrent and sequential partnerships were possible.

The changes in the numbers of HIV-negative individuals, HIV-positive individuals in the acute phase, and HIV-positive individuals in the latent phase between time intervals t_i and t_{i+1} are $\Delta_{\text{HIV-}}(t_i) = N_{\text{R-HIV-}}(t_i) - N_{\text{dth-HIV-}}(t_i) - N_{\text{hiv}}(t_i)$, $\Delta_{\text{HIV+A}}(t_i) = N_{\text{R-A}}(t_i) + N_{\text{hiv}}(t_i) - N_{\text{A-L}}(t_i) - N_{\text{dth-A}}(t_i)$, and $\Delta_{\text{HIV+L}}(t_i) = N_{\text{R-L}}(t_i) + N_{\text{A-L}}(t_i) - N_{\text{dth-L}}(t_i)$, respectively.

The fourth step involves parameter values as follows:

1. *Risk group*. The probability of an individual being in risk group k, (f^k_{rg}), was chosen to be similar to distributions of needle-sharing behaviors in VIDUS (unpublished data, M. T. Schechter, 1998). The percentage of the population assumed not to share needles was $f^0_{\text{rg}} = 17.5\%$ ($\text{RR}^0_0 = 0$), and $f^1_{\text{rg}} = 17.5\%$ was assumed to have one long-term needle-sharing partner at a time ($\text{RR}^1_p = 1$ if $p = 0$ and 0 if $p > 0$). The remaining 65% of the population was assumed to have multiple needle-sharing partners. Of the population, 40% ($f^2_{\text{rg}} = 40\%$) was assumed to be at low risk of being selected for pair formation ($\text{RR}^2_p = 1$ for all p). The probability of being selected to be a member of a pair was assumed to be increased by a multiple $\text{RR}^{3,\ldots,6}_p = 2$, 3, 4, and 5 for all p for $f^3_{\text{rg}} = 15\%$, $f^4_{\text{rg}} = 5\%$, $f^5_{\text{rg}} = 2.5\%$, and $f^6_{\text{rg}} = 2.5\%$ of the population, respectively. This variation in probabilities of being selected for pair formation mimics the concept of a heterogeneous higher risk group for which the numbers of needle-sharing partners and the rate of acquiring new partners can vary between individuals. This allows for gradation of risk, rather than just high and low risk.
2. *Dissolution of partnerships*. The probability of dissolution pd_p for an individual who currently is in p partnerships was equal to .0002 if the IDU had no other partners, to .0035 if the IDU had $1 \le p \le 4$ other partners, and to .05 if the IDU had more than 5 other partners ($p > 5$).
3. *Needle-exchange program*. The needle-exchange program was introduced into the simulated population at $t_{\text{NEP}} = 1989$, as was the case in Vancouver. In the baseline scenario, the probabilities that an IDU in risk group $k = 1, \ldots, 6$ was assigned to be a never ($f^k_{\text{N-NEP}}(t_c)$), sometimes ($f^k_{\text{S-NEP}}(t_c)$), and always ($f^k_{\text{A-NEP}}(t_c)$) user of the NEP were chosen to reflect NEP attendance in VIDUS (unpublished data, M. T. Schechter, 1998). In VIDUS, 10% of the population remained never users. Between 1989 and 1996, attendance at the NEP increased gradually from no use until 60% of the population were sometimes users (between less than once a month and every few days), and 30% of the population were always or daily users (VIDUS, unpublished data, M. T. Schechter, 1998). Therefore, $f^k_{\text{A-NEP}}(t)$ and $f^k_{\text{S-NEP}}(t)$ linearly increased from 0% at time $t_c = 1989$ to 30% and 60%, respectively, at $t_c = 1996$ for all $k = 1, \ldots, 6$, and $f^k_{\text{N-NEP}}(t_c)$ declined from 100% at $t_c = 1989$ to 10% when $t_c = 1996$ and remained at 10% for all $t_c > 1996$ for all k.
4. *Frequency of needle-sharing incidents*. The number of needle-sharing incidents per partnership per month for never users of the NEP followed a Poisson distribution with mean $\lambda_{\text{N-NEP}}(t_c) = 2.5$ before $t_c = 1994$ and increased linearly to a mean of $\lambda_{\text{N-NEP}}(t_c) = 5.5$ by $t_c = 1996$. For sometimes users of the NEP, the mean number of needle-sharing incidents per partnership per month, since the inception of the NEP at $t_c = 1989$, was decreased linearly from $\lambda_{\text{S-NEP}}(t_c) = 2.5$ to $\lambda_{\text{N-NEP}}(t_c) = 1.615$ between $1989 < t_c < 1994$ and was increased linearly to $\lambda_{\text{N-NEP}}(t_c) = 3.9$ by 1996. The increase in the

needle-sharing incidents among sometimes and never users between the periods 1994 and 1996 is due to the introduction of cocaine into the drug-using community in Vancouver during this period since cocaine injectors are known to inject repeatedly within a short span of time. Always users of the NEP were assumed to have no needle-sharing incidents and thus were effectively moved into the group of nonsharers.

5. *Needle-sharing partners.* At the beginning of the simulation, the average number of needle-sharing partners per IDU per month in the population was $\mu(1984) = 2$ and ranged from 0 to 16, corresponding to the distribution of the number of needle-sharing partners of VIDUS participants (unpublished data). The average number of partners per IDU was linearly increased to $\mu(1996) = 3.85$ per month between 1994 and 1996 to reflect the increase in partners associated with the introduction of injected cocaine into the drug-using community in Vancouver.[17] Because cocaine is injected more frequently and is associated with bingeing, cocaine users tend to have more needle-sharing partners.[31–33]
6. *Transmission of HIV.* Individuals are believed to be most infectious in primary infection, the period immediately following infection, when the level of viral load peaks[34,35] and less infectious later in disease after the level of viral load has declined to a set point[36] ($\beta_A > \beta_L$)). The probability of transmission of HIV has been estimated to be between .003 and .004 per accidental needle-stick injury[37] and .0067 per needle-sharing incident among IDUs.[38] Following the work of Kretzschmar and Weissing,[27] we assumed that the probability of HIV transmission per needle shared was $\beta_A = .054$ if the HIV-positive individual was in the acute phase of infection and $\beta_L = .00126$ per needle shared if the HIV-positive individual was in the latent phase. The increase in the probability of transmission of HIV by a factor of 40 is conservative given that data from VIDUS has shown that the plasma viral load (pVL) of individuals in the acute phase of infection is approximately 100 times higher than the pVL of individuals who had been infected for 6 months or longer (VIDUS, unpublished data, M. T. Schechter, 1997).
7. *Mortality.* The mortality rates of HIV-negative and HIV-positive individuals were set to $\delta_1 = 0.0017$ and $\delta_0 = 0.0042$ per month, respectively.[39]
8. *Influx of IDUs into the population.* The number of IDUs joining the population each month was assumed to follow a Poisson process with mean $\Lambda = 12$. On average, 10 of these individuals were assumed to be HIV negative, 1 was HIV positive in the acute phase, and 1 was HIV positive in the latent phase.
9. *Time of progression.* The time of progression from the acute to the latent phase T was assumed to be normally distributed with a mean μ_T of 90 days and a variance σ_T^2 of 100 days.[36]

The baseline parameter values used in the simulation are summarized in Table 1.

DIFFERENT NEEDLE-EXCHANGE PROGRAM SCENARIOS INVESTIGATED

The effect of the NEP on incidence and prevalence of HIV was estimated after varying four assumptions: the frequency of attendance at the NEP, the number of

TABLE 1. Parameter values used in baseline scenario

Parameter	Value	Symbol	Reference
Size of simulated population	10,000	$N(t_1)$	—
Start date of simulation	1984	t_1	—
Date of introduction of NEP	1989	t_{60}	18
Initial prevalence of HIV in the simulated population	1%		16, 17
Proportion of population			
With no partners	17.5%	f_{rg}^0	18
Who are sequentially monogamous (risk group 1)	17.5%	f_{rg}^1	
In risk group 2	40.0%	f_{rg}^2	
In risk group 3	15.0%	f_{rg}^3	
In risk group 4	5.0%	f_{rg}^4	
In risk group 5	2.5%	f_{rg}^5	
In risk group 6	2.5%	f_{rg}^6	
Relative risk of being selected to be part of a needle-sharing partnership			
Risk group 0	0	RR^0	–
Risk group 1	1	RR_0^1	
	0	RR_1^1	
Risk group 2	1	$RR_{p,\ p\geq 0}^2$	
Risk group 3	2	$RR_{p,\ p\geq 0}^3$	
Risk group 4	3	$RR_{p,\ p\geq 0}^4$	
Risk group 5	4	$RR_{p,\ p\geq 0}^5$	
Risk group 6	5	$RR_{p,\ p\geq 0}^6$	
Per capita mortality rate			
HIV-negative individuals	0.0017	δ_0	29
HIV-positive individuals	0.0042	δ_1	
Rate of needle-sharing partners			
Before 1994	2	$\mu(t_c)$	VIDUS study unpublished data (M. T. Schechter, 1998)
After 1996	3.85	$\mu(t_c)$	
Between 1994 and 1996	Linear increase		
Rates of needle-sharing incidents $\lambda_{nsi}(t_c)$			
Never users before 1994	2.5	$\lambda_{N\text{-}NEP}(t_c)$	VIDUS study unpublished data (M. T. Schechter, 1998)
Never users after 1996	5.5		
Sometimes users before NEP ($t_c < 1989$)	2.5	$\lambda_{S\text{-}NEP}(t_c)$	
Sometimes users by 1994	Decrease to 1.62		
Sometimes users by 1996	Increase to 3.9		
Probability of HIV transmission during a single needle-sharing incident			
HIV+ individual in acute phase	.054	β_A	27
HIV+ individual in latent phase	.00126	β_L	
Duration of acute phase	N(90,100)	T	36
Probability of a partnership dissolving if each member of pair has p partners			
1 Partner	.0002	pd_1	—
2–5 Partners	.0035	$pd_p,\ p = 2,\ldots,5$	
>5 Partners	.05	$pd_p,\ P > 5$	

TABLE 1. ***Continued***

Parameter	Value	Symbol	Reference
Rate of influx of new IDU			
HIV negative	Poisson(10)	τ_0	—
HIV positive in acute phase	Poisson(1)	τ_1	
HIV positive in latent phase	Poisson(1)	τ_2	
Overall NEP attendance			
Before 1989	0%	$F_{\text{N-NEP}}(t_c)$	VIDUS study unpublished data
By 1996 (baseline scenario)			
Never users	10%	$F_{\text{N-NEP}}(t_c)$	
Sometimes users	60%	$F_{\text{S-NEP}}(t_c)$	
Always users	30%	$F_{\text{A-NEP}}(t_c)$	

IDU, injection drug user; NEP, needle-exchange program.

additional needle-sharing partners, the probability of NEP attendance per risk group, and the reduction of needle-sharing incidents due to NEP attendance.

Frequency of Needle-Exchange Program Attendance

The overall proportions of the IDU population who were never ($F_{\text{N-NEP}}$), sometimes ($F_{\text{S-NEP}}$), or always users ($F_{\text{A-NEP}}$) of the NEP in 1996 were set, respectively, at 10%, 60%, and 30% (moderate NEP use, baseline scenario); 10%, 30%, and 60% (high NEP use); or 20%, 70%, and 10% (low NEP use).

Number of Additional Needle-Sharing Partners

The effect of the introduction of an NEP was estimated with and without the assumption that NEP attendance results in the formation of new needle-sharing partnerships among IDUs that attend the NEP. While data from VIDUS has shown that the NEP did not result in new needle-sharing partnerships among the IDUs in Vancouver [30], we wanted to determine the impact of acquiring new partnerships at the NEP. Accordingly, the number of additional needle-sharing partnerships per month as a result of NEP attendance was assumed to be $\Delta = 0$ (baseline scenario), 0.5, or 1. The mean number of needle-sharing partnerships per month among IDUs who attended the NEP was then $\mu(1989) = \mu(1984) + \Delta$, where $\mu(1984)$ was the mean rate of needle-sharing partnerships per month before attending the NEP.

Probability of Needle-Exchange Program Attendance per Risk Group

The probability of NEP attendance for each risk group was also varied: equal probability of NEP attendance by risk weights, greater probability of NEP attendance among high-risk IDUs (baseline scenario), or greater probability of NEP attendance among low risk IDUs. The probabilities of attending the NEP for each risk group are shown in Table 2 for each scenario.

Simulations for each of the 27 combinations of the above three parameters were performed.

Frequency of Needle-Sharing Incidents

In addition to the 27 combinations described above, different assumptions about the reduction ($\Delta_{\lambda\text{S-NEP}}$, $\Delta_{\lambda\text{A-NEP}}$) in frequency of needle-sharing incidents among some-

TABLE 2. Probability of Needle-Exchange Program (NEP) attendance by risk level *k* for scenarios in which attendance varies by risk level

		Overall percentages of never, sometimes, and always users of the NEP								
		$F_{\text{N-NEP}}$ 10%, $F_{\text{S-NEP}}$ 60%, $F_{\text{A-NEP}}$ 30%, Probability by risk level			$F_{\text{N-NEP}}$ 10%, $F_{\text{S-NEP}}$ 30%, $F_{\text{A-NEP}}$ 60%, Probability by risk level			$F_{\text{N-NEP}}$ 20%, $F_{\text{S-NEP}}$ 70%, $F_{\text{A-NEP}}$ 10%, Probability by risk level		
NEP attendance scenarios	Risk level *k*	$f^k_{\text{N-NEP}}$	$f^k_{\text{S-NEP}}$	$f^k_{\text{A-NEP}}$	$f^k_{\text{N-NEP}}$	$f^k_{\text{S-NEP}}$	$f^k_{\text{A-NEP}}$	$f^k_{\text{N-NEP}}$	$f^k_{\text{S-NEP}}$	$f^k_{\text{A-NEP}}$
High-risk IDUs more likely to attend NEP	1, 2	.11	.61	.28	.13	.29	.58	.22	.717	.075
	3	.10	.60	.30	.05	.35	.60	.20	.70	.10
	4	.05	.65	.30	.05	.30	.65	.10	.70	.20
	5	.05	.50	.45	.00	.25	.75	.05	.65	.30
	6	.05	.35	.60	.00	.20	.80	.00	.60	.40
All risk groups equally likely to attend NEP	1, . . . ,6	.10	.60	.30	.10	.30	.60	.20	.70	.10
Low-risk IDUs more likely to attend NEP	1, 2	.065	.61	.325	.075	.30	.625	.165	.725	.11
	3	.09	.60	.31	.10	.29	.61	.19	.71	.10
	4	.20	.60	.20	.10	.35	.55	.30	.65	.05
	5	.35	.55	.10	.20	.40	.40	.35	.60	.05
	6	.515	.42	.065	.575	.16	.265	.715	.265	.22

times and always users as a result of attending the NEP were investigated. In the models described above, we assumed that the number of needle-sharing incidents per month per partnership among sometimes users decreased from $\lambda_{S\text{-}NEP}(t_c) = 5.5$ when $t_c < 1989$ to 3.9 when $t_c = 1996$ (a $\Delta_{\lambda S\text{-}NEP} = 30\%$ reduction) as a result of attending the NEP, and that there were no needle-sharing incidents among partnerships in which at least one member was an always user of the NEP (a $\Delta_{\lambda A\text{-}NEP} = 100\%$ reduction). We varied the percentage reduction in needle-sharing incidents among sometimes users of the NEP from $\Delta_{\lambda S\text{-}NEP} = 30\%$ to 70% and among always users of the NEP from $\Delta_{\lambda A\text{-}NEP} = 90\%$ to 100%.

The baseline scenario that most closely reflects the epidemic in Vancouver with respect to input parameters is the one in which there were no new partners as a result of attending the NEP, higher risk IDUs were more likely to attend the NEP, and there was moderate NEP use. We performed 100 simulations for each combination of parameters investigated. For each set of simulations, the mean and standard deviation of the prevalence and incidence of HIV in the simulated population by calendar year were calculated. HIV incidence was calculated based on the incidence density approach in terms of person-years of observation. The simulation programs were written in the C programming language and performed on a SparcStation Unix-based computer. Separate random number generating routines were used to generate random numbers from the uniform, normal, and Poisson distributions.

RESULTS

The mean overall incidence of HIV between 1984 and 2000 from sets of 100 simulations of the population is shown in Fig. 2 for four scenarios: no NEP, high NEP use, moderate NEP use (baseline), and low NEP use. In these scenarios, individuals

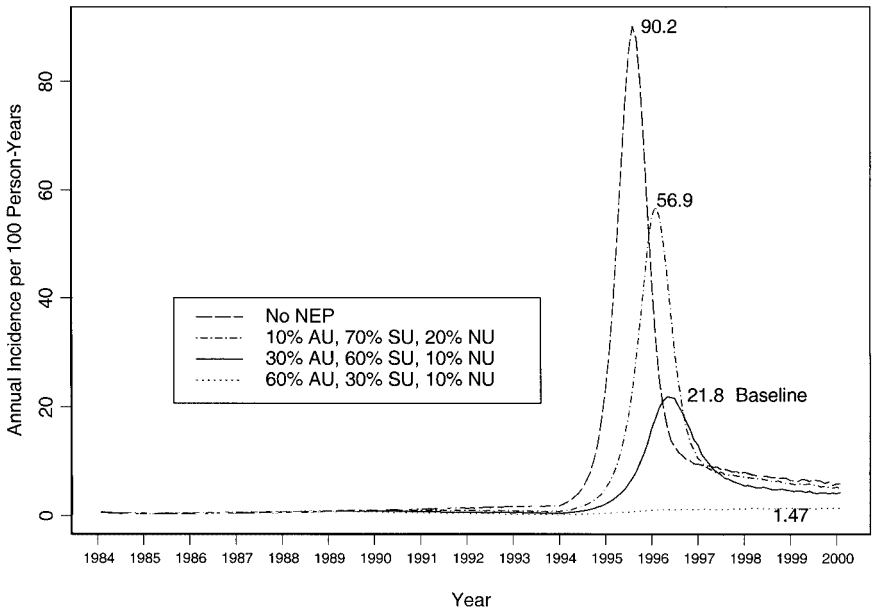

FIGURE 2. Mean seroincidence by percentages of injecting drug users (IDUs) who always (AU), sometimes (SU), or never (NU) attend the needle-exchange program (NEP).

with the highest risk scores are assumed to be most likely to attend the NEP, and NEP attendance was assumed to yield no new needle-sharing partners.

With no NEP, incidence peaked at 90.2 per 100 person-years in September 1995. With low NEP use, incidence peaked at 56.9 per 100 person-years in March 1996. With baseline and high NEP use, incidence peaked at 21.8 per 100 person-years in September 1996 and 1.47 per 100 person-years in June 1997, respectively. In the scenarios without an NEP, the prevalence of HIV in January 2000 was 64%, and the number of cumulative infections since 1984 was 6,491. With low, moderate (baseline), and high use of the NEP, the estimated prevalences in January 2000 were 52.9%, 36.6%, and 10.7%, respectively, and the numbers of cumulative infections were 5,454, 3,677, and 998. Under the baseline scenario, for which the input parameters most closely reflect the situation in Vancouver, the peak incidence of 21.8 per 100 person-years closely approximates the peak incidence observed in VIDUS,[18] and the estimated prevalence of HIV in January 2000 agrees with prevalence estimates from the VIDUS study (unpublished data, M. T. Schechter, 2000).

Figure 3 shows the mean HIV incidence between 1984 and 2000 for three scenarios: NEP use more likely among high-risk IDUs (baseline), NEP use more likely among low-risk IDUs, and NEP use equally likely across risk groups. For these simulations, it was assumed that there was moderate NEP use, and that NEP attendance did not result in any additional needle-sharing partners. Incidence peaked in January 1996 at 35.1 per 100 person-years, when low-risk IDUs were more likely to attend the NEP; in July 1996 at 28.2 per 100 person-years, when attendance was equally likely across risk groups; and in September 1996 at 21.8 per 100 person-years in the baseline case, when high-risk IDUs were more likely to attend the NEP. The prevalence of HIV in January 2000 was 40.4% when low-risk IDUs were more likely to attend the NEP, 38.4% when all IDUs were equally likely

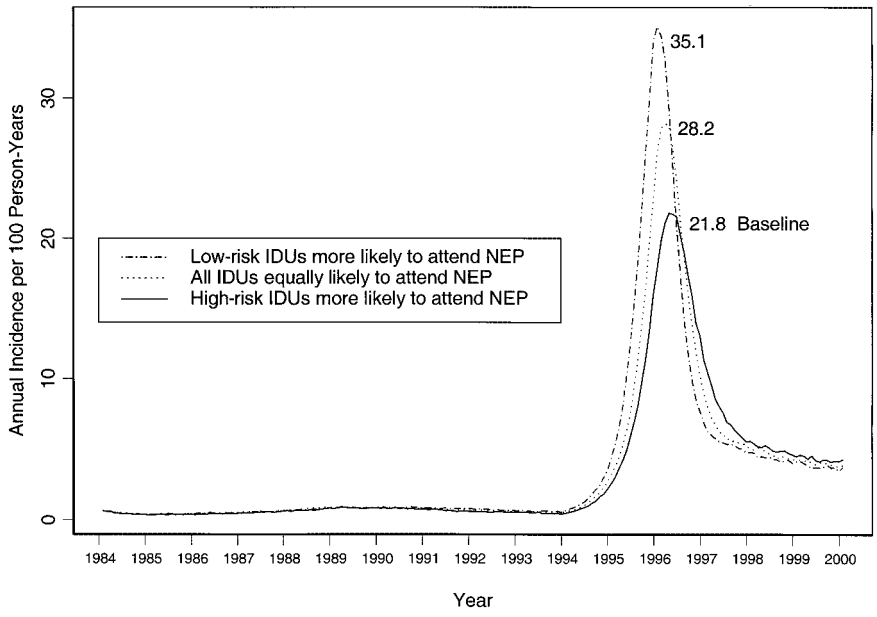

FIGURE 3. Mean seroincidence by varying likelihood of different risk groups to attend the needle-exchange program (NEP).

to attend the NEP, and 36.6% when high-risk IDUs were more likely to attend the NEP. The corresponding numbers of cumulative infections were 4,120, 3,895, and 3,677.

Figure 4 shows the mean HIV prevalence between 1984 and 2000 for three other scenarios: the baseline scenario in which IDUs gained no additional partners as a result of NEP attendance and the scenarios when either 0.5 or 1 additional partner per month was gained as a result of NEP attendance, starting in 1996. For these simulations, it was assumed that there was moderate NEP use, and that high-risk individuals were more likely to attend the NEP. Incidence peaked in January 1996 at 32.3 per 100 person-years, in May 1996 at 23.8 per 100 person-years, and in September 1996 at 21.8 per 100 person-years, respectively, when 1, 0.5, and 0 additional partners were acquired as a result of attending the NEP. The prevalence of HIV in January 2000 was 64% if NEP was not introduced and 41.8%, 39.7%, and 36.6% when an NEP was introduced and 1, 0.5, and 0 additional needle-sharing partners, respectively, per month were acquired as a result of attending the NEP. The corresponding numbers of cumulative infections per month were 4,292, 4,042, and 3,677.

Table 3 shows the estimated prevalences of HIV in January 2000 from all 27 combinations of parameters. Even under the worst-case scenario that NEPs result in 1 additional needle-sharing partnership per month, low-risk IDUs most likely to use the NEP and low NEP use, the NEP was still shown to be more effective than not having an NEP at all.

Table 4 shows the prevalence of HIV among never users, sometimes users, and always users of the NEP, assuming 30% to 70% reductions in the number of needle-sharing incidents among sometimes users and 90% to 100% reductions in the numbers of needle-sharing incidents for always users. For these scenarios, we as-

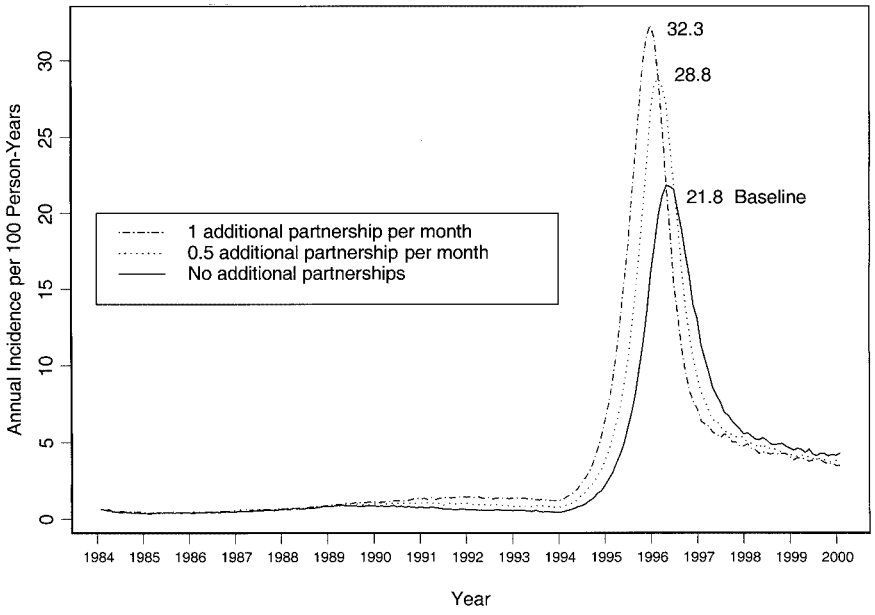

FIGURE 4. Mean seroincidence by number of additional partnerships as a result of needle-exchange program attendance.

TABLE 3. Overall prevalence of HIV in simulated injection-drug-using population in January 2000

Number of additional partners from attending the NEP	Likelihood of different risk groups to attend the NEP	Percentages of never, sometimes, and always users of the NEP, $F_{N\text{-}NEP}/F_{S\text{-}NEP}/F_{A\text{-}NEP}$		
		10%/30%/60%	10%/60%/30%	20%/70%/10%
0	High risk more likely	10.7 (1.63)*	36.6 (0.77)†	52.9 (0.53)
	Equal probability	13.8 (1.34)	38.4 (0.70)	54.4 (0.57)
	Low risk more likely	18.4 (1.07)	40.4 (0.58)	54.8 (0.52)
0.5	High risk more likely	14.0 (1.70)	39.7 (0.66)	54.9 (0.48)
	Equal probability	17.4 (1.13)	41.2 (0.65)	56.1 (0.43)
	Low risk more likely	21.3 (0.85)	42.7 (0.59)	56.4 (0.43)
1	High risk more likely	17.1 (1.34)	41.8 (0.70)	56.2 (0.46)
	Equal probability	20.3 (1.18)	43.0 (0.67)	57.1 (0.47)
	Low risk more likely	23.4 (0.82)	44.4 (0.56)	57.5 (0.50)

Prevalence in January 2000 with no NEP introduced = 64.0

NEP, needle-exchange program.
*Mean (standard deviation).
†Baseline scenario.

TABLE 4. Prevalence of HIV in January 2000 by needle-exchange program (NEP) attendance for various reductions in needle-sharing incidents among sometimes and always users of the needle-exchange program

Percentage reduction in frequency of needle sharing		Prevalence of HIV in 2000, %			
Among S-NEP, $\Delta_{\lambda S\text{-}NEP}$	Among A-NEP. $\Delta_{\lambda A\text{-}NEP}$	Never users, N-NEP	Sometimes users, S-NEP	Always users, A-NEP	Overall
30*	100	51.4	50.1	6.6	36.6
30	90	47.1	65.3	40.5	59.3
40	100	47.9	45.0	6.4	33.3
40	95	46.6	62.1	37.5	56.5
40	90	46.2	62.1	38.7	56.6
50	100	43.6	38.6	6.3	29.2
50	95	45.7	56.7	34.9	52.0
50	90	45.5	57.1	36.5	52.4
60	100	36.7	30.2	6.2	23.5
60	95	44.0	48.3	31.6	44.5
70	95	38.9	35.2	26.0	33.6

*Baseline scenario.

sumed that higher risk IDUs are more likely to attend the NEP, there was moderate NEP use, and no additional partnerships were formed as a result of attending the NEP. The prevalence of HIV among always users is highly sensitive to small reductions from perfect compliance (100% to 95%), but less sensitive to further reductions in compliance (95% to 90%). The reduction in prevalence due to a larger reduction in the needle-sharing incidents among sometimes users is outweighed by a smaller reduction in the needle-sharing incidents among always users. The prevalence of HIV among never users was similar to the prevalence of HIV among sometimes users, and for three scenarios in which the always users had less than 100% reduction in needle-sharing incidents, the prevalence of HIV among sometimes users of the NEP exceeded that among never users of the NEP. This is due in part to the fact that higher risk individuals are more likely to attend the NEP.

To measure how much safe needle use has been accomplished, we divided the total number of "injecting incidents" into cases in which a clean needle is used for each individual or those in which a needle is shared. Since needle-sharing incidents were only simulated for HIV-discordant partners, the only partnerships for which HIV transmission can occur, the total number of needle-sharing incidents for the entire simulated population is not known. However, under the assumption that HIV-concordant partners share needles at the same rate as HIV-discordant partners, we can extrapolate the total number of needle-sharing incidents. The total number of needle-injecting incidents per month is shown in Fig. 5 for discordant and concordant partnerships assuming that high-risk IDUs were more likely to attend the NEP, that there was moderate NEP use, and that NEP attendance did not result in any new needle-sharing partners. The numbers of injecting occasions during which needles were shared and for which sharing of needles was avoided are

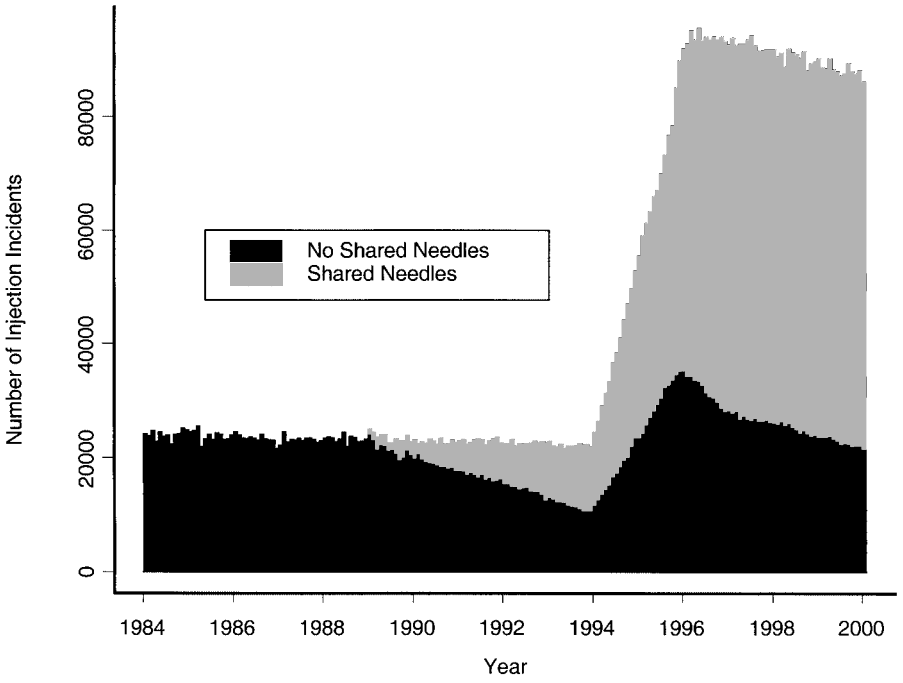

FIGURE 5. Total number of injection incidents per month.

shown in Fig. 5 and are indicated by the shading of the bars. From this graph, we can see how much protection is offered by the NEP and how much more protection is still needed.

DISCUSSION

We conducted a Monte Carlo simulation study of the effect of a needle-exchange program on reducing the spread of HIV in an IDU population. We based as many parameters as possible on empiric data from VIDUS, and while our conclusions may be applicable to epidemics in other centers, extrapolation of our conclusions to settings with different patterns of drug use and needle sharing should be undertaken with caution. In our model, NEPs were shown to be effective even under the most pessimistic conditions. We have shown that the effect of NEPs lies on a continuum that depends on the proportion of the population who are regular attenders of the NEP, the type of IDUs who are most likely to frequent the NEP, the number of new partners acquired by attending the NEP, and the percentage reduction in needle-sharing incidents among NEP attenders.

Of the factors we varied in the simulation, the proportions of IDUs who were never, sometimes, or always users of the NEP and the percentage reduction in needle-sharing incidents among NEP attenders had the greatest impact on the spread of HIV in the IDU population. By varying the proportions of IDUs who are sometimes and always users of NEPs, we were able to determine that it is more effective to increase the frequency of attendance of fewer NEP users than to increase the total number of IDUs attending the NEP, some of whom may have irregular attendance. It is more effective to eliminate needle sharing completely among a small proportion of higher risk IDUs than to reduce partially the frequency of sharing among a larger group of IDUs. The number of new partners as a result of NEP attendance and the dependence of attendance at the NEP on the risk score of the IDU had comparably smaller impacts on the spread of HIV in the population.

Our models also showed how HIV incidence can spike due to relatively small changes in population behaviors after a long period of low prevalence. Thus, cities that report long periods of low prevalence of HIV among their population who uses injecting drugs[41] should not be complacent, but should be prepared for outbreaks, as have been witnessed in Vancouver, Montreal, and other cities.

NEPs may appear to lead to increased incidence in some settings if the timing of the implementation of the NEP coincides with other changes that increase the incidence of HIV, such as the influx of cocaine into a community, when in fact the incidence could have been even higher had the NEP not been introduced. In some settings, such as in the study by Bruneau et al.,[6] NEP users have been shown to have higher incidence than non NEP-users, even after controlling for a number of risk behaviors. It is difficult to say whether the increased risk is truly due to factors associated with NEP attendance or to the difficulty of adequately controlling for high-risk activities. However, from our models, it appears that increased incidence among NEP users is not due to the acquisition of new partners as a result of attending the NEPs. Logistic regression models fit to the simulated data to examine the risk of HIV seroconversion associated with NEP use after adjusting for risk score and numbers of partners did not reproduce the results reported by Bruneau et al. It may be that other changes in the structure of the network, such as a change in the mixing pattern from a proportionate pattern to a more assortative pattern, contributed to more explosive growth among NEP users.

There are limitations to simulation models. In general, it is difficult to perfectly model behavior as variable and sporadic as needle sharing among injection drug users and to estimate each parameter precisely in a dynamic environment. We have assumed that transmission of HIV occurs largely through needle sharing in this population and have not modeled HIV transmission through sexual partnerships. However, since sharing of drug injection equipment is a much more effective mode of transmission of HIV than heterosexual intercourse, which is believed to comprise the majority of sexual activity in this population, we do not believe the omission of transmission of HIV through sexual partnerships in our model will have a significant impact on our conclusions. Although we allowed movement in and out of the population, we did not model migration back and forth to a high-risk setting, such as jail, which might be a significant factor for some populations. Despite these limitations, simulation studies offer a unique opportunity to study the independent effects of a parameter in absence of confounding. Furthermore, models permit the study of the natural dynamics of the infection in absence of important social factors or secular trends, such as changing public health policies, the availability of drugs on the street, and other factors. Since simulation studies are able to avoid contamination from such variables, they are valuable tools to aid in the interpretation of epidemiological data.

Needle-exchange programs have been operating in many cities since the late 1980s. Many initial opponents of NEPs now support the programs,[42] and the number of NEPs in the United States has increased by about 20% per year in recent years. While NEPs have been demonstrated to be a cost-effective strategy to reduce the spread of HIV,[43] they are not sufficient to provide enough clean needles to IDUs.[44,45] A multifaceted approach to risk reduction among IDUs needs to be implemented. Safe injection sites,[9] relaxation of strict syringe possession laws,[46,47] and addiction treatment programs are also important strategies in addition to NEPs in attempting to stem the spread of HIV and other bloodborne pathogens among IDUs.[47]

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