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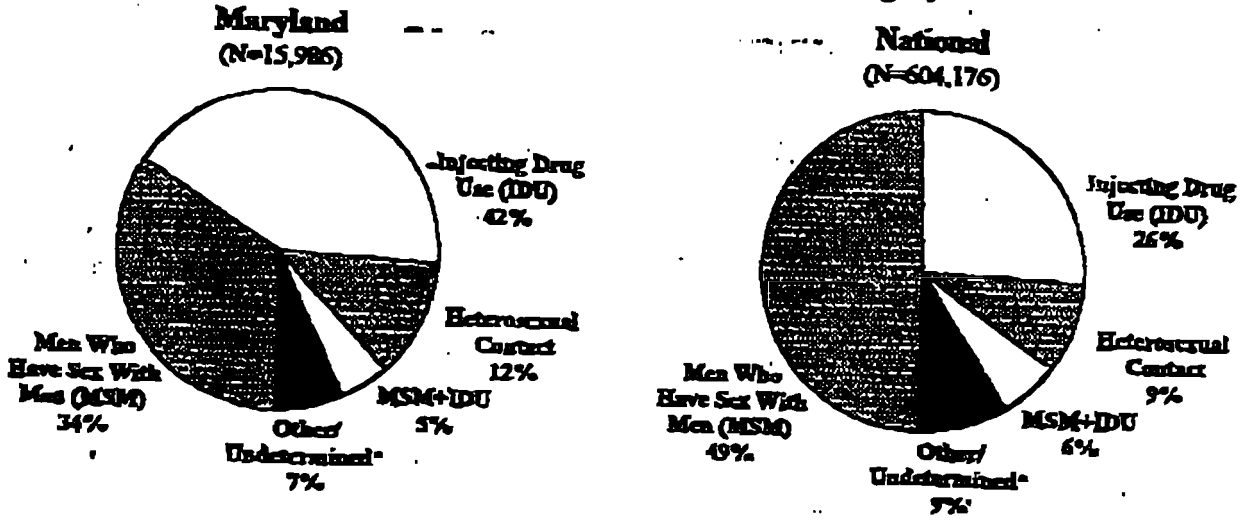
CESAR FAX
October 20, 1997
Vol. 6, Issue 41
Distribution: 3,000
A Weekly FAX from the Center for Substance Abuse Research
University of Maryland, College Park

Injecting Drug Use Associated with More AIDS Cases in Maryland than Nationally

The most recent data from the Maryland AIDS Administration show that of the nearly 16,000 AIDS cases diagnosed since 1981, 42% were associated with injecting drug use (IDU). This differs dramatically from the national trend; injecting drug use accounts for 26% of AIDS cases nationally. It is possible that the high rate of IDU-related AIDS cases in Maryland is due to the considerable degree of heroin use in Baltimore (see CSAT by Fax, Volume 2, Issue 17). The majority (52%) of Maryland AIDS cases are from Baltimore City.

Percentage of Cumulative Adult/Adolescent AIDS Cases Through June 30, 1997, by Exposure Category



*The category "Other/Undetermined" includes hemophilia/coagulation disorder and blood transfusion recipient.

SOURCE: Adapted by CESAR from data from the "Maryland HIV/AIDS Update," AIDS Administration, State of Maryland Department of Health & Mental Hygiene, August 1997; and the "HIV/AIDS Surveillance Report," 9(1). WWW document (Adobe Acrobat); URL http://www.cdc.gov/nchstp/hiv_aids/stats/hasrlink.htm (downloaded 9/25/97). For Maryland AIDS information, contact Carol Christmyer at 410-767-5198. For national AIDS information, contact the CDC National AIDS Clearinghouse at 800-458-5231.

CDC National AIDS Clearinghouse Offers HIV/AIDS Information and Materials

The Centers for Disease Control and Prevention's (CDC) National AIDS Clearinghouse provides information and materials on HIV and AIDS from databases maintained by the Clearinghouse, as well as from information sources maintained by other organizations, both public and private. The Clearinghouse services can be accessed by calling 1-800-458-5231.

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CESAR FAX is supported by a grant from the Governor's Office of Crime Control & Prevention.

Effectiveness of needle-exchange programmes for prevention of HIV infection

Susan F Hurley, Damien J Jolley, John M Kaldor

Summary

Background Needle-exchange programmes (NEPs) are potentially a key strategy for containing the spread of HIV infection among injecting drug users, but their implementation has been limited by uncertainty about their effectiveness. We used an ecological study design to compare changes over time in HIV seroprevalence in injecting drug users worldwide, for cities with and without NEPs.

Methods Published reports of HIV seroprevalence in injecting drug users were identified, and unpublished information on HIV seroprevalence for injecting drug users entering drug treatment in the USA between 1988 and 1993 was obtained from the Centers for Disease Control and Prevention. Details of the implementation of NEPs were obtained from published reports and experts. For each of the 81 cities with HIV seroprevalence data from more than 1 year and NEP implementation details, the rate of change of seroprevalence was estimated by regression analysis. The average difference in this rate for cities with and without NEPs was calculated.

Findings On average, seroprevalence increased by 5·9% per year in the 52 cities without NEPs, and decreased by 5·8% per year in the 29 cities with NEPs. The average annual change in seroprevalence was 11% lower in cities with NEPs (95% CI −17·6 to −3·9, p=0·004).

Interpretation A plausible explanation for this difference is that NEPs led to a reduction in HIV incidence among injecting drug users. Despite the possibility of confounding, our results, together with the clear theoretical mechanisms by which NEPs could reduce HIV incidence, strongly support the view that NEPs are effective.

Lancet 1997; 349: 1797–1800

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Introduction

The HIV epidemic in injecting drug users has reached crisis proportions, moving from its original focal points in Europe and North America to major outbreaks in Asian cities.[1] In the USA alone, use of injection-drugs was the direct or indirect cause of almost 26 000 cases of AIDS in 1995, comprising 35% of all new cases.[2] Needle-exchange programmes (NEPs) are potentially a key strategy for containing this epidemic, but they are not universally accepted. Government-funded NEPs are well established in several countries, including the UK, the Netherlands, and Australia.[3] However, there is still strong opposition to their implementation in the USA, where federal funding of NEPs has been prohibited until "the Surgeon General determines that such programs are effective in preventing the spread of HIV and do not encourage the use of illegal drugs".[4] State prescription and paraphernalia laws, which restrict the possession and distribution of needles and syringes, are a further impediment to the operation of NEPs in the USA.[5] Although NEPs had been established in 55 US cities by 1994,[6] many operate illegally, with tenuous funding, and on a small scale.[6,7]

Several observational studies have attempted to assess the effectiveness of NEPs in preventing HIV transmission. Most of these studies relied on surrogate endpoints such as self-reported risk behaviours,[8,9] or the occurrence of infections with hepatitis B or C virus.[9] The few studies that used HIV endpoints either compared HIV seroincidence rates or HIV seroprevalence in small numbers of NEP participants and non-participants, or correlated time trends in HIV seroprevalence for a single city with the introduction of NEPs.[10,11] Three reviews of NEP effectiveness commissioned by the US federal government since 1993[6,12,13] found that the evidence in favour of the effectiveness of NEPs was weak by accepted scientific standards. The goal of our study was to examine the effectiveness of NEPs with an approach that overcame some of the methodological limitations of previous studies. We used an ecological study design to compare changes over time in HIV seroprevalence in injecting drug users worldwide, for cities with and without NEPs.

Methods

Our analysis compared cities that had NEPs with those that had no NEPs. Programmes that distributed needles and syringes free of charge were regarded as NEPs, irrespective of how they operated (ie, from a fixed or mobile site, whether return of a used needle was mandatory, or the range of additional preventive services offered). We identified published reports of HIV seroprevalence surveys in injecting drug users that included 50 or more drug users and details of the implementation of NEPs in the corresponding city were obtained from reports and through communication with public-health officials and NEP researchers. We searched cities on Medline from between 1984 and May, 1994, HIV seroprevalence studies of injecting drug users and implementation of NEPs. Unpublished information on HIV seroprevalence was obtained from the Centers for Disease

Characteristics of cities	Cities with NEPs	Cities without NEPs
Location of cities		
North America	17	27
South America	0	1
Europe	8	18
Asia and the South Pacific	4	6
Total	29	52
Surveys, by type of recruitment site		
Drug treatment centres	402	316
Prisons	5	10
MSM/IDU services	38	43
Other sites	119	114
Total	563	483
Characteristics of surveys		
Average number of surveys per city	19·4	9·3
Total number of drug users surveyed	192738	139154
Average number of drug users surveyed per city	6648	2503
Average seroprevalence period, in years, per city	7·2	5·3
Average HIV seroprevalence at start of seroprevalence periods (%)	15·7	18·4
Average HIV seroprevalence at end of seroprevalence periods (%)	25·7	24·9

Table 1: Characteristics of cities and HIV seroprevalence surveys, by NEP status

Control and Prevention on injecting drug users entering drug treatment in 27 cities in the USA from 1988 to 1993.[9]

Cities were included in our analysis if HIV seroprevalence had been measured in injecting drug users in 2 or more calendar years, and basic information on NEP implementation was available. We defined a survey as a measurement of HIV prevalence among injecting drug users in a single city at a single point in time. If data were gathered during a specific time period, the midpoint was used as the survey date. For each survey in a given city and year, the number of drug users, percentage seropositive for HIV, and type of recruitment site or sites were recorded. Population size, estimated number of injecting drug users and indices of NEP *scope* (presence/absence and the number of needles distributed in each year) for the relevant city were recorded from published material and information provided by experts.

For each city, the seroprevalence period was defined as the time in years from the first to the last available survey. The rate of change of HIV seroprevalence over this period was estimated by regression analysis, with the equation: $\text{logit}(p_{ij}) = \alpha_i + \beta_i t_{ij}$, where p_{ij} is the ith measurement of prevalence in a city j.[10] The parameter β_i represents the rate of change in prevalence on a log odds scale. Calendar years, t_{ij}, were centred to 1990, so that the intercept terms represented the predicted seroprevalence in this year.

Average slopes (rate of change in HIV seroprevalence) were then calculated for cities with NEPs established during the period spanned by the surveys, and those without NEPs. The averages were weighted by the inverse of the squared SE of β_i to reflect the relative accuracy of each city's slope estimate. The difference in average slopes between the two groups was calculated and tested for significance with a linear model.[10] To assess the effect of introducing NEPs when HIV seroprevalence was still low, a subgroup analysis was done among cities in which the first measured seroprevalence was less than 10% and the seroprevalence period was more than 3 years. The average annual rate of change of seroprevalence was then compared between cities in which no NEP was introduced during the seroprevalence period and those in which an NEP had been introduced when seroprevalence among injecting drug users was below 10%.

Results

About 3500 published papers were reviewed, and information that satisfied the inclusion criteria for the study was obtained from 214 of these (references available from the authors on request). A total of 81 cities with HIV seroprevalence measurements from more than 1 year and information on NEP implementation were identified. 54% of these cities were in North America, 32% in Europe, and 12·4% in Asia and the South Pacific (table 1). In these cities, 1046 surveys of HIV prevalence involving 332892 drug users had been done between 1980 and 1995, 75% in drug treatment centres (table 1). Some serum specimens had been collected and stored, and were analysed when HIV tests became available. There were NEPs during the seroprevalence period in 29 (36%) cities; the mean duration of NEP implementation was 3·8 years (range 1–8). Seroprevalence was slightly higher at the start of the seroprevalence period in cities without NEPs than in cities with NEPs, and by the end of the seroprevalence periods average HIV seroprevalence had changed little in cities with NEPs, but had increased in cities without NEPs (table 1).

To illustrate the regression analyses, the results for two cities are shown in figure 1. In Bern, Switzerland, where

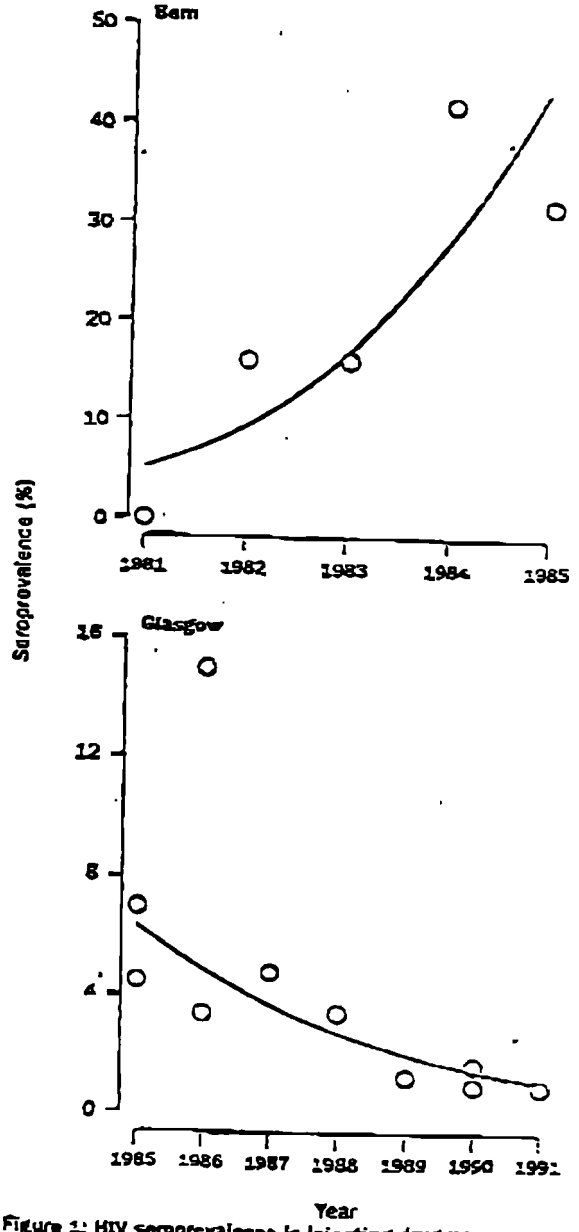

Figure 1: HIV seroprevalence in injecting drug users per year of survey for Bern, Switzerland, and Glasgow, UK
Lines represent fitted values from the logistic regression models. Note vertical scales are not the same for both cities.

	Cities with NEPs	Cities without NEPs
Number of cities with increase in seroprevalence according to regression modelling*	14 (48%)	30 (58%)
Estimated annual rate of change (%) in seroprevalence (95% CI)		
All cities	−5·8 (−10·1 to −1·4)	5·8 (−0·5 to 12·6)
Cities with initial seroprevalence <10% and seroprevalence surveys longer than 3 years (95% CI)	−1·1 (−21·2 to 24·2)	16·2 (3·0 to 31·2)

*Shape of plot of estimated log odds of seroprevalence vs time.

Table 2: Effect of NEPs on HIV seroprevalence

NEPs were not operating during the seroprevalence period, the rate of change of the log odds of seroprevalence was estimated to be 0·677 per year (SE 0·123), corresponding to a 96·8% increase each year (95% CI 53·8–150·0). In Glasgow, UK, NEPs were introduced in 1987. The estimated rate of change in the log odds of seroprevalence was −0·286 (0·042), corresponding to a 24·9% annual decrease in seroprevalence (−18·3 to −30·9).

Seroprevalence was estimated to have increased in 58% of cities without NEPs and 48% of cities with NEPs (table 2). The regression model showed that seroprevalence increased on average by 5·9% per year in the 52 cities without NEPs, and decreased by 5·8% per year in the 29 cities with NEPs—a difference of 11% (−17·6 to −3·9, p=0·004). The number of needles distributed over the seroprevalence period per 1000 injecting drug users was known for 21 cities, but was not a significant predictor of the rate of change of seroprevalence.

When analysis was restricted to cities with seroprevalence periods of more than 3 years with an initial seroprevalence below 10% we found that, on average, seroprevalence decreased by 1%, in the eight cities with NEPs compared with a 16% increase in the 18 cities without NEPs (figure 2), but this difference (−14·8 [95% CI −34 to 10]) was not significant. However, the regression modelling gave estimates of more than 10% for seroprevalence at the start of the period for four cities without NEPs, and one city with NEPs, apparently because the earliest surveys included fewer drug users and were consequently given less weight in estimation of slopes. Any bias would have caused the effectiveness of NEPs to be underestimated.

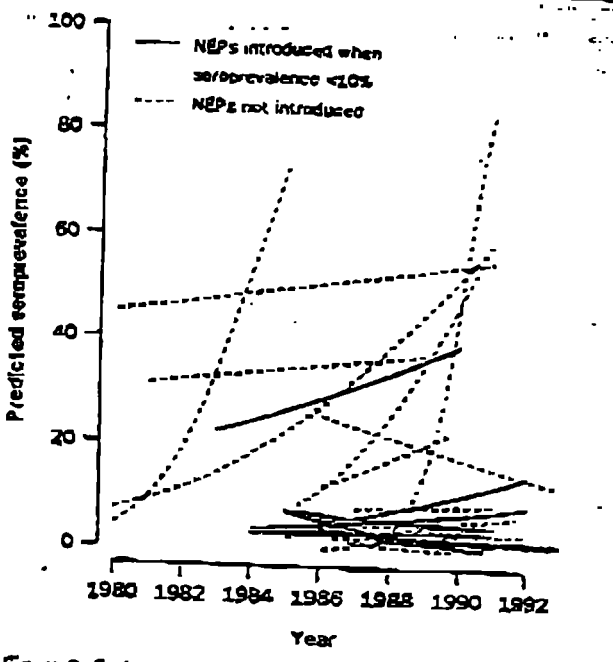

Figure 2: Estimated HIV seroprevalence per year of survey for cities where first seroprevalence was <10%* and seroprevalence periods were longer than 3 years
*Estimated seroprevalence is more than 10% at start for some cities because of regression modelling.

Discussion

We found that in cities with NEPs HIV seroprevalence among injecting drug users decreased on average, whereas in cities without NEPs HIV seroprevalence increased. A plausible explanation for this difference is that the NEPs led to a reduction in HIV incidence among injecting drug users.

NEPs have the potential to decrease directly HIV transmission by lowering the rate of needle sharing[11] and the prevalence of HIV in needles available for reuse,[12] as well as indirectly through activities such as bleach distribution, referrals to drug treatment centres, provision of condoms, and education about risk behaviour. Although these mechanisms have strong theoretical support, the published evidence for NEP effectiveness is limited. Previous studies of the effect of NEPs on HIV incidence used observational designs or statistical models. Observational designs included case studies, cross-sectional, serial cross-sectional, and cohort studies (often without comparison groups); and case-control studies.[4] Only one study assessed the impact of NEPs on HIV incidence. Des Jarlais and colleagues[7] estimated that the hazard for incident HIV infection was 3·3 for injecting drug users in four high-seroprevalence cities without NEPs, compared with continuous users of NEPs in New York City. One case study investigated HIV prevention activities for five cities with low seroprevalence, but did not formally compare these with other cities that had high seroprevalence.[13] The most frequently cited statistical model for assessment of NEP effectiveness was developed by the New Haven NEP evaluators, and is based on the theory that NEPs decrease HIV transmission rates by lowering the time that needles are in circulation.[14]

The conclusion of a 1993 review by a University of California team[5] was that NEPs are associated with decreased HIV drug risk behaviour and are not associated with negative outcomes, but that there is no clear evidence that they decrease HIV infection rates.[5] Few new data were available for the most recent US review by the Panel on Needle Exchange and Bleach Distribution Programs,[4] which concluded that NEPs are effective, but acknowledged that the evidence was weak.

Our study is distinguished from previous work by its worldwide scope and its design, which compares changes in HIV seroprevalence in cities with and without NEPs, rather than changes within a single city. Nevertheless, our analysis clearly has limitations. First, the seroprevalence data were collected according to different protocols in diverse populations. However, any inaccuracies would be unlikely to differ systematically between cities with NEPs and those without, so the consequent bias would be in the direction of underestimating the effectiveness of NEPs. Second, cities were selected for analysis by the existence of HIV seroprevalence surveys, and bias may have been introduced by the decision to do a survey in a particular

city. Furthermore, HIV seroprevalence may have remained low in some of the cities with NEPs, irrespective of their introduction. Finally, implementation of NEPs was almost certainly confounded by the implementation of other HIV prevention strategies, and the sale of injection equipment through pharmacies is one such strategy that could work similarly to NEPs. Therefore, the difference in rate of change of seroprevalence between cities with and without NEPs may not be due solely to NEPs.

Despite these limitations, our study provides evidence that NEPs reduce the spread of HIV infection. With the theoretical mechanisms by which NEPs could reduce HIV incidence, and the interpretation of previous studies by the Panel on Needle Exchange and Bleach Distribution Programs,[4] the view that NEPs are not effective no longer seems tenable.

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FAST TRACK

Needle exchange is not enough: lessons from the Vancouver injecting drug use study

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Objective: To describe prevalence and incidence of HIV-1, hepatitis C virus (HCV) and risk behaviours in a prospective cohort of injecting drug users (IDU).

Setting: Vancouver, which introduced a needle exchange programme (NEP) in 1988, and currently exchanges over 2 million needles per year.

Design: IDU who had injected illicit drugs within the previous month were recruited through street outreach. At baseline and semi-annually, subjects underwent serology for HIV-1 and HCV, and questionnaires on demographics, behaviours and NEP attendance were completed. Logistic regression analysis was used to identify determinants of HIV prevalence.

Results: Of 1006 IDU, 65% were men, and either white (65%) or Native (27%). Prevalence rates of HIV-1 and HCV were 23 and 88%, respectively. The majority (92%) had attended Vancouver's NEP, which was the most important syringe source for 78%. Identical proportions of known HIV-positive and HIV-negative IDU reported lending used syringes (40%). Of HIV-negative IDU, 39% borrowed used needles within the previous 6 months. Relative to HIV-negative IDU, HIV-positive IDU were more likely to frequently inject cocaine (72 versus 62%; $P < 0.001$). Independent predictors of HIV-positive serostatus were low education, unstable housing, commercial sex, borrowing needles, being an established IDU, injecting with others, and frequent NEP attendance. Based on 24 seroconversions among 257 follow-up visits, estimated HIV incidence was 18.6 per 100 person-years (95% confidence interval, 11.1–26.0).

Conclusions: Despite having the largest NEP in North America, Vancouver has been experiencing an ongoing HIV epidemic. Whereas NEP are crucial for sterile syringe provision, they should be considered one component of a comprehensive programme including counselling, support and education.

AIDS 1997, 11:F59–F65

Keywords: HIV-1, injecting drug users, incidence, prevalence, needle exchange, needle sharing, harm seduction

Introduction

Vancouver introduced a legal, free-standing needle exchange programme (NEP) and a street nurse programme in 1988 and 1989, respectively [1,2]. At that time, the estimated HIV prevalence was 1–2% among the city's population of 6000–10 000 injecting drug users (IDU) [3]. Vancouver's NEP appears to be the

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largest in North America, having exchanged over 1 million needles per year since 1993, and 2.3 million in 1996. Until recently, NEP was considered to be a major factor accounting for Vancouver's low HIV prevalence rate [4]. In 1993, among 16 NEP in North America that were independently evaluated by the US Centers for Disease Control and Prevention, the Vancouver NEP ranked in the top three in terms of the number of syringes exchanged and returned, the estimated proportion of IDU reached, and number of client referrals to drug treatment and support services [5].

However, following an initial period of stable, low HIV prevalence, a rapid increase in HIV infection among IDU has been documented in Vancouver since September 1994. Surveillance of HIV testing data in the province of British Columbia indicated that the proportion of self-identified IDU testing HIV-seropositive rose from 2 to 7% in an 18-month period [6]. As a result, in October 1994 the street nurse programme was bolstered. In addition, centralized bulk purchase of syringes for all 14 NEP in British Columbia was undertaken by the provincial government, allowing NEP to provide syringes in sufficient numbers to meet client needs. Although sterile syringes are exempt from paraphernalia laws in Canada, deregulation of syringe sales in British Columbia pharmacies was undertaken in December 1995 to further expand syringe access to IDU.

An outbreak investigation was conducted in 1995, which found needle sharing and social determinants such as unstable housing to be independently associated with recent HIV seroconversion among Vancouver's IDU [6]. Concern regarding the potential for continued HIV transmission in Vancouver's IDU population prompted the initiation of a new cohort study in 1996. Herein, this study reported upon baseline prevalence of HIV and hepatitis C virus (HCV) and associated risk behaviours among 1006 IDU, as well as first estimates of HIV incidence.

Methods

Study sample

Beginning in May 1996, persons who had injected illegal drugs at least once in the previous month and resided in the Greater Vancouver region were recruited into the Vancouver IDU Study through self-referral and street outreach. Evidence of recent injecting drug use was required by inspection of needle tracks. Eligible subjects provided written informed consent. At the baseline visit and semi-annually thereafter, subjects provided blood samples for HIV and HCV antibody testing, and underwent an interviewer-administered questionnaire. HIV tests reactive on enzyme-linked immunosorbent assay were confirmed by Western blot. Purified protein derivative (PPD) tuberculin skin testing was also performed at baseline. Subjects were reimbursed CDN$ 20 for each study visit, at which time referrals were provided for universal medical care, HIV/AIDS care, available drug and alcohol treatment, and counselling.

Study instrument

The study instrument was developed from a questionnaire used in our previous case–control investigation [6,7]. Questionnaires were administered by trained interviewers, all of whom were blind to the HIV serostatus of participants. Questionnaire information pertained to risk behaviours and living conditions in the previous 6 months. Detailed information was collected on demographics, injecting and non-injecting drug use, borrowing and lending of needles and other paraphernalia, re-use of one's own needle, syringe disinfection, source of needles, access and barriers to clean needle use, attendance at two local NEP, incarceration, housing, self-reported frequency of HIV testing, drug treatment, methadone maintenance and other drug/alcohol programmes.

Since our previous investigation revealed that attendance at shooting galleries *per se* was not a common practice [7], respondents were asked whether they had injected in places where they 'generally did not know the people and there was injecting in groups'. Persons who reported injecting for the first time in the previous 2 years were considered new IDU; the remainder were considered established IDU. Sexual behaviour and condom use were assessed for regular, casual and sex trade partners of the same and opposite sexes. Finally, subjects were asked about a variety of mental and social issues, including an abbreviated seven-item version of the Center for Epidemiological Study Depression Scale (CES-D) [8], suicidal ideation, sexual abuse, and self-reported diagnosis of mental illness.

Statistical analysis

IDU who tested HIV-seropositive at enrolment were compared with those who tested HIV-negative using contingency table analysis for categorical variables, and the Wilcoxon rank-sum test for continuous variables. NEP attendance was considered as follows: (i) ever attending any NEP, and (ii) frequent versus less frequent attendance (i.e., more than once per week versus less frequently). The latter categorization was chosen following inspection of the distribution of self-reported attendance. As in previous analyses [6,7], unstable housing was defined as living primarily in a hotel, boarding room, hostel, transition house, jail or on the street in the previous 6 months. CES-D scores were summed, and scores above the 75th percentile were considered to represent elevated depression scores.

Independent predictors of HIV prevalence at baseline were assessed using unconditional logistic regression. Variables that were significant at the 5% level in univariate models were entered into multivariate models in a stepwise, hierarchical fashion. In the final model, all relevant two-way interactions were evaluated. HIV incidence was calculated based on the incidence density approach, in terms of person-years of observation. All 95% confidence intervals (CI) were calculated based on the Poisson distribution.

Results

By February 1997, 1006 eligible IDU had completed baseline interviews and provided blood specimens for HIV and HCV antibody testing. Baseline HIV prevalence was 23.2% (95% CI, 20.6–25.8), of whom 58% were previously aware of their HIV-positive serostatus. HCV serology was conducted on the first 500 participants only, among whom HCV prevalence was 88% (95% CI, 85.2–90.8). PPD skin test reactivity was 25%.

Among 257 subjects who tested HIV-negative at baseline and attended their first semi-annual follow-up visit, 24 seroconversions were confirmed among 129.4 person-years of observation, yielding an estimated HIV incidence of 18.6 per 100 person-years (95% CI, 11.1–26.0). As of 28 February 1997, the overall follow-up rate among those who were eligible to return was 83%. Subjects eligible for follow-up who had not yet returned did not differ from those who had returned with respect to gender, ethnicity, frequency of injection, types of drugs used, or frequency of NEP attendance; however, they were significantly younger ($P = 0.01$).

Table 1. Comparison of HIV-positive and HIV-negative injecting drug users (IDU) at baseline in the Vancouver IDU Study (n = 1006).

Variable*	n (%)† HIV-positive subjects (n = 233)	HIV-negative subjects (n = 773)	Total	P‡
Sex				
Male	135 (58)	518 (67)	653 (65)	0.02
Female	96 (42)	257 (33)	353 (35)	
Sociodemographics				
Median (range) age (years)	34 (16–55)	35 (14–58)	35 (16–58)	0.64
Ethnicity				
White	139 (60)	518 (67)	657 (65)	0.01
Native	80 (34)	192 (25)	272 (27)	
Other	14 (6)	63 (8)	77 (8)	
Unstable housing	165 (72)	454 (59)	619 (62)	0.001
Education (< high school)	201 (86)	617 (80)	818 (81)	0.03
Incarceration	78 (33)	241(31)	319 (32)	0.51
High depression score	70 (30)	208 (27)	278 (28)	0.35
Homo-/bisexual activity (men only)	36 (27)	109 (21)	145 (22)	0.20
Non-consensual sex ever	99 (44)	270 (36)	369 (37)	0.03
IDU sex partner	74 (32)	236 (30)	310 (31)	0.72
Been paid for sex	74 (32)	161 (21)	235 (23)	< 0.001
Drug-using behaviours				
Median (range) age at first injection	19 (7–51)	18 (9–51)	18 (7–51)	0.73
Main drug injected				
Cocaine	167 (72)	470 (62)	637 (64)	< 0.001
Heroin	34 (15)	213 (28)	247 (25)	
Speedball	32 (14)	81 (11)	113 (11)	
Injecting with others	178 (76)	512 (67)	690 (69)	0.005
Established IDU (>2 years)	213 (91)	628 (81)	841 (84)	< 0.001
Attend NEP (ever)	218 (96)	691 (91)	909 (92)	0.01
Frequent NEP attendance (more than once per week)	189 (81)	544 (71)	733 (73)	0.002
NEP most frequent source of syringes	186 (80)	591 (77)	777 (78)	0.33
Obtained syringes from pharmacy	112 (48)	364 (47)	476 (47)	0.79
Cited any difficulties obtaining sterile syringes	64 (28)	176 (23)	240 (24)	0.35
Cited difficulties purchasing syringes from pharmacies	55 (32)	169 (31)	224 (31)	0.70
Borrowed used needles (ever)	175 (76)	509 (67)	684 (69)	0.007
Borrowed used needles	95 (41)	304 (39)	399 (40)	0.69
Lent used needles	88 (39)	293 (40)	381 (40)	0.89
Consistent bleach use§	10 (11)	76 (25)	86 (22)	0.003
Methadone maintenance (ever)	45 (19)	138 (18)	183 (18)	0.61
Current methadone maintenance	34 (15)	84 (11)	118 (12)	0.12

*Unless otherwise stated, behaviours refer to previous 6 months. †Unless otherwise indicated. ‡Based on χ^2 tests. §Restricted to 381 IDU who reported borrowing used needles. NEP, Needle exchange programme.

Table 2. Final multivariate logistic regression model of predictors of HIV-positive serostatus at baseline among injecting drug users (IDU) in Vancouver.

Variable	Adjusted odds ratio (95% CI)	P
Unstable housing*	1.61 (1.15–2.98)	0.005
Education (< high school)	1.79 (1.14–2.82)	0.006
Commercial sex*	1.66 (1.18–2.35)	0.008
Ever used borrowed needles	1.49 (1.04–2.14)	0.03
Inject with others*	1.62 (1.13–2.32)	0.008
Established injector†	2.24 (1.34–3.74)	0.002
Frequent NEP* attendance (more than once per week)	1.68 (1.13–2.51)	0.011

*Based on previous 6 months. †First injection >2 years previously. NEP, Needle exchange programme.

Demographic and behavioural characteristics at baseline for the 1006 IDU are shown in Table 1. Of these, the majority were men (65%); however, subjects testing HIV-positive at baseline were more likely to be women ($P = 0.02$). Although most subjects were white (65%), HIV-positive subjects were disproportionately of Native origin. HIV-positive subjects were significantly more likely to have less than a high school education, unstable housing, and to reside in a downtown Vancouver neighbourhood, which is the poorest postal district in Canada.

With respect to drug use, the most frequently injected drug was cocaine, which was more common among HIV-positive IDU ($P < 0.001$; Table 1). Relative to HIV-negative IDU, HIV-positive IDU were significantly more likely to be established IDU, were more likely to report engaging in commercial sex work, and were more likely to inject with others. The proportions of HIV-positive and HIV-negative IDU who reported lending and borrowing used needles in the previous 6 months were nearly identical, regardless of self-reported HIV serostatus. Almost one-half (45%) reported sharing other injection paraphernalia.

HIV-positive IDU were more likely to have ever attended NEP, and to attend NEP on a more regular basis, compared with HIV-negative IDU. However, there were no differences between these groups with respect to self-reported barriers in accessing sterile injection equipment, or difficulties purchasing syringes from pharmacies. Almost one-half of HIV-positive and HIV-negative IDU reported purchasing syringes from pharmacies in the previous 6 months. Despite widespread needle availability, however, subjects reported re-using their own needle a median of three times [interquartile range (IQR), 2–4]. A conservative estimate of injection frequency based on regular drug use patterns was 2.5 injections per day (IQR, 1–6). There were no differences between HIV-positive and HIV-negative IDU in terms of current or previous enrolment in methadone maintenance or other drug/alcohol programmes, or difficulties accessing drug treatment.

Multiple logistic regression was conducted in a hierarchical stepwise fashion to identify independent predictors of HIV-positive serostatus (Table 2). In the final model, sociodemographic variables that remained significantly associated with HIV-positive serostatus were unstable housing and low education. In examining

Table 3. Profile of documented seroconverting injecting drug users (IDU) observed in the Vancouver Injection Drug User Study*.

	Sex	Age (years)	Race	New IDU†	Main source of syringes	Difficulty accessing syringes	Drug of choice	Shared injection equipment	Housing
1	Male	48	White	No	NEP	No	Methadone	Yes	Unstable
2	Female	46	Native	No	NEP	No	Heroin	Yes	Unstable
3	Male	36	Native	No	NEP	No	Cocaine	Yes	Unstable
4	Female	43	White	No	NEP	No	Cocaine/heroin	Yes	Unstable
5	Female	44	White	No	NEP	No	Cocaine/heroin	No	Unstable
6	Male	40	White	No	NEP	No	Cocaine/heroin	Yes	Unstable
7	Male	46	White	No	NEP	Yes	Cocaine/heroin	No	Unstable
8	Male	35	Native	No	NEP	No	Cocaine	Yes	Unstable
9	Male	21	White	Yes	NEP	No	Cocaine/heroin	Yes	Unstable
10	Female	42	White	Yes	NEP	Sometimes	Cocaine/heroin	Yes	Stable
11	Male	43	White	No	NEP	Yes	Heroin/speedball	Yes	Unstable
12	Female	35	Native	No	NEP	No	Cocaine	Yes	Unstable
13	Male	43	White	No	NEP	No	Cocaine	No	Unstable
14	Male	27	White	Yes	Pharmacy	No	Cocaine/speedball	Yes	Unstable
15	Male	29	White	No	NEP	No	Cocaine/heroin	Yes	Unstable
16	Female	40	White	No	NEP	No	Heroin	No	Unstable
17	Female	43	White	Yes	NEP	No	Cocaine	Yes	Unstable
18	Male	32	White	No	NEP	Sometimes	Cocaine	No	Unstable
19	Male	36	Native	No	NEP	No	Heroin/speedball	Yes	Unstable
20	Male	26	Asian	No	NEP	No	Cocaine/heroin	No	Stable
21	Male	32	White	No	NEP	Sometimes	Cocaine	No	Unstable
22	Female	48	White	No	NEP	No	Heroin/speedball	Yes	Unstable
23	Female	31	Native	No	NEP	No	Cocaine/heroin	Yes	Unstable
24	Male	22	Native	No	NEP	No	Cocaine/heroin	Yes	Unstable

*Characteristics refer to the seroconversion interval (i.e., period between baseline HIV-negative test and first HIV-positive test at follow-up). †Injected for the first time in previous 2 years. NEP, Needle exchange programme.

behavioural variables, commercial sex work, borrowing used needles, injecting with others, being an established IDU, and attending NEP more than once per week were all independently associated with HIV-positive serostatus. These associations were unchanged after adjusting for age, gender, frequency of injecting, main drug injected or other factors. No significant two-way interactions were observed. The likelihood ratio statistic, which tests the global null hypothesis that the coefficients are not significantly different from zero, was highly significant ($P < 0.001$), providing support for adequate goodness of fit.

Although the limited number of HIV seroconversions observed to date precluded a formal statistical analysis, a profile of sociodemographic and behavioural characteristics was generated, based on the period between the last negative HIV test at baseline, and first positive HIV test at follow-up (denoted seroconversion interval; Table 3). Of the 24 seroconverters identified to date, similarities were noted relative to the overall cohort in terms of the proportions who were women, those who were Native, those who were established IDU, and those who most commonly injected cocaine. All but two individuals reported unstable housing, residing primarily in single room occupancy hotels in Vancouver. Only three reported commercial sex work during the seroconversion interval. It is particularly striking that 23 of the 24 seroconverters reported NEP as their most frequent source of sterile syringes, and only five reported having any difficulty accessing sterile syringes.

Discussion

In our prospective study of more than 1000 IDU in Vancouver, baseline prevalence rates of HIV and HCV were very high, at 23 and 88%, respectively. After 8 months of follow-up, our preliminary estimate of HIV incidence was 18.6 per 100 person-years. Such an estimate could have been biased upward by selective return for follow-up of those at highest risk of HIV seroconversion; however, differences in baseline risk behaviour between subjects who did and did not return for follow-up when eligible were not found. The estimate could also have been inflated if individuals who suspected they had become HIV-infected selectively returned for follow-up.

To address these possible biases, the incidence calculation was repeated under a best case scenario, assuming all eligible persons who had not returned would have tested HIV-negative at their 6-month follow-up visit. Even under this optimal scenario, the HIV incidence was 16.5 per 100 person-years (95% CI, 9.9–23.2). Although these incidence estimates were based on small numbers, even the lower bound of the lowest possible 95% CI (9.9%) was much higher than that observed among prospective IDU studies in Baltimore, Montreal, Amsterdam and New York [9–12]. It was concluded that these preliminary results were entirely consistent with an ongoing and serious outbreak of HIV infection among IDU in Vancouver [6].

Also of great concern in our study was the high level of reported needle-sharing behaviours. The proportions of IDU who reported borrowing and lending used needles were similar to those observed in our 1995 case–control investigation, which was based on the same target population [6,7]. At baseline in the present study, the proportion of HIV-positive IDU who reported lending used needles was nearly identical to that of HIV-negative IDU, regardless of self-reported HIV serostatus. This suggests that little, if any, behaviour change occurred among individuals in our sample who had received an HIV-positive test result. As in our previous study [7], consistent use of bleach among IDU borrowing used needles was low, and sharing of other injection paraphernalia was common.

Our data are particularly disturbing in light of two facts: first, Vancouver has the highest volume NEP in North America; second, HIV prevalence among this city's IDU population was relatively low until recent years. The fact that sharing of injection equipment is normative, and HIV prevalence and incidence are high in a community where there is an established and remarkably active NEP is alarming. A vast body of literature has suggested that NEP are associated with reduced incidence of HIV and HCV and do not lead to increased drug use [5,12–15]. Several studies have also shown NEP to be associated with decreased needle borrowing [9,12,15]. In cities where NEP is part of a comprehensive programme that includes HIV testing, counselling, education and drug treatment options, HIV incidence and associated risk behaviours have declined significantly over time [9,16,17]. Provided that services are available and IDU are willing, NEP can act as a stepping stone to addictions treatment, which can serve as the ultimate prevention if IDU choose to cease injecting.

In Vancouver, NEP was introduced early, but access to drug and alcohol treatment, methadone maintenance and counselling services remains inadequate. As early as 1990, the lack of appropriate services for addictions treatment in British Columbia, especially for cocaine users, was identified as a major barrier encountered by Vancouver's NEP attenders, among whom there was already a marked demand for HIV-related counselling [1]. This situation continues at present [6]. Our results do not argue against the overall effectiveness of NEP as an HIV intervention, but rather, they lead us to propose that without adequate and appropriate community-wide

interventions such as addictions treatment, detoxification and counselling, stand-alone NEP may be insufficient to maintain low HIV prevalence and incidence for an indefinite period. Our study, and recent findings of higher HIV incidence among Montreal's NEP attenders compared with non- or infrequent attenders [10], strongly suggest that the concept of harm reduction requires a broader perspective beyond NEP alone [14,17,18]. Support for this was provided from Amsterdam, where a continuum of harm-reduction activities was associated with lower HIV incidence and needle-sharing behaviours, but there was no evidence of a protective effect for single interventions such as NEP or methadone maintenance [9].

Why is it that Vancouver is experiencing an ongoing HIV outbreak despite a high volume NEP and pharmacy access? Although it is too early to draw inferences from our seroconversion data, some clues arise from our analysis of determinants of HIV-positive serostatus at baseline. Like other studies, our study found that factors such as borrowing needles [6,9,10,19–21] and injecting with others [20] were associated with HIV prevalence. It was also found that established IDU were more likely to be HIV-infected relative to new IDU, although this may have been a reflection of duration of exposure. Although cocaine injection *per se* did not appear as an independent risk factor, it is noteworthy that cocaine was more likely to be the drug of choice among HIV-positive IDU. Other studies have reported an elevated risk of HIV seroconversion associated with cocaine injection [22,23]. Indeed, a shift from heroin use to increasing dependence on cocaine may be an important factor in Vancouver's escalating HIV prevalence and incidence, since cocaine is commonly associated with more frequent injections [22]. If the conservative estimate of 2.3 injections per day in our cohort may be generalized to the city's estimated IDU population of 6000–10 000, approximately 5–10 million needles per year would be needed to meet the ideal scenario of 'one-set one-shot'. Whether it is realistic to expect, even with expanded pharmacy access, that this goal can be achieved in cities where cocaine is the drug of choice, remains to be determined. Finally, since commercial sex work was also independently related to HIV prevalence, it may be that sexual transmission plays an important role.

In the midst of an ongoing HIV outbreak, it is important not to overlook social and contextual factors that may be directly or indirectly related to HIV transmission [24–26]. As previously found in this setting [6], unstable housing was independently associated with HIV-positive serostatus. The predominance of single-room occupancy hotel rooms, which have been reported to serve as shooting galleries in Vancouver's poorest neighbourhood, may contribute to needle sharing [6]. Risks associated with less secure injecting locations have also been noted by others [18,27]. The hypothesis that specific social networks of IDU may be risk factors for HIV seroconversion, possibly as a result of mixing between HIV-negative individuals and those who are newly infected and have high viral loads, is also currently being explored. Ethnographic research is needed in the study of social networks to complement existing quantitative data.

Our study was not intended to evaluate the effectiveness of NEP, since the majority of subjects attended NEP at least once, and there were no estimates of HIV incidence among IDU in Vancouver prior to the introduction of NEP in 1988. In fact, without the presence of an active NEP that was implemented early, HIV incidence among IDU in Vancouver may have been much higher, much earlier. The fact that frequent NEP attendance was independently associated with HIV prevalence should not be interpreted as causal, because risk behaviours and exposure to HIV interventions could have changed following an HIV-positive diagnosis. In addition, NEP attendance was self-reported; validation of self-reports through record linkage with NEP's administrative databases will improve attempts to correlate NEP attendance with HIV incidence. Finally, it has been suggested that NEP attract higher risk IDU [10,28–31]. NEP could thus be associated with HIV infection, even in multivariate models, if residual confounding persists.

If NEP attract higher risk IDU, then an appropriate public health response should be to capitalize on this window of opportunity by using NEP as a vehicle to change social norms surrounding needle sharing. From this perspective, it is crucial that NEP be maintained as a cornerstone in HIV prevention. Appropriate education, counselling and treatment options should be implemented simultaneously with the introduction of NEP. Allocation of adequate resources is required to allow NEP and other community agencies to enhance services other than the sole provision of needles. The present data have suggested that even in cities with sustained low HIV prevalence, outbreaks of HIV can occur. Long-term evaluation of NEP is therefore necessary to allow HIV prevention activities to adapt to changes in the local environment. If the effectiveness of NEP diminish over time, as others have found [29], other complementary strategies will be need to be bolstered to reduce HIV transmission among IDU populations.

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