LETTERS TO THE EDITOR

RE: "HIGH RATES OF HIV INFECTION AMONG INJECTION DRUG USERS PARTICIPATING IN NEEDLE EXCHANGE PROGRAMS IN MONTREAL: RESULTS OF A COHORT STUDY"

The central finding of the study by Bruneau et al. (1) is the existence of a statistical association between attendance at needle exchange programs (NEPs) and higher HIV incidence in injection drug users (IDUs). This association cannot be removed by addition to the multivariate models of potential confounding variables relating to differences in risk behaviors relevant to HIV infection in NEP attenders versus nonattenders. The assumption then made is that the potential causal link is operating in the direction NEP $\Rightarrow$ HIV incidence, and thus the conclusion is drawn that NEP attendance must somehow increase the risk of becoming infected with HIV.

As pointed out by Lurie (2), an alternative explanation is that the NEP attenders, in specific contexts that may vary from city to city, have a higher risk of HIV infection in comparison with nonattenders, before they ever attend NEPs. This is suggested by the data of Bruneau et al. (1), in that both the frequency of risk behaviors relevant to HIV infection and the prevalence of HIV infection were higher in NEP users than in non-NEP users at study enrollment. Furthermore, this possibility has been directly demonstrated in a recent paper by Hahn et al. (3), in which HIV incidence in IDUs who subsequently used or did not use NEPs was measured before NEP attendance. The HIV incidence before NEP attendance was indeed higher in the group that subsequently became NEP attenders than in those who did not (relative risk = 24.6 for HIV seroconversion in NEP users vs. nonusers). Thus, while this paper shows the same type of statistical association between NEP use and HIV incidence as that by Bruneau et al. (1), the difference is that, since Hahn et al. (3) have pre-NEP use incidence data, it is possible to assume that the potential causal link is, in fact, operating in the HIV $\Rightarrow$ NEP direction, i.e., the direction opposite to that postulated by Bruneau et al. (1). As the authors state, "The high seroconversion rate among future exchangers reflects a self-selection of high-risk users into the exchanges, not an effect of exchange itself" (3, p. 162).

The Montreal data (1), as stated by Lurie (2), do indeed show that NEP users are at higher risk of HIV infection than are non-NEP users. Unfortunately, however, in the absence of data on HIV incidence prior to NEP attendance, Bruneau et al. (1) are nevertheless forced to explain this observation in terms of what NEPs might be doing to cause a higher HIV incidence. However, risk behaviors in this context (of an observational study not designed to directly evaluate NEPs, such as this study) are merely a proxy for HIV incidence, and it cannot be assumed that any questionnaire, however complete and well-designed, could ever collect comprehensive drug-use interactions and their potential effects on HIV incidence amongst IDUs, ethnographic and sociologic studies are clearly required in addition to quantitative epidemiologic data (4, 5). Thus, while we do not wish to underestimate the importance of, for example, the study of social networks, their impact on HIV transmission (6), and the possible effects of NEPs on their formation (7) or, indeed, to be uncritical of NEPs in terms of potentially deleterious practices, such as restricted needle distribution in conjunction with limited opening times, we do wish to state that the study by Bruneau et al. (1), particularly in the light of the results of the paper by Hahn et al. (3), does not present convincing evidence that NEP attendance increases the risk of HIV infection per se.

A further piece of evidence that counters the idea that NEP use has a negative effect on (i.e., increases) HIV incidence is that the strength of the association observed by the study by Bruneau et al. (1) decreases over time of NEP attendance. When the results from the study by Hahn et al. (3) are taken into account, this is to be expected if NEPs are effective in reducing HIV incidence (figure 1). The decrease over time in the strength of the association is consistent with the fact that recruitment for the study by Bruneau et al. (1) commenced at about the same time (a few months before) as the NEP opened in Montreal.

The difference in interpretation of the direction in which the potential causal link between HIV infection and NEPs may be operating is not purely "academic." As made clear by Lurie (2), scientific data are being used by federal authorities to justify continued lack of funding for NEPs in the United States. With regard to this, it is salutary to compare the conclusions drawn from the two excellent studies (1, 3) discussed here. Bruneau et al. (1), although
stat\gathering clearly that their study was not designed specifically
to evaluate NEPs, have little option but to draw cautious and
somewhat negative conclusions. On the other hand, Hahn et al. (3)
state positively that because NEPs, at least in some
settings, clearly attract high-risk injectors, they are an ex-
cellent place to target intense behavioral interventions in
addition to providing clean needles. In the highly sensitive
political and social context of drug addiction and NEP use
in general, we as epidemiologists have a duty to be even
more than usually cautious about putting the cart before the
horse when interpreting our data.

REFERENCES
infection among injection drug users participating in needle
exchange programs in Montreal: results of a cohort study.
2. Lurie P. Invited commentary: Le mystère de Montréal. Am J
3. Hahn JA, Vranizan KM, Moss AR. Who uses needle
exchange? A study of injection drug users in treatment in San
not infected with HIV": implications for long-term HIV risk
reduction and HIV vaccine trials. J Acquir Immune Defic
drug sharing among injecting drug users: patterns, social con-
text and implications for transmission of blood-borne patho-
networks and risk for HIV infection. Am J Public Health
1997;87:1289–96.
7. Bruneau J, Franco E, Lamothe F. Assessing harm reduction
strategies: the dilemma of observational studies. Am J Epide-

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RE: “INVITED COMMENTARY: LE MYSTÈRE DE
MONTREAL”

We would like to respond to a recent commentary (1) on
a study of HIV seroconversion in the Montreal needle
exchange program (NEP). Like the Montreal study (2), ours
is one of the three studies on needle exchange reviewed by
the Institute of Medicine in 1995 (3). The commentary
states that our study (4) "suggests potential benefits for
NEPs" (1, p. 1003).

We found that injection drug users who used the needle
exchanges were at a higher risk for human immunodefi-
ciency virus infection than those who did not. Cross-
sectional analysis showed greater injection frequency,
homelessness, and awareness of human immunodeficiency
virus serostatus in needle exchange users. Additionally, a
longitudinal cohort analysis of seroconversion prior to nee-
dle exchange use showed high risk among injectors who
used needle exchange. The seroconversion rate was 9.38
percent per person-year (95 percent confidence interval
2.84–21.80 percent) prior to needle exchange use among
injectors who subsequently used needle exchange compared
with 0.38 percent per person-year (95 percent confidence
interval 0.02–1.73 percent) among those who never used
needle exchange. We therefore concluded that high-risk
injectors were more likely to use needle exchange.

This finding might be described as suggesting potential
benefits for needle exchange. We instead interpret it as
suggesting that the important task of accessing those at
highest risk was successful. We caution against making
further conclusions from our data about the benefits of
needle exchange.

REFERENCES
1. Lurie P. Invited commentary: Le mystère de Montréal. Am J
infection among injection drug users participating in needle
exchange programs in Montreal: results of a cohort study.
3. Hahn JA, Vranizan KM, Moss AR. Who uses needle
exchange? A study of injection drug users in treatment in San
not infected with HIV": implications for long-term HIV risk
reduction and HIV vaccine trials. J Acquir Immune Defic
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text and implications for transmission of blood-borne patho-
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RE: “INVITED COMMENTARY: LE MYSTÈRE DE
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In his invited commentary, Lurie (1) speaks out on the
uncertain benefits and harms associated with needle
exchange programs (NEP). The setting is the apparently
unexpected findings of Bruneau et al. (2), who observed
statistically significant increased human immunodeficiency
virus (HIV) prevalence and incidence associated with nee-
dle exchange attendance in Montreal. In Lurie’s view, "di-
verse studies generate a picture that overwhelmingly sup-
ports the effectiveness of NEP’s" (1, p. 1005). The theses in
his commentary are 1) that the findings of Bruneau et al. (2)
are the artifacts of selection bias and inadequate control for
confounding; 2) that our randomized trial of needle ex-
de
change currently underway in Anchorage, Alaska, is uneth-
ical and methodologically flawed; and 3) that, in Montreal,
"what is needed to reduce the terrible toll of HIV among
Montreal IDU’s is not less needle exchange but more" (1,
page 1005).

The explicit dismissal of the findings of Bruneau et al. (2) as the result of selection bias in Lurie's advocacy of more needle exchange misses a critical public health obligation to identify the behaviors of this group of injectors in Montreal and similar populations elsewhere. Granting Lurie's view that, with adequate access, needle exchange is effective in reducing HIV incidence, what constitutes adequate access is not well understood. It is likely a complex interplay of availability, knowledge, attitudes, readiness for change, and finally, behavior. Thus, it is premature and possibly incorrect to presume that the Montreal cohort, for whom needle exchange participation has been shown to be associated with increased risk of HIV infection, is necessarily best served by still more needle exchange. Rather, we should be looking to the unique database of Bruneau et al. (2) for clues to the complexities of unsafe injection practices and HIV transmission.

Similarly, additional dismissal by Lurie (1) of our randomized trial of needle exchange versus legal pharmacy sales (D. G. Fisher, Protocol funded by the National Institute on Drug Abuse, 1996) is also inappropriate. Briefly, our trial seeks to compare the efficacies of two methods for delivering clean injection paraphernalia to drug injectors, needle exchange versus legal pharmacy sales. The following corrections to Lurie's commentary are indicated: 1) individuals randomized to the needle exchange condition are not barred from obtaining syringes by any other means, including through pharmacy sales; 2) secondary exchange, that is, having a participant in the needle exchange condition exchange syringes for a participant in the pharmacy sales condition, is not prohibited; and 3) the pharmacy sales condition is an intervention that includes training in the purchase of syringes from a pharmacist. The significance of our experimental paradigm is a comparison of the effects of two plans of delivering clean injection paraphernalia. In its formulation, we sought to inform decision making in the real world conditions faced by public health practitioners concerned with reducing HIV risk. Thus, understanding the relative successes of the two plans is among our primary aims and the phenomenon of crossover, far from being an analytic nightmare, is an outcome of special interest. Specifically, participants randomized to the needle exchange condition who elect to obtain clean works from a pharmacist offer insights into the limitations of the needle exchange approach, and vice versa. Among our secondary analyses will be an exploration of 1) the predictors of choosing to obtain clean works and 2) the choice of method of access to clean injection paraphernalia, needle exchange, or pharmacy sales. We also wish to clarify that in defining our two study arms (needle exchange, pharmacy sales), we sought to compare two delivery methods, each under optimal conditions. Accordingly, randomization to pharmacy sales is actually to an enhanced pharmacy sale intervention. In addition to being informed of sympathetic pharmacy locations, these randomizes are taught effective methods of purchasing syringes, including what to say, how to behave, etc. Finally, because of state law, we reiterate that all drug injectors in Anchorage, Alaska independent of their participation in our trial. Our team has researched local pharmacies and has identified which are favorably inclined toward the sale of syringes. Thus, for participants and nonparticipants alike, it will be easier to obtain sterile syringes as a result of this trial. In addition, we offer free hepatitis B vaccination to all participants, including free taxicab rides to the clinic. External oversight of its ethical merit is also assured, through the appointment of a Data Safety and Monitoring Board that meets every 6 months. To date, no ethical concerns have been voiced.

Too often, the need for policy decision making cannot wait for results of research. Nevertheless, it is our view that this particular commentary, "Le Mystere de Montreal" (1), is a policy interpretation of a research finding. As such, its contribution to our understanding of the benefits and harms associated with needle exchange is limited. We are reminded of several important studies demonstrating the benefits of needle exchange but are then asked to dismiss, first, the unique opportunities that present themselves in the rich data base of Bruneau et al. (2) and, second, a unique randomized trial of two feasible approaches to delivering clean injection paraphernalia, needle exchange versus legal pharmacy sales. We caution against the dismissal of the study by Bruneau et al. (2) and our own as a potentially dangerous setback to our understanding of the needle exchange and HIV infection in drug injectors.

REFERENCES


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DR. LURIE REPLIES

It is perplexing that Dr. Fisher sees three of his comments as "corrections," as these same three points were made in my editorial. Still more amazing is his defense of his study in a manner that reinforces its unethical nature. He concedes in his letter that "with adequate access, needle exchange is effective in reducing HIV incidence" (1, p. 715). This echoes the statement in his National Institutes of Health grant proposal that the pharmacy arm (as opposed to the needle exchange program [NEP] arm) "represents the withholding of a potentially life-saving service" (D. G. Fisher, Protocol funded by the National Institute on Drug Abuse, 1995). Thus, by his own admission, his research violates the
As for the comments of Hahn et al., the NEP’s success in “accessing those at highest risk” (7, p. 714) was precisely the “potential benefit” I was suggesting.

REFERENCES


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DRS. BRUNEAU, LAMOTHE, AND FRANCO REPLY

We agree with Fisher and Bigelow (1) that a prime public health obligation is to understand the particular set of circumstances and behaviors that lead intravenous drug users to choose needle exchange programs (NEP) in specific urban settings. Consistent with the observation that NEP participation was associated with a higher risk of human immunodeficiency virus (HIV) seroconversion in our cohort (2), we also agree with their contention that it would be premature to conclude that what is needed in Montreal is more, not less, NEP (1). Lowndes and Alary (3), on the other hand, raise the more troubling issue that our approach to interpreting the association may have been flawed—that we assumed the causal link to operate in the direction NEP to HIV, rather than from HIV to NEP. They refer to a recent cross-sectional analysis (4) that showed that NEP users had more risk behaviors than did nonusers and asserted that our findings can only be the result of selection bias (3), despite our overly conservative approach to scrutinize the NEP-HIV association.

How would this selection bias operate? The high prevalence of risk behaviors among NEP users at the outset of program participation would presumably lead to a high HIV seroincidence that was already latent, as a consequence of exposures prior to entry into the program. Even when the temporal directionality of a NEP to HIV is preserved, as it is in a prospective cohort investigation, the possibility remains that the relatively high incidence observed among NEP users may reflect the high frequency of early seroconverters. Their final disease status in our analyses cannot be ascribed to the effects of the intervention, since not enough latency had been given for it to operate. It is conceivable, therefore, that selection bias may have resulted from the
large proportion of injection drug users who became early seroconverters and were counted among the NEP users. Our study has now reached the point where we can explore whether this excess of early seroconverters among NEP users may have biased the direction of our relative risk estimates to the point of making them consistent with the interpretation of lack of benefit for NEPs.

When we analyze the association on the basis of all 166 incident cases of HIV infection in the cohort, the annual incidence rates among NEP users and non users are 5.6 and 3.1 percent, respectively. The adjusted hazard ratio (HR) (for age, cohort period, gender, and language) is 1.78 (95 percent confidence interval 1.30–2.44). This point estimate is similar to the one reported in our original analysis (2). We then entertained latency in the analysis by removing early seroconverters whose outcome may have resulted from the remote circumstances that were associated with NEP attendance. We chose a purposely long latency period of 2 years and removed from the analysis all seroconversions occurring within that period, under the assumption that they would have had an infectious onset preceding establishment of the cohort. The resulting HR estimates will thus only reflect late seroconversions and sufficiently long NEP attendance. This left 65 late seroconverters for the cohort analysis. The new annual seroincidence rates were 5.2 and 2.6 percent, respectively, only slightly lower than the original averages including all incident cases. More important, however, was the fact that the underlying adjusted HR was 1.86 (95 percent confidence interval 1.12–3.09), which speaks against the possibility of selection bias tilting the association toward lack of benefit for NEPs. Additional restrictive analyses similar to the ones we conducted in the original article with the aim of probing for cumulative NEP use are consistent with the latter interpretation.

In light of these new results, we have to stand by our original interpretation and conclude that selection bias cannot be playing as severe a role, as suggested by Lowndes and Alary (3). We are fully aware of the potential policy implications of our findings and can only hope that the broader discussion on the putatively preventive effect of NEPs will be grounded more on scientific reasoning than on blind ideology. Perhaps, only then the discussion may for once concede as plausible the possibility that the “horse” may be dangerously before the “cart.”

REFERENCES

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