Selection Effect of Needle Exchange in Anchorage, Alaska

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ABSTRACT Participation bias (selection bias) may be a problem in studies that attempt to evaluate the effects of needle-exchange programs (NEPs). The present study looked at only those injection drug users (IDUs) who were randomly placed in the needle-exchange condition in a two-arm randomized clinical trial of needle exchange. Time to follow-up between the experimental NEP condition ($n = 296$; median = 261 days) and pharmacy sales condition ($n = 304$; median = 256 days) was not statistically different [$\chi^2(1, N = 600) = 0.42, P = .52$]. Within the NEP condition, a similar analysis comparing time to follow-up between IDUs who used the NEP ($n = 65$; median = 199 days) and those who refrained from using the NEP ($n = 231$; median = 286 days) was highly significant, $\chi^2(1, n = 296) = 17.3, P = .0001$. The final logistic regression model predicting use of the NEP was the log 10 transformation of the number of times injected heroin in the last 30 days (odds ratio [OR] = 4.9, confidence interval [CI] 2.8, 8.9), ever injected amphetamine in the last 30 days (OR = 4.9, CI 1.09, 22.5), and ever shared injection equipment in the last 30 days (OR = 2.9, CI 1.5, 5.5). Within the NEP condition, follow-up rates differed between those who used the NEP and those who did not use it. Of drug users randomly assigned to an NEP, the ones who actually used the NEP had higher levels of drug use. Predictors of who used the NEP were consistent with the studies of Hagen et al. This study demonstrates that selection bias occurs among IDUs who use NEPs.

INTRODUCTION

Selection bias among individuals participating in voluntary or other nonrandomized studies is a threat to the validity of that study.¹ Campbell and Stanley² noted that selection bias is a threat to the validity of any study not using a randomized control design as only randomized studies allow unbiased comparisons between treatment and control groups.² The factor jeopardizing external validity is “the interaction effects of selection biases and the experimental variable.”^{2(p6)} This threat to external validity occurs when “of those initially designated as experimental groups participants, one eliminates those who fail to show up for the experimental session, then one selectively shrinks the experimental group in a way not comparably done in the control group, biasing the experimental group.”^{2(p16)}

Studies that have attempted to evaluate needle-exchange programs (NEPs) have been either observational studies of voluntary participation in NEPs^{3–6} or case-con-

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trol studies^{7,8} using serological markers of blood-borne pathogens among injection drug users (IDUs) and examining whether those who showed serological evidence of infection had reported use or nonuse of an NEP. Several studies have explicitly explored the selection bias inherent in sampling among voluntary NEP participants,^{1,9} while others have reported the results of the study without specifically mentioning the selection bias inherent in voluntary participation studies.¹⁰

Hagan and colleagues¹ reported bias in a nonrandomized study of those IDUs who used a voluntary NEP in Seattle, Washington. They found that IDUs who were homeless or who reported sharing injection equipment were more likely to use the NEP. Hahn et al.¹¹ also reported participation bias among IDUs who used a San Francisco, California, needle exchange. NEP use was associated with homelessness, higher frequency of injection, and knowledge of serostatus. NEPs attracted a subgroup of IDUs at very high risk, with seroconversion rates among the NEP users being significantly higher than among those who never used the NEP. Schechter et al.¹² found high frequencies of injection among IDUs who participated in an NEP in Vancouver, British Columbia. This group described frequent NEP use in Vancouver as occurring among men who reported frequent cocaine injection and among women who reported high frequencies of any drug injection, shooting gallery attendance, and having a nonlegal source of income.¹³ Flynn et al.⁵ also reported that the NEP in Baltimore, Maryland, attracted a group of IDUs at very high risk. These IDUs exhibited both high-frequency drug use and high levels of other risk behaviors.

The purpose of this study was twofold. First, we wanted to investigate time to follow-up between those individuals randomly assigned to an experimental NEP and those randomly assigned to an enhanced pharmacy sales condition and then explore the time to follow-up among only those individuals assigned to the experimental NEP, stratifying whether the individuals used the NEP at least once compared to those who were assigned to the NEP condition but refrained from using the NEP. Second, we wanted to investigate predictors of which individuals used the NEP compared to those who did not use the NEP among those individuals randomly assigned to the experimental NEP condition. We also report follow-up rates (proportion of subjects enrolled in each group who completed a follow-up interview) comparing NEP versus pharmacy sales subjects.

METHODS

A total of 600 IDUs were randomly placed in either an experimental NEP or a legal pharmacy sales condition. Only those randomly placed in the NEP were eligible to exchange syringes personally at the NEP. They were also able to purchase syringes at local pharmacies. Eligibility to participate in the study included being at least 18 years of age, reporting current injection, and having visible signs of injection (track marks). Pictures of the track marks were taken by trained medical photographers and rated for visual evidence of injection by dermatologists.¹⁴ Informed consent was obtained using an informed consent form approved by the University of Alaska Anchorage Institutional Review Board (IRB). After eligibility was determined, participants were interviewed using the National Institute on Drug Abuse (NIDA) Risk Behavior Assessment (RBA),¹⁵ a structured face-to-face interview administered to all participants regardless of assignment. The Risk Behavior Assessment has been shown to have good test-retest reliability¹⁶⁻¹⁸ and good validity of the drug use variables.¹⁹

Participants received pretest counseling for human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV) testing. After the counseling session, participants had their blood drawn by a certified phlebotomist, were paid \$25 for their time, and were given a reminder card to return for posttest counseling in 1 week and a referral card for hepatitis B vaccination (described in Trubatch et al.²⁰). Approximately 1 week later, participants returned for posttest counseling. At that time, the intervention counselor gave them their blood test results and opened the assignment envelope that revealed the experimental assignment for the participant.

Participants were also asked to return for a follow-up interview between 150 and 365 days later (nominally 6 months). When they completed the follow-up session, they were paid \$25. Kaplan-Meier survival analysis using a Cox-Mantel log-rank χ^2 was used to compare time to follow-up between the experimental NEP and the pharmacy sales arms of the study. Within the NEP condition, a similar analysis compared time to follow-up between IDUs who used the NEP at least once and those who refrained from using the NEP. Also, using only those participants assigned to the NEP condition, a logistic regression model was developed to predict who would use the NEP at least once during the study period. Variables considered as predictors included demographics, drug and sex risk factors, psychological symptomatology (including depression), and residential proximity to the NEP location. Univariate and bivariate statistical tests were used in model building, and the final model was based on empirical results.

RESULTS

Figure 1 shows the flow of participants through the study and the loss to follow-up at different points in time by assignment. There were 600 participants who were randomly assigned to the two arms of the study. The pharmacy sales condition had 79.9% (243/304) followed up at least once. The NEP condition had 83.4% (247/296) followed up at least once.

Survival Analysis

Survival analysis was used to compare time to follow-up between the experimental NEP ($n = 296$; median = 261 days) and pharmacy sales ($n = 304$; median = 256 days) conditions, $\chi^2(1, N = 600) = 0.42, P = .52$ (see Fig. 2).

Within the NEP condition, a similar analysis compared time to follow-up between IDUs who used the NEP at least once ($n = 65$; median = 199 days) and those who refrained from using the NEP ($n = 231$; median = 286 days), $\chi^2(1, n = 296) = 17.3, P = .0001$ (see Fig. 3). The proportion of individuals assigned to the NEP condition who used the program was 22% (65/296). Of those who used the NEP, 95.4% (62/65) had at least one follow-up session, 90.8% (59/65) were followed at 6 months, and 89.2% (58/65) were followed at 12 months.

Logistic Regression

Several variables were significant in bivariate analysis, but were not retained in the final multivariate model. Living situation, described as either living in a shelter or living on the street, was significant on χ^2 tests of association, but was not retained in the final model [$\chi^2(1) = 5.15, P = .02$]. NEP users were more likely to have in-

FIGURE 1. Proportion of participants lost by assignment.

come from illegal sources [$\chi^2(1) = 10.46$, $P = .005$] and to have higher mean 30-day incomes ($M = \$1359.37$, $SD = 1,512.43$) than nonusers ($M = \$893.47$, $SD = 1,069.91$) [$t(292) = 2.79$, $P = .02$]. They were less likely to identify themselves as unemployed but looking for work [$\chi^2(1) = 7.84$, $P = .005$]. Living in a census tract in or adjacent to the NEP location was significant on the Wilcoxon rank sum test ($z = -2.39$, $P = .02$), but was also not retained in the final multivariate model.

There was also a significant association between NEP use and pharmacy use for those in the NEP condition [$\chi^2(1) = 23.40$, $P = .0001$]. This was not considered as a candidate variable for the logistic regression model because it was not possible to obtain this at baseline, and it could only be obtained at follow-up. As we were

FIGURE 2. Proportion of participants lost by needle-exchange program use.

FIGURE 3. Comparison of time to follow-up between injection drug users who used the needle-exchange program at least once and those who refrained from using the needle-exchange program.

trying to develop a predictive model, this would not have been consistent with our desired time perspective for the analysis. An anonymous reviewer suggested that those (assigned to the NEP condition) who used both were more compliant. An alternative hypothesis appears to stand up better to examination; that is, the source of syringes was related to the intensity of injection, measured as the number of

injections in the 30 days prior to the 6-month follow-up ($F_{3,210} = 25.22$, $P = .0001$). Those who used neither were the lowest ($M = 1.8$, $SD = 7.1$), followed by those who only used the NEP ($M = 5.8$, $SD = 11.3$), followed by those who only used the pharmacy ($M = 6.4$, $SD = 18.3$), and finally followed by those who used both the NEP and the pharmacy ($M = 39.5$, $SD = 52.8$).

Three variables were retained in the final logistic regression model predicting use of the NEP: the log 10 transformation of the number of times injected heroin in the last 30 days ($OR = 4.9$, 95% CI 2.8, 8.9); ever injected amphetamine in the last 30 days ($OR = 4.9$, 95% CI 1.09, 22.5); and ever shared injection equipment in the last 30 days ($OR = 2.9$, 95% CI 1.5, 5.5).

CONCLUSION

Several previous studies of NEP use have commented on or acknowledged the presence of selection bias among participants of an NEP.^{1,5} This is the only randomized study of NEP conducted to date. As such, this is the only study that used the intention-to-treat method of randomized clinical trials. The other studies of voluntary participation bias, because of the lack of a randomized design, are similar to on-treatment analyses. Some studies of NEPs that have acknowledged the presence of selection bias have rationalized their findings because the selection bias appeared to be in the preferred direction; that is, NEP programs in those studies were attended by higher risk IDUs.^{12,21} These studies concluded that the rates of HIV/AIDS (acquired immunodeficiency syndrome) in these voluntary, high-risk participants would have been even higher if the NEPs had not existed.²²

Selection bias would be more of an issue in the United States if the bias were in the other direction (i.e., NEPs were documented to attract a lower risk population of IDUs). In Scotland, low-risk IDUs were more frequent attendees of an NEP than nonattendees.²³ Flynn et al.⁵ noted the tendency of a Baltimore NEP to attract a group of IDUs at very high risk and the associated problem of identifying an appropriate comparison group for NEP evaluations. Our randomized clinical trial found that, of those drug users randomly assigned to an NEP, the ones who actually used the NEP had higher levels of drug use. We also found that, of those individuals assigned to the NEP condition, those who used both the NEP and the pharmacy to obtain sterile syringes injected significantly more often. This would indicate that it was need, rather than compliance, that led to using multiple sources of sterile syringes.

In our study, no differences in time to follow-up were found between assignment conditions. However, IDUs who participated in the NEP returned earlier for follow-up than IDUs who did not use the NEP. The difference in follow-up rates between NEP users and nonusers is further evidence of selection effects elicited by participation in NEPs. The lack of difference between assignment arms is a demonstration of one advantage of random assignment.

The proportion of IDUs randomly assigned to the NEP condition who used the NEP (65/295 or 21.9%) is consistent with another study. Schoenbaum et al.¹⁰ reported that 21.9% of IDUs attending a methadone maintenance program in the Bronx, New York, also attended the local NEP. A major similarity between these two studies is that they were both prospective studies. Schoenbaum et al. established their cohort years before an illegal, replaced by a legal, needle exchange provided NEP access to their cohort. Most other NEP studies are either cross sectional or retrospective, or they establish their cohort after the NEP is in existence.

There were also significant differences in characteristics of those who used the NEP and those who did not use it. These findings are consistent with the findings of others^{1,11,12} who found higher frequencies of injection among users of NEPs when compared to nonusers. Our findings replicate and strengthen the arguments of Hagan et al.,¹ who demonstrated selection bias among participants of nonrandomized NEP studies. Our finding that, among those assigned to the NEP condition, use of both the pharmacy and the NEP demonstrated much higher frequencies of injection also needs to be further investigated and replicated.

It is possible that the beneficial effects of NEPs are small and are overwhelmed by local selection effects. It is also possible that, in the absence of NEPs, HIV rates would be no different from those rates found in high-risk cohorts with access to NEPs. These are alternative explanations for findings in NEP evaluation studies that should be dealt with in discussion sections of published reports and should not be ignored.

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REFERENCES

1. Hagan H, McGough JP, Thiede H, Hopkins SG, Weiss NS, Alexander ER. Volunteer bias in nonrandomized evaluations of the efficacy of needle-exchange programs. *J Urban Health*. 2000;77(1):103–112.
2. Campbell DT, Stanley JC. *Experimental and Quasi-Experimental Designs for Research*. Chicago, IL: Rand McNally College Publishing Company; 1963.
3. Bruneau J, Lamothe F, Franco E, et al. High rates of HIV infection among injection drug users participating in needle exchange program in Montreal: results of a cohort study. *Am J Epidemiol*. 1997;146(12):994–1002.
4. Des Jarlais DC, Marmor M, Paone D, et al. HIV incidence among injecting drug users in New York City syringe-exchange programmes. *Lancet*. 1996;348:987–991.
5. Flynn C, Junge MB, Riley E, Cohn S, Beilenson P, Vlahov D. Selection bias in needle exchange participation as observed in two cohorts of injection drug users. Paper presented at: International Conference on AIDS; June 28–July 3, 1998; Geneva, Switzerland.
6. Watters JK, Estilo MJ, Clark GL, Lorvick J. Syringe and needle exchange as HIV/AIDS prevention for injection drug users. *JAMA*. 1994;271(2):115–120.
7. Hagan H, Des Jarlais DC, Friedman SR, Purchase D, Alter M. Reduced risk of hepatitis B and hepatitis C among injection drug users in the Tacoma syringe exchange program. *Am J Public Health*. 1995;85:1531–1537.
8. Van Ameijden E, van den Hoek AJAR, Van Haastrecht H, Coutinho RA. The harm reduction approach and risk factors for human immunodeficiency virus (HIV) seroconversion in injecting drug users, Amsterdam. *Am J Epidemiol*. 1992;136(2):236–243.
9. Bruneau J, Franco E, Lamothe F. Assessing harm reduction strategies: the dilemma of observational studies. *Am J Epidemiol*. 1997;146:1007–1010.
10. Schoenbaum EE, Hartel DM, Gourevitch MN. Needle exchange use among a cohort of injecting drug users. *AIDS*. 1996;10:1729–1734.
11. Hahn JA, Vranizan KM, Moss AR. Who uses needle exchange? A study of injection

- drug users in treatment in San Francisco, 1989–1990. *J Acquir Immune Defic Syndr Hum Retrovirol.* 1997;15(2):157–164.
12. Schecter M, Cornelisee P, Van Haastrecht H, et al. A comparison of active injection drug users attending needle exchange and methadone maintenance programs in Vancouver versus Amsterdam. Paper presented at: International Conference on AIDS; June 28–July 3, 1998; Geneva, Switzerland.
 13. Archibald C, Ofner M, Strathdee SA, et al. Factors associated with frequent needle exchange program attendance in injection drug users in Vancouver, Canada. *J Acquir Immune Defic Syndr.* 1998;17:160–166.
 14. Cagle HH, Fisher DG, Senter TP, Thurmond RD, Kastar AJ. Classifying skin lesions of injection drug users: a method for corroborating disease risk. Washington, DC: National Clearinghouse for Alcohol and Drug Information; 2002.
 15. National Institute on Drug Abuse. *Risk Behavior Assessment.* Rockville, MD: National Institute on Drug Abuse; 1991.
 16. Fisher DG, Needle R, Weatherby N, Brown B, Booth R, Williams M. Reliability of drug user self-report. Paper presented at: Ninth International Conference on AIDS; 1993; Berlin, Germany.
 17. Needle R, Fisher DG, Weatherby N, et al. The reliability of self-reported HIV risk behaviors of drug users. *Psychol Addict Behav.* 1995;9(4):242–250.
 18. Weatherby NL, Needle R, Cesari H, et al. Validity of self-reported drug use among injection drug users and crack cocaine users recruited through street outreach. *Eval Program Plann.* 1994;17(4):347–355.
 19. Dowling-Guyer S, Johnson ME, Fisher DG, et al. Reliability of drug users' self-reported HIV risk behaviors and validity of self-reported recent drug use. *Assessment.* 1994;1(4):383–392.
 20. Trubatch BN, Fisher DG, Cagle HH, Fenaughty AM. Vaccination strategies for targeted and difficult-to-access groups. *Am J Public Health.* 2000;90(3):447.
 21. Bluthenthal RN, Kral AH, Gee L, Erringer EA, Edlin BR. The effect of syringe exchange use on high-risk injection drug users: a cohort study. *AIDS.* 2000;14(5):605–611.
 22. Lurie P. Invited commentary: le mystere de Montreal. *Am J Epidemiol.* 1997;146(12):1003–1006.
 23. Frischer M, Elliott L. Discriminating needle exchange attenders from non-attenders. *Addiction.* 1993;88:681–687.