VOLUNTEER BIAS IN NONRANDOMIZED EVALUATIONS OF THE EFFICACY OF NEEDLE-EXCHANGE PROGRAMS

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ABSTRACT

Objective. Nonrandomized comparisons of the incidence of HIV and hepatitis B and C between injection drug users (IDUs) who do and do not attend voluntary needle-exchange programs may be subject to bias. To explore possible sources of bias, we examined characteristics associated with voluntarily beginning or ceasing to participate in the Seattle needle exchange.

Methods. In a cohort of 2,879 IDUs, a standardized questionnaire measured characteristics present at enrollment. We examined the relation of these characteristics to the proportion of IDUs who began to use the program during the ensuing 12-month follow-up period and to the proportion of current exchangers who dropped out during that period of time.

Results. Of the 494 never-exchangers at baseline, 32% attended the exchange program during follow-up; those who reported sharing syringes or who were homeless at enrollment were more likely to become new exchange users (adjusted risk ratio [ARR] for becoming an exchange user = 1.8 for those who shared syringes, and ARR = 2.2 for those who were homeless). Of 1,274 current exchangers, 16% stopped using the exchange during follow-up, with daily injectors (ARR = 0.6) and those who reported backloading (ARR = 0.6) being relatively less likely to drop out of the exchange.

Conclusions. The analysis suggests that IDUs participating in needle-exchange programs at a given point in time may include a particularly high proportion of those injectors whose pattern of drug use puts them at elevated risk of blood-borne viral infections.

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BACKGROUND

Voluntary needle-exchange programs began in Amsterdam in 1984 in an attempt to reduce transmission of blood-borne agents.[1] The earliest studies consistently reported that needle exchanges attracted a disproportionate number of injection drug users (IDUs) who injected more frequently and who shared drug injection equipment more often than IDUs not using the programs.[2–4] A study of San Francisco IDUs recruited in 1989–1990 found that those who went on to use the exchange reported a greater degree of high-risk injection behavior and had a 25-fold higher human immunodeficiency virus (HIV) incidence prior to beginning use of the exchange compared to the incidence over a comparable period of time among those who remained nonexchangers.[5] Two studies noted that, in the case of long-standing exchange programs, differences between exchange users and nonexchangers may be still greater.[4,6]

The comparison of the incidence of blood-borne viral infections between IDUs who volunteer to participate in exchange programs versus those who do not has been the focus of many needle-exchange evaluations.[5,7–12] Nonrandomized studies of the efficacy of voluntary health screening and promotion programs may be subject to confounding since health concerns or a pattern of health-seeking behavior may distinguish volunteers from other persons.[13] Multivariate analytic methods may remove the confounding effect of differences in high-risk behavior between groups, but only when such behaviors are measured and are measured accurately.[14] When measurement error exists, efforts to remove confounding will only be partly successful. In this paper, we studied whether, in our population over a 1-year period, the needle-exchange program attracted high-risk IDUs and the extent to which low-risk IDUs disproportionately migrated from the exchange.

METHODS

Seattle Needle Exchange and the RAVEN Study

Needle exchanges first began operating in Seattle in early 1989; the programs were declared legal in 1992. In Seattle during the 1990s, a prescription has not been required to buy syringes; however, it is unlawful for any person to sell syringes to anyone they suspect of being a drug user. During the enrollment period for this study, there were six 1-for-1 needle-exchange programs operating in the city of Seattle and the surrounding area. These included an outdoor sidewalk exchange in the downtown area, four van-based exchange programs,

and a mobile exchange that visited other neighborhoods that drug users were known to frequent. Staffing, locations, and hours of operation were stable throughout the study period; referral to drug treatment and other medical and social services was provided at all sites. These programs exchanged an average 1,047,000 syringes per year over the enrollment period, and approximately 70% of the estimated 12,000–15,000 IDUs living in the Seattle–King County region attended the programs at least once.

The RAVEN (Risk Activity Variables, Epidemiology, and Network) Study is a cohort study of health outcomes and risk behaviors among IDUs. Recruitment was carried out June 1994 to May 1997 in methadone treatment clinics, a drug detoxification center, a drug and alcohol assessment agency, and the county corrections facility and at a street outreach and social service agency serving a downtown Seattle area with a highly visible drug-using population. A scheme based on random numbers was used to select the *n*th individual from agency census or client lists; in the street outreach site, the client entering the premises at the *n*th minute was selected. Needle-exchange programs were not used as recruitment locations. Once selected, individuals were screened for eligibility: They must have injected an illicit drug at least once in the previous year (by self-report), have been English or Spanish speaking, have been aged 14 years or older, and not already enrolled in the study. In Washington State, parental consent is required for minors younger than 14 years to participate in this type of research. Participants who consented to enrollment were paid $10 to complete the study visit.

Study Interviews

At enrollment, a standardized questionnaire was administered by a trained interviewer. The questionnaire covered demographic information; history of incarceration, drug treatment, and drug use; injection risk behavior during the previous 30 days, including frequency and recency of injection and sharing of equipment used to inject or prepare drugs; and information about where they had obtained syringes for drug injection. Data on backloading—a term used to describe use of a syringe to divide drugs between two or more drug injectors—was also collected. Follow-up on participants 1 year later included a second interview about behavior during the follow-up period. Payment of $25 was given to participants on completion of the follow-up visit.

During the June 1994 to May 1997 recruitment period, 2,995 interviews were completed; 116 (4%) were later excluded from the study because the data provided were judged by the interviewer to be unreliable or because it was discovered in

subsequent interviews that the subject had never injected drugs or had already been interviewed. Subjects included in this analysis are shown in the Figure. From among the 2,879 who comprised the eligible cohort, data from subjects who had begun to use (n = 269) or stopped using the exchange (n = 190) less than 6 months prior to the baseline interview were excluded from the analysis since their baseline behavior overlapped with the period in which their exchange use status changed. Those who reported not injecting any drugs during the month prior to the baseline interview (n = 375) or who had missing data on the date of first exchange use (n = 18) were also excluded. Thus, data from 2,027 individuals were used; they included 1,555 IDUs who had used an exchange at least once before study enrollment (exchange users) and 472 who had never used an exchange (never-exchangers). There were 385 of 472 never-exchangers (82%) who completed a follow-up visit by the end of April 1998; 123 (32%) began to use the exchange (at least one visit) between baseline and follow-up (new exchangers). Among those who were exchange users at baseline, 1,199 completed follow-up (77%); 182 (15%) stopped using the exchange after the baseline interview (former exchangers).

ANALYSES

To examine predictors of becoming an exchange user, we compared sociodemographic characteristics and risk behaviors reported at baseline by 123 new users

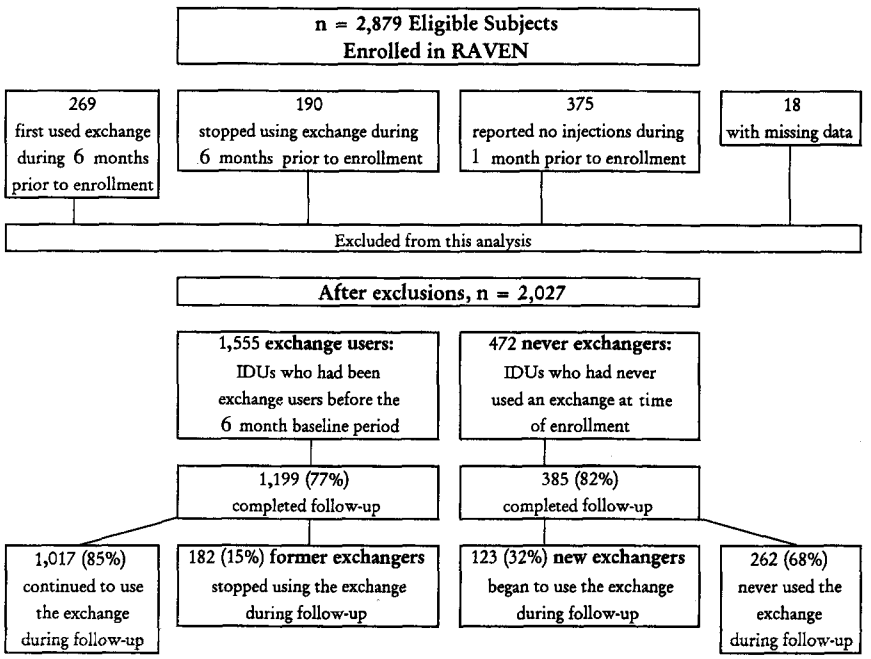

FIGURE 1 Subjects included in analysis of losses and gains to the Seattle needle exchange.

of the exchange versus 262 IDUs who still had not ever used the program by the end of the 12-month follow-up period. The same characteristics were considered as possible predictors of stopping use of the exchange among the 1,199 persons who were using the exchange at baseline. The risk ratio (RR) and its 95% confidence limit (CL) were used to evaluate the association between baseline characteristics and change in exchange use status, that is, becoming an exchange user or stopping use of the exchange. Multivariate logistic regression analysis was used to obtain the adjusted RR (ARR) for all other factors considered in the univariate analysis (gender, race, age, residence, and baseline drug use characteristics as shown in the table).

RESULTS

Results of the univariate and multivariate analyses of the association of baseline characteristics to beginning or stopping use of the exchange are shown in the Table. During the 12-month follow-up period, 123 IDUs began using the needle-exchange program for the first time (32%). Gender, race, and age were not associated to any substantial degree with becoming a new exchange user. In univariate analysis, heroin injection, daily injection, pooling money with other IDUs to buy drugs, syringe sharing, and backloading were associated with beginning to use the exchange. After adjustment for all the characteristics in the Table, IDUs who reported living on the streets or in a shelter were twice as likely as other IDUs to begin to use an exchange, and those who reported heroin as their primary injection drug were 2.6 times more likely to become a new exchange user. Recent syringe sharing (injection with a syringe used by another injector) was also associated with beginning to use the exchange (ARR = 1.8). In either univariate or multivariate analysis, participants who shared drug cookers or filtration cotton were no more likely to become exchange users than other IDUs.

Of those who had been users of the exchange, 15% (182) did not attend the program at all during the follow-up period (Table). Gender and homelessness were unrelated to stopping use of the exchange. In univariate analysis, African-American and other non-white injectors were more likely to stop using the program. Heroin injectors, daily injectors, those who pooled their money with other IDUs to buy drugs, or those who backloaded were more likely to remain exchange users during follow-up. After adjustment for other factors, African-Americans were more likely than white IDUs to stop using the program (ARR = 1.7), while injectors aged 24 or younger were less likely to stop using it (ARR = 0.4). Heroin injectors were also less likely to stop using the exchange than injectors of other drugs (ARR = 0.6), as were daily injectors (ARR = 0.6) and

TABLE Characteristics of Seattle Injection Drug Users in Relation to Beginning or Stopping Use of the Needle Exchange

	Never-Exchangers at Baseline		RR (Beginning to Use Exchange)		Exchange Users at Baseline		RR (Stopping Exchange Use)	
	N	Began to Exchange, %	RR (95% CL)	ARR (95% CL)	N	Stopped Exchanging, %	RR (95% CL)	ARR (95% CL)
	385	31.9			1199	15.2		
Demographics								
Gender								
Male	235	33.6	1.2 (0.8–1.6)	1.2 (0.7–2.2)	725	13.9	0.8 (0.6–1.1)	0.8 (0.5–1.1)
Female	150	29.3	1.00	1.00	474	17.1	1.00	1.00
Race/ethnicity								
White	271	32.5	1.00	1.00	756	11.9	1.00	1.00
African-American	68	29.4	0.9 (0.6–1.4)	1.4 (0.6–3.1)	290	21.7	**1.8 (1.4–2.4)**	**1.7 (1.1–2.7)**
Other	46	32.6	1.0 (0.6–1.6)	1.2 (0.5–2.9)	153	19.0	**1.6 (1.1–2.3)**	1.2 (0.6–2.1)
Age, years								
≤24	26	38.5	1.2 (0.7–2.0)	1.2 (0.4–3.5)	120	10.8	0.7 (0.4–1.2)	**0.4 (0.1–0.9)**
>24	359	31.5	1.00	1.00	1079	15.7	1.00	1.00
Lived on street/in shelter								
Yes	52	40.4	1.3 (0.9–1.9)	2.2 (1.0–4.9)	208	13.9	0.9 (0.6–1.3)	1.0 (0.6–1.7)
No	331	30.4	1.00	1.00	981	15.2	1.00	1.00
Baseline drug use characteristics								
Usual drug injected								
Heroin	283	36.0	**1.8 (1.2–2.7)**	**2.6 (1.3–5.5)**	1056	13.6	**0.5 (0.3–0.6)**	**0.6 (0.3–0.9)**
Other	99	19.8	1.00	1.00	118	29.7	1.00	1.00

Injected every day								
Yes	224	37.5	**1.6 (1.1–2.1)**	1.5 (0.9–2.7)	916	13.6	**0.7 (0.5–0.9)**	**0.6 (0.4–0.9)**
No	161	24.2	1.00	1.00	283	20.1	1.00	1.00
Usually pooled money with another IDU to buy drugs								
Yes	261	35.6	**1.6 (1.1–2.4)**	1.3 (0.6–2.8)	930	13.3	**0.6 (0.4–0.8)**	0.8 (0.5–1.5)
No	99	22.2	1.00	1.00	173	22.5	1.00	1.00
Injected with a syringe previously used by another injector								
Yes	161	41.0	**1.5 (1.1–2.1)**	**1.8 (1.01–3.4)**	485	12.4	**0.8 (0.6–1.0)**	1.1 (0.7–1.7)
No	180	26.7	1.00	1.00	661	16.0	1.00	1.00
Shared a drug cooker or filtration cotton with another injector								
Yes	247	34.0	1.1 (0.8–1.6)	0.8 (0.4–1.7)	790	13.8	0.8 (0.6–1.1)	0.9 (0.6–1.5)
No	95	30.5	1.00	1.00	266	17.3	1.00	1.00
Backloaded								
Yes	149	41.6	**1.6 (1.1–2.1)**	1.4 (0.8–2.5)	632	11.9	**0.7 (0.5–0.9)**	**0.6 (0.4–0.9)**
No	175	26.9	1.00	1.00	481	18.3	1.00	1.00

Bold type highlights RRs and ARRs with 95% confidence limits that did not include 1.00.

ARR were obtained in a multivariate logistic regression model that included gender, race/ethnicity, age (≤24, >24), and residence (street or shelter vs. other), and these baseline drug use characteristics: usual drug injected (heroin vs. others), daily injector, usually pooled money with other IDUs, injected with a used syringe, shared a cooker or cotton, and backloading.

those who reported backloading (ARR = 0.6). After statistical adjustment, neither sharing of syringes or cooker/cotton nor reporting pooling one's money with other injectors to buy drugs were associated to any appreciable degree with remaining in the exchange program.

DISCUSSION

We studied one aspect of possible confounding in studies evaluating the efficacy of voluntary needle-exchange programs by examining factors related to in- and out-migration to and from the Seattle exchange. In our analysis, we examined drug use and risk behaviors collected before subjects began or ceased using the needle exchange. Over the 12-month follow-up period, 32% of nonexchangers began to use the program, and 15% of current exchangers stopped using the program. In both cases, the change in exchange use status was related to some extent to baseline risk behavior and to heroin injection. IDUs who injected heroin more often than other drugs were more likely to begin to use the exchange and less likely to stop exchange use. IDUs who reported they had injected recently with a used syringe and those who were homeless were more likely than others to initiate exchange use. Among current exchange users at study enrollment, daily injectors and those who reported backloading with another IDU were more likely to continue using the program. Thus, the program attracted new clients from the pool of IDUs who were at elevated risk of blood-borne viral infection, and losses from the exchange clientele included a disproportionate number of low-risk IDUs.

Information on needle-exchange use after the baseline interview was available for only 77% of those who were nonexchangers at baseline and for only 82% of those who were exchange users at baseline. However, the probability of loss to follow-up did not vary in relation to any of the factors shown in the Table, so it is unlikely that differential follow-up led to bias in the observed associations.[15] Differences in risk behavior between subjects as assessed at the baseline interview may not have applied to their behavior at the time their exchange use status changed; this was a limitation inherent in the 1-year follow-up design of the study. Reasons for disproportionate losses of African-American IDUs from the exchange could not be explained by differences in risk behavior or other characteristics, and they merit further study.

Consistent with a hypothesis of increasingly high-risk needle-exchange clients is a time-dependent effect of needle exchange reported in a previous study of Amsterdam IDUs, which showed a lower rate of HIV infection in exchange users versus other IDUs was noted only in the period soon after the program began.[6]

It is conceivable that reduced risk associated with use of needle exchange noted in evaluations carried out in the early years of the programs would appear to wane in the presence of underlying changes in the risk characteristics of exchange users. Recent studies have reported elevated HIV prevalence associated with current use of needle exchange in Vancouver and Montreal, Canada,[7,8] and no difference in hepatitis B virus or hepatitis C virus incidence in Seattle.[12] In Vancouver, confounding due to high-risk characteristics of exchange users may have contributed to earlier reports of increased HIV prevalence and incidence in Vancouver needle-exchange users.[16]

CONCLUSION

From this study, we conclude that volunteer bias may be at work in the formation of exchange user samples, with losses and gains to an exchange program resulting in retention of higher risk IDUs. Therefore, the "natural history" of needle-exchange programs presents several methodological challenges to evaluations of the efficacy of needle exchange in reducing transmission of blood-borne viruses, risk behaviors, or drug use frequency. The tendency for current users of an exchange to be persons at higher risk of HIV and other viral infections than other IDUs likely is distorting, downward and to an unknown degree, the observed efficacy of needle exchange, particularly in studies that rely on cross-sectional samples of IDUs. Overcoming these challenges to the discovery of possible benefits of needle-exchange programs will require careful measurement and control for risk characteristics that exist prior to exchange use.

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