EDITORIAL REVIEW

A circulation theory of needle exchange

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Introduction

HIV infection and AIDS are transmitted, amongst other routes, through sharing of drug-injection equipment. Almost one-third of the AIDS cases reported in the United States has been associated directly or indirectly with drug injection [1]. Needle-exchange programs have been established with the aim of slowing the spread of AIDS by enabling drug injectors to trade used for clean needles [2–4]. Such programs have existed for some time in Europe and Australia, where they are widely accepted as preventive. More recently, programs have started in Canada and the United States [5,6]. Aside from the political controversy that accompanies 4iscussion of these programs in the United States [7,8] is the question of effectiveness: do needle-exchange programs reduce HIV transmission among participating drug injectors?

Several published studies suggest that these programs offer considerable protection against HIV infection [9–15]. Many of these studies rely on needle-exchange participants' self-reported changes of risky behavior as a principal data source [16]. However, in an environment in which injectors are repeatedly informed of the health risks associated with needle sharing, it is perhaps not surprising to learn that clients report reductions in needle-sharing rates after exposure to needle exchange. That the potential for social desirability biases in self-reporting exists

in no way proves that the behavioral studies are wrong. However, since it is difficult to verify self-reported behavioral changes, there is a role for studies that rely on other data sources. (We recognize that the policy relevance of this argument is less pressing outside the United States.)

Another concern is that, even if behavioral data are reported accurately, it is not clear what role needle-exchange operations play in eliciting behavior changes [17]. To establish the efficacy of needle exchange requires a clear linkage between the distribution and return of needles on the one hand and HIV risk reduction on the other. It is the specific effect of needle exchange on HIV transmission dynamics that should be estimated.

Here, we formulate a circulation theory of needle exchange that highlights the fundamental impact such programs have on the behavior of needles, and present data derived from 20 months of needle-exchange operations in New Haven (Connecticut, USA), which are free from self-reporting concerns. We begin with a discussion of our primary data source, the syringe tracking and testing system. In the following sections, we integrate an intuitive account of the theory with more formal mathematical developments facilitating empirical tests of the theory developed. We also consider competing hypotheses, which, if correct, could explain some of the observed data without ascribing any benefit to

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needle exchange. Our conclusion is that the data support the circulation theory, adding weight to the contention that needle exchange *per se* lowers the rate of HIV transmission among participating drug injectors.

The syringe tracking and testing system

New Haven's legal needle-exchange program began on 13 November 1990, following an act of the Connecticut Legislature, and allows participating clients to exchange, on a one-for-one basis, up to five needles per visit (with the exception of client enrollment when a new client with no needles to exchange receives a single needle). The program operates from a mobile van (for more details relating to program operations, see [17]).

Health department officials vetoed the idea of sequentially testing program participants to determine HIV incidence directly for fear of dissuading broad participation by injectors [18]. Instead, we designed a data collection system for 'interviewing the needles'. This syringe tracking and testing system (STT) works as follows [17]: all participating clients receive unique code names of their own choosing, while all distributed needles are also coded. When needles are distributed, the date, location, needle codes and recipient's client code are recorded; when needles are returned, the corresponding date, location, needle codes and client code are again recorded. Thus, for all needles distributed and returned to the program, it is known who received and returned each needle, when needles were received and returned, and where the exchanges took place. The client code, date, and location for non-program needles returned to the exchange are also recorded (as the program allows clients to exchange any needles). Finally, systematic samples of returned needles are tested for HIV proviral DNA using polymerase chain reaction (PCR) [19]. The sampling procedure accounts for the fact that a purely random sample of returned needles would be heavily biased in favor of those exchanging the most needles in the following manner. Needles are typically exchanged in batches ranging from one to five per batch. We first sample all needles from batches consisting of two needles at most, along with two needles from batches greater than two. We then systematically select every tenth needle from those sampled previously. This increases the chance of sampling needles from clients who exchange less frequently beyond what would be obtained by random sampling.

The STT enables the objective determination of several important quantities, such as needle circulation times, the fraction of distributed needles returned to the program, the number of clients participating in the program, the needle distribution and return rates, the number of client visits, and the fraction of needles testing positive for HIV proviral DNA. Our study utilizes STT data collected from November 1990 to June 1992 inclusive. We confine our report to this period because the Connecticut Legislature legalized the purchase of needles and syringes without a prescription in pharmacies as of 1 July 1992, an event that changed the environment in which the needle exchange was operating.

Needle removal processes

Consider a population of needles circulating among drug injectors in the absence of needle exchange. Each needle faces a variable lifetime following introduction to the population after which the needle is removed from circulation (because of breakage, wear, misplacement, etc.). Let δ represent the removal (or loss) rate per circulating needle per unit time prior to the introduction of a needle-exchange program. The expected lifetime of a needle is then given by $1/\delta$.

Introducing needle exchange affects the existing needle removal process because the program offers a new exit route for circulating needles. Consequently, the length of time needles spend in circulation will fall. Formally, let ρ represent the exchange rate per circulating needle per unit time, while δ continues to represent the removal rate per needle per unit time for all reasons other than needle exchange. The total removal rate increases from δ to $\rho + \delta$. Thus, the expected circulation time is reduced from $1/\delta$ to $1/(\rho + \delta)$. In addition, the probability that any circulating needle will be exchanged equals $\rho/(\rho + \delta)$.

To estimate ρ and δ from STT data, we note that STT enables direct calculation of return probabilities and needle circulation times for returned needles. Defining t_i as the average circulation time per needle distributed by the program in month i (calculated as the mean duration of time between needle distribution and return divided by the mean number of needles distributed per visit to adjust for batch size effects), and r_i as the fraction of needles distributed in month i that ultimately return to the program, we equate

$$t_i = 1/(\rho_i + \delta_i) \text{ and } r_i = \rho_i/(\rho_i + \delta_i) \quad (1)$$

which yield estimates of the needle return and loss rates in month i as

$$\rho_i = r_i/t_i \text{ and } \delta_i = (1 - r_i)/t_i \quad (2)$$

Estimates of the needle exchange and loss rates over the first 20 months of the New Haven needle-exchange program as derived from equations 1 and 2 are presented in Fig. 1. It is clear that the needle-

exchange rates have increased substantially over time, reflecting an increase in the turnaround of needles in the population due to needle exchange. However, the needle-loss rates have remained stable relative to the exchange rates. The implications of these trends will be discussed shortly, but for now it suffices to note that the operations of the needle exchange have substantially increased the total rate with which circulating needles are removed from the population.
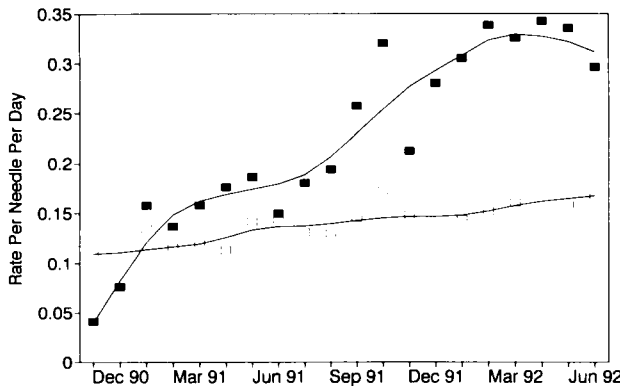

Fig. 1. Needle return and loss rates. The daily return rate per needle ρ (■) and loss rate per needle δ (□) are shown for each month as computed from equation 2 in the text. The lines show statistically smoothed versions of these time series obtained from the '4253H, twice' smoothing algorithm [22].

Conservation of needles in a needle exchange

The New Haven program operates on a one-for-one exchange basis, forcing a simple conservation of needle flow to apply in theory [17]: the total number of needles distributed by the program equals the total number of needles returned to the program. The number of needles distributed and returned in New Haven from November 1990 to June 1992 is shown in Fig. 2. This figure shows that needle flow is approximately conserved, but that there is some 'leakage' in the system (as represented by the thin strip between the curves of Fig. 2). One reason for this is that clients joining the program with no needles to exchange are given a single 'free' needle to initiate exchange activities, although all exchanges beyond the first are meant to be one-for-one. However, some clients do obtain more needles than they return on certain visits, suggesting either counting errors, deception, or a combination of the two.

A more formal view of needle conservation proceeds as follows: let D equal the number of drug injectors participating in the program, N equal the number of needles circulating among program
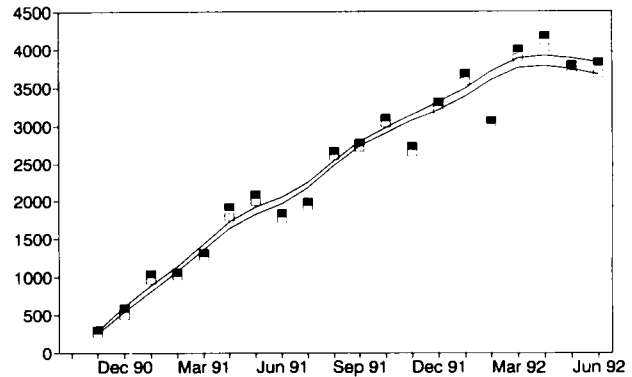

Fig. 2. Monthly needle distribution and return. The total number of needles distributed (■) and returned (□) are shown, along with statistically smoothed values.

clients, and ν represent the needle distribution rate per program client per unit time. Since ρ is the return rate per circulating needle per unit time, the rates with which needles are distributed by and returned to the program will balance if

$$D\nu = N\rho \tag{3}$$

at any moment in time. While both D and N may vary over time, needle exchange should have little if any effect on the ratio N/D which represents the average number of circulating needles per drug injector in the program population. If $\kappa = N/D$, equation 3 can be expressed as

$$\nu = \kappa\rho \tag{4}$$

The empirical relationship between the needle distribution rate per client and the needle return rate per needle, along with a least-squares fit of equation [4] are shown in Fig. 3. We estimate that $\hat{\kappa} = 1.32$ circulating needles per program client (SE, 0.03), a quantity of interest in its own right.
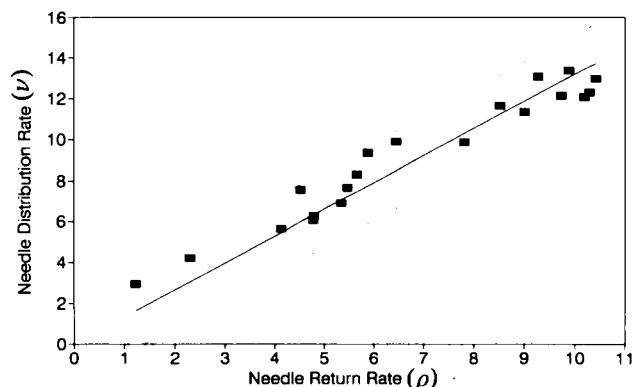

Fig. 3. Conservation of needle flow. Monthly needle distribution rates per client ν are plotted against monthly return rates per needle ρ. The least squares fit of equation 4 is shown with accompanying 95% prediction intervals.

Return probability, program penetration and needle circulation time

Combining needle removal processes with needle conservation allows some interesting insights into the operations of needle exchange. According to equation 1 the probability that a distributed needle is eventually returned to the program is given by $r = \rho/(\rho + \delta)$. As the program is a needle *exchange*, the quantity r also represents the fraction of all circulating needles that are program needles, a measure of program penetration. As discussed earlier, needle exchange also reduces mean needle circulation time from $1/\delta$ to $1/(\rho + \delta)$. Thus, we derive the relative reduction in mean circulation time due to the introduction of needle exchange as

$$\left[1/\delta - 1/(\rho + \delta) \right] / (1/\delta) = \rho/(\rho + \delta) = r \quad (5)$$

Thus, information about the reduction in needle circulation times is encoded in the fraction of distributed needles returned to the program [20]. These results show that the fraction of distributed needles returned to a needle exchange is a valuable statistic for evaluating such programs. The return probability estimates the relative reduction in circulation times and the penetration of program needles into the population, in addition to the fraction of distributed needles that are returned to the program.

Integrating needle behavior with the frequency of client exchanges

In a needle-exchange program, the rate at which needles are exchanged is a function of client participation in the program. Both the number of clients participating in the program each month (by virtue of having made at least one exchange visit), and the total number of visits made by these clients each month are shown in Fig. 4. While the number of program clients leveled, the number of visits made by these clients to the program continued to grow. This suggests that clients visited the program more often as time progressed, which in turn suggests that needle circulation times must have fallen as a result of the increasing needle exchange rate (and recall from Fig. 1 that the needle-exchange rates increased). In addition, as suggested by equation 5, declining circulation times should be accompanied by an increase in the fraction of distributed needles returned to the program, and such an increase in turn would signal an increase in the penetration of program needles in the population of circulating needles.

The impact of the program on needle circulation patterns is summarized in Fig. 5. Based on the 49 405 needles distributed from November 1990 through June 1992, there is no question that mean nee-
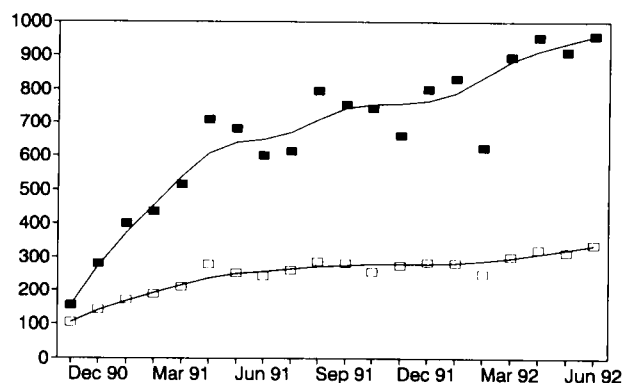

Fig. 4. Client participation and visitation. The total number of client visits (■), and the number of clients visiting the program at least once (□) are shown, along with statistically smoothed values.

dle circulation times have fallen substantially while needle-exchange probabilities have increased. The near mirror-imaging of these two time trends is in accord with the predictions of our theory according to equations 1 and 5.
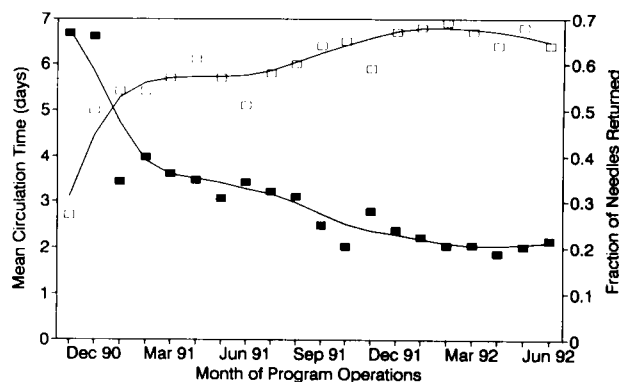
Fig. 5. Circulation time and return probability. Mean needle circulation times in days (■) and the fraction of needles distributed by the program that are ultimately returned (□) are shown, along with statistically smoothed values.

Needle exchange reduces HIV prevalence in circulating needles

Needle exchange clearly reduced needle circulation times; but the question is why this should translate into a reduction in the risk of acquiring HIV infection among needle-sharers. An intuitive answer is that reducing the length of time any needle is available for use reduces the number of opportunities a given needle can be re-used. If fewer people use each needle, then each needle should have a lower probability of becoming infected with HIV. Conse-

quently, those who continue to share needles will be less likely to encounter an infected needle when sharing.

More formally, let λ denote the rate at which uninfected needles become infected per uninfected needle per unit time, and μ denote the rate that infected needles become uninfected per infected needle per unit time. The main determinants of λ include the prevalence of HIV in the injecting population (which is assumed to remain constant over the relatively short duration of study), and the rate at which infected people inject with and contaminate uninfected needles. The determinants of μ (absent needle exchange) include the fraction of uninfected drug injectors in the population, effective needle cleaning (for example, careful use of bleach), needle decontamination owing to dilution effects when uninfected drug users inject with infected equipment, natural inactivation of the virus contained in residual blood in the needle, or replacement of used needles with new ones from non-program sources. Note that the loss rate δ could contribute to both λ and μ in this model because some lost needles will be replaced by infectious equipment, while others will be replaced by uninfected needles. In the absence of needle exchange, the probability that a circulating needle is infected will reach the steady-state value p_I where

$$p_I = \lambda/(\lambda + \mu) \qquad (6)$$

Given the high frequency of drug injection, this steady-state value will be obtained relatively quickly compared to our monthly observation periods [technically, the 'relaxation time' for this process equals $1/(\lambda + \mu)$, which for our data is estimated to equal approximately 3 days, as reported below].

The operation of the needle exchange offers a new route by which infected needles become uninfected, via the exchange of contaminated used needles for new uninfected ones. Thus, needle exchange augments the rate at which infected needles are decontaminated by the return rate ρ. This in turn reduces the fraction of circulating needles that are infected to

$$p_I^*(\nu) = \lambda / (\lambda + \mu + \rho) = \lambda / (\lambda + \mu + \nu/\kappa) \qquad (7)$$

with the latter equality in equation 7 following from equation 4. Substituting equation 6 into 7 shows that

$$p_I^*(\nu) = a\,p_I / (a + \nu) \qquad (8)$$

where $a = (\lambda + \mu)\kappa$ and p_I is the fraction of needles infected in the absence of needle exchange as given in equation 6. The model of equation 8 suggests a prevalence-drop law, which states that in a one-for-one needle-exchange program with a needle distribution rate equal to ν needles per client

per unit time, relative reduction in the fraction of circulating needles that are infected of roughly $100 \times \nu$ $(a + \nu)\%$ should be expected.

Of the 49 405 needles distributed by the needle exchange between November 1990 and June 1992, 2813 (5.7%) have been tested for HIV using PCR. Of the 2813 needles tested, 1163 (41.3%) were HIV-positive. In month i, let x_i be the number of needles that tested HIV-positive, y_i the number that tested negative, and ν_i equal the number of needles distributed per program client in month i. Estimates for the quantities a and p_I in equation 8 were then found by maximizing the likelihood function $L(a,p_I)$ given by

$$L(a, p_I) = \prod_{i=1}^{20} p_I^*(\nu_i)^{x_i} \left(1 - p_I^*(\nu_i)\right)^{y_i} \qquad (9)$$

The resulting maximum likelihood estimates are $\hat{a}$ = 13.25 (SE, 3.17) and $\hat{p}_I = 0.693$ (SE, 0.065). Note that the relaxation time $1/(\lambda + \mu)$ equals κ/a, which is estimated as 0.0996 months (approximately 3 days).

This model suggests that prior to the operation of the needle exchange, 69.3% of circulating needles were HIV-infected. Of considerable interest is the fact that independently of the data used to fit equation 8, 160 non-program 'street needles' returned to the exchange at the beginning of program operations were tested for HIV. Of these 160 needles, 108 (67.5%) tested positive, well within the noise level of our estimate $\hat{p}_I$.

The measured level of HIV infection in returned needles in each of the 20 months of program operations, estimates from the model of equation 8, and 95% prediction intervals for these estimates are shown in Fig. 6. The model replicates the measured level of infection in most of the months of observations, although there are four clear outliers in January 1991, April 1991, November 1991, and January 1992 that we cannot explain.
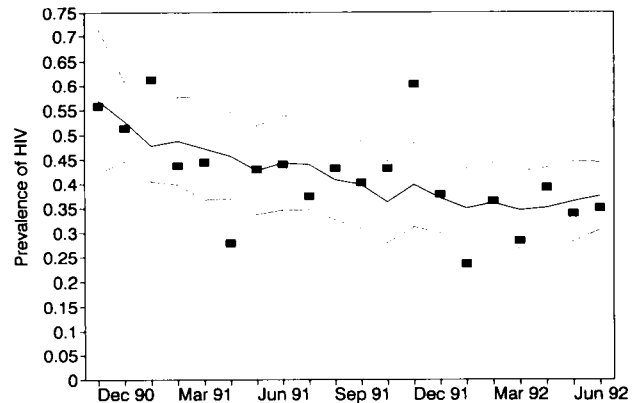

Fig. 6. HIV prevalence in needles. The fraction of needles that test positive for HIV using polymerase chain reaction in each month (■) are shown, along with the predictions of the model of equation 8 and associated 95% prediction intervals as obtained by maximum likelihood.

Implications for HIV incidence reduction

To become infected through needle sharing requires injection using infected needles. It therefore follows that the HIV incidence rate among drug injectors who persist in needle sharing is proportional to the level of infection among circulating needles. However, if HIV incidence is proportional to the prevalence of HIV in needles, then changes in HIV incidence are proportional to changes in the prevalence of HIV infection in circulating needles. Consequently, our analysis suggests that HIV incidence among program clients has been reduced by more than 40% as a result of the needle-exchange program.

Competing hypotheses

We have attempted to construct and test competing hypotheses that would explain the observed HIV prevalence drop in needles without implying any salutory benefits due to the needle exchange [21]. Suppose that there are broadly speaking two types of clients deemed high risk (likely to be infected) and low risk (less likely to be infected). If the types of program clients changed over time such that the mixture of high-risk and low-risk injectors moved from predominantly high risk at the start of the program to predominantly low risk after several months of program operations, one might expect a temporal drop in the level of infection in the needles observed in our data even if needle exchange offered no protective benefits. Such changes in the client population should be detectable from self-reported behavioral data collected from program clients at enrollment. Even if the self-reported data are not intrinsically accurate, there is no reason to expect that clients with truly different levels of risky behavior should provide similar self-reported responses. Thus, changes in the profile of baseline self-reported risky behaviors over time should correspond to changes in the true infection risk of the client base over time. Alternatively, failure to detect such changes in the profile argues against the suggestion that a changing needle-exchange client base could account for the observed HIV prevalence decline in returned needles.

We therefore considered six self-reported behavioral variables for program participants over time. The variables are the duration of injection (in years), the daily frequency of injection, the fraction of time spent injecting in shooting galleries, the fraction of injections that are shared, the fraction of clients injecting cocaine, and the daily frequency of risky injection (defined for each client as the product of daily injection frequency, the fraction of injections that are shared, and the fraction of shared injections

that are not cleaned prior to injection). These data were obtained by surveying clients at their first visit to the program. To analyze changes over time, the mean values (and SE of these means) of these six variables were determined for the clients who actually visited the needle exchange in each of the 20 months in our study (Table 1). We restricted the analysis to include only clients who visited at least three times during the 20 months, since these clients contributed the overwhelming majority (95%) of the needles tested. We emphasize that temporal changes in these variables, if they occur, are not indicative of behavioral changes since all data were obtained when clients enrolled. Rather, as argued above, such changes would reflect shifts in the overall client base using the needle exchange.

The results of a one-way analysis of variance for each of the six variables are also reported in Table 1. The hypothesis tested in each case is that the mean of the variable in question has not changed over time. In all six instances, this hypothesis cannot be rejected, suggesting that the client base has not changed. We have conducted more sophisticated analyses testing for simultaneous stability in these measures using multivariate analysis of variance, arriving at similar results [21].

Conclusions

We have formulated a circulation theory of needle exchange that focuses on the behavior of needles rather than the behavior of drug injectors. We have shown how needle exchange increases the turnaround of circulating needles by increasing their removal rate. This increase in turnaround leads to both a reduction in needle circulation times and an increase in the penetration of program needles into the population of all needles. Decreasing needle circulation times lead to a reduction in the fraction of circulating needles infected with HIV because shorter circulation times reduce the opportunities for needles to share people. Assuming that HIV incidence via needle sharing is proportional to the level of infection in circulating needles, the HIV prevalence drop in needles translates into a reduction in the rate of new HIV infections.

Several aspects of this theory were shown to be consistent with observed data, including conservation of needle flow and the HIV prevalence decline in needles. Of interest was the ability of our model in equation 8 to correctly predict the level of infection measured in circulating non-program 'street' needles. The strongest evidence for the circulation theory is summarized in Figs 3, 5 and 6, which present data that are explained simultaneously by circulation theory.

We considered competing hypotheses to explain the drop in the level of infection observed in needles,

Table 1. Self-reported behavioral variables.

Month	Duration of injection	Frequency of injection	Fraction			Risky injection frequency
			Gallery use	Injections shared	Using cocaine	
November 1990	8.649	1.833	0.1373	0.1152	0.8358	0.0335
	(0.334)	(0.167)	(0.0324)	(0.0261)	(0.0456)	(0.0253)
December 1990	8.040	1.824	0.1220	0.725	0.7600	0.0381
	(0.319)	(0.140)	(0.0259)	(0.0131)	(0.0429)	(0.0187)
January 1991	7.435	2.203	0.1247	0.1040	0.7008	0.0459
	(0.306)	(0.129)	(0.0239)	(0.0179)	(0.0408)	(0.0201)
February 1991	7.580	2.171	0.1024	0.0849	0.7755	0.0546
	(0.283)	(0.121)	(0.0209)	(0.0130)	(0.0345)	(0.0221)
March 1991	7.656	2.260	0.0945	0.1397	0.7765	0.0638
	(0.254)	(0.112)	(0.0177)	(0.0178)	(0.0312)	(0.0230)
April 1991	7.419	2.2958	0.0750	0.1187	0.7847	0.0510
	(0.242)	(0.0988)	(0.0141)	(0.0143)	(0.0285)	(0.0173)
May 1991	7.227	2.3158	0.0702	0.1137	0.7526	0.0466
	(0.260)	(0.0993)	(0.0129)	(0.0144)	(0.0311)	(0.0173)
June 1991	7.580	2.2977	0.0759	0.1273	0.7500	0.0352
	(0.241)	(0.0990)	(0.0143)	(0.0161)	(0.0307)	(0.0211)
July 1991	7.439	2.244	0.0642	0.1235	0.7837	0.0370
	(0.243)	(0.102)	(0.0125)	(0.0149)	(0.0286)	(0.0143)
August 1991	7.381	2.2420	0.0694	0.1248	0.7655	0.0476
	(0.231)	(0.0943)	(0.0126)	(0.0150)	(0.0282)	(0.0177)
September 1991	7.201	2.1808	0.0829	0.1367	0.7660	0.0338
	(0.233)	(0.0927)	(0.0146)	(0.0154)	(0.0277)	(0.0124)
October 1991	7.263	2.2490	0.0645	0.1370	0.7634	0.0264
	(0.240)	(0.0953)	(0.0122)	(0.0165)	(0.0285)	(0.0106)
November 1991	7.593	2.2878	0.0777	0.1404	0.7421	0.0623
	(0.230)	(0.0940)	(0.0144)	(0.0167)	(0.0295)	(0.0239)
December 1991	7.451	2.2899	0.0759	0.1378	0.7217	0.0301
	(0.229)	(0.0913)	(0.0132)	(0.0163)	(0.0296)	(0.0126)
January 1992	7.469	2.3458	0.0643	0.1369	0.7447	0.0415
	(0.235)	(0.0936)	(0.0122)	(0.0164)	(0.0285)	(0.0193)
February 1992	7.303	2.3242	0.0717	0.1504	0.7944	0.0384
	(0.243)	(0.0987)	(0.0136)	(0.0178)	(0.0277)	(0.0153)
March 1992	7.586	2.2493	0.0754	0.1251	0.7276	0.0371
	(0.217)	(0.0895)	(0.0123)	(0.0147)	(0.0278)	(0.0120)
April 1992	7.382	2.2968	0.0672	0.1371	0.7154	0.0304
	(0.219)	(0.0860)	(0.0111)	(0.0158)	(0.0277)	(0.0115)
May 1992	7.506	2.2963	0.0655	0.1354	0.7194	0.02643
	(0.226)	(0.0880)	(0.0118)	(0.0159)	(0.0283)	(0.00898)
June 1992	7.363	2.3650	0.0618	0.1154	0.7185	0.0303
	(0.222)	(0.0839)	(0.0102)	(0.0142)	(0.0274)	(0.0104)
F statistic	0.83	1.10	1.46	1.03	0.91	0.46
Degrees of freedom	19, 4052	19, 4039	19, 4037	19, 4018	19, 4043	19, 4015
P	0.667	0.343	0.092	0.425	0.565	0.977

The six variables reported are: duration of drug injection (in years); frequency of injection (daily); fraction of time injecting in shooting galleries; fraction of injections that are shared; fraction of injectors using cocaine; and daily risky injection frequency, defined as the product of daily injection frequency, fraction of injections that are shared, and one minus the fraction of shared injections that are cleaned. The data were obtained by survey from clients during their first visit to the program. For each variable, monthly mean values are reported, while the SE of these means appear in parentheses. Also reported are one-way analysis of variance results testing the hypothesis of no change in these variables over time. For each of the six variables, one cannot reject the null hypothesis.

but self-reported behavioral data do not support the suggestion that changes in the client base over time were responsible for the prevalence drop. Circulation theory remains, to our knowledge, the only theory able to account, in a unified manner, for the data we have observed. More importantly, circulation theory prescribes that the operations of needle exchange caused the trends observed in the data.

To refute this claim, an alternative theory capable of explaining the same data while omitting the effect of needle exchange must be advanced and subjected to analysis. In the absence of such an alternative theory, however, we believe that the data support the proposal that needle-exchange programs can reduce HIV transmission risks among program participants.

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