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Fast-tracked article

Risk factors for elevated HIV incidence rates among female injection drug users in Vancouver

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Abstract

Background: In 1997, we found a higher prevalence of HIV among female than among male injection drug users in Vancouver. Factors associated with HIV incidence among women in this setting were unknown. In the present study, we sought to compare HIV incidence rates among male and female injection drug users in Vancouver and to compare factors associated with HIV seroconversion.

Methods: This analysis was based on 939 participants recruited between May 1996 and December 2000 who were seronegative at enrolment with at least one follow-up visit completed, and who were studied prospectively until March 2001. Incidence rates were calculated using the Kaplan–Meier method. The Cox proportional hazards regression model was used to identify independent predictors of time to HIV seroconversion.

Results: As of March 2001, seroconversion had occurred in 110 of 939 participants (64 men, 46 women), yielding a cumulative incidence rate of HIV at 48 months of 13.4% (95% confidence interval [CI] 11.0%–15.8%). Incidence was higher among women than among men (16.6% v. 11.7%, $p = 0.074$). Multivariate analysis of the female participants' practices revealed injecting cocaine once or more per day compared with injecting less than once per day (adjusted relative risk [RR] 2.6, 95% CI 1.4–4.8), requiring help injecting compared with not requiring such assistance (adjusted RR 2.1, 95% CI 1.1–3.8), having unsafe sex with a regular partner compared with not having unsafe sex with a regular partner (adjusted RR 2.9, 95% CI 0.9–9.5) and having an HIV-positive sex partner compared with not having an HIV-positive sex partner (adjusted RR 2.7, 95% CI 1.0–7.7) to be independent predictors of time to HIV seroconversion. Among male participants, injecting cocaine once or more per day compared with injecting less than once per day (adjusted RR 3.3, 95% CI 1.9–5.6), self-reporting identification as an Aboriginal compared with not self-reporting identification as an Aboriginal (adjusted RR 2.5, 95% CI 1.4–4.2) and borrowing needles compared with not borrowing needles (adjusted RR 2.0, 95% CI 1.1–3.4) were independent predictors of HIV infection.

Interpretation: HIV incidence rates among female injection drug users in Vancouver are about 40% higher than those of male injection drug users. Different risk factors for seroconversion for women as opposed to men suggest that sex-specific prevention initiatives are urgently required.

Recent reports in Canada and numerous other countries indicate that HIV is increasingly affecting women.¹ Before 1995, adult women in Canada had 9.6% of all positive HIV tests for which the age and sex of the person being tested were known. By 1995, this proportion had increased to 18.5% and reached 23.9% in 2000. In addition, 39% of all new HIV infections among women in 2000 were attributed to injection drug use.² These data are consistent with findings in the United States where, in 1999, women accounted for 23% of all reported AIDS cases in adults, of which 42% were attributed to injection drug use.³

These data clearly indicate that the face of the epidemic is changing. Whereas some factors unique to the transmission of HIV to women are known, basic and behavioural research efforts addressing sex-related and drug-related vulnerabilities among female injection drug users (IDUs) are lacking.⁴ At a time when women's vulnerability to HIV infection is becoming increasingly apparent worldwide,^{5,6} a better understanding of the processes and factors that cause drug-related harm among women in industrialized countries is urgently required.

Since the mid-1990s, the Downtown Eastside of Vancouver, British Columbia, has experienced an explosive and ongoing HIV epidemic among IDUs with annual HIV incidence rates reaching as high as 19% in 1997.^{7,8} When subjects were enrolled in the Vancouver Injection Drug User Study (VIDUS), it was found that the baseline HIV prevalence was higher among women than men (35.2% v. 25.8%).⁷ Follow-up of this cohort now allows an investigation aimed at identifying the predictors of HIV seroconversion among female and male IDUs. Therefore, we sought to compare HIV incidence rates among male and female IDUs in Vancouver and to compare risk factors associated with HIV seroconversion.

Methods

Beginning in May 1996, individuals who had injected illicit drugs in the previous month were recruited into VIDUS. Overall, 1437 study subjects have been enrolled in the study, most of whom were recruited through self-referral and street outreach from Vancouver's Downtown Eastside, the biggest community of IDUs in the country.⁷ Individuals were eligible if they had injected illicit drugs at least once in the previous month, resided in the greater Vancouver region and provided written informed consent. Subjects were reimbursed Can\$20 for each study visit. The study was approved by the University of British Columbia/Providence Health Care Research Ethics Board. At baseline and semi-annually, subjects provided blood samples for HIV and HCV antibody testing and completed an interviewer-administered questionnaire. All eligible respondents had private interviews and pre- and post-test counselling with trained nurses.

The present study included all individuals from the VIDUS cohort who met the following eligibility criteria for this analysis. First, only participants who were HIV-negative at enrolment into the cohort study were included. Second, only participants who returned for at least one follow-up visit during the period between May 1996 and December 2000 were included.

The questionnaires were designed

to elicit demographic data and information about drug use, behaviour leading to an increased risk of HIV and drug treatment. Sociodemographic variables of interest in this analysis included age, Aboriginal ethnicity, incarceration in the last 6 months and stable versus unstable housing. We evaluated Aboriginal ethnicity in order to adjust for potential confounding that could have arisen because Aboriginal individuals represent different proportions of men and women in the cohort. Aboriginal status was based on self-report. Clients who reported having stable housing were those who were living in their own house or apartment. Unstable housing was defined as living arrangements that included single room occupancy hotels, transitional living arrangements such as staying with relatives, and homelessness. Risky injection variables included borrowing and lending syringes that had been used by someone else, overdose experience, and drug use behaviours such as frequent injection and bingeing behaviour. As we have done previously,^{9,10} we described clients who reported injecting cocaine or heroin once or more per day as frequent cocaine and heroin users respectively. Bingeing was defined as periods when drugs were injected more frequently than usual. Risk factors regarding sexual behaviour included having an HIV-positive sexual partner, being a man who has sex with men and having unsafe sex. Unsafe sex was defined as not using condoms with regular sexual partners, casual sexual partners or sex trade clients in the last 6 months. Regular partners were defined as those partners with whom the sexual relationship lasted for more than 3 months. Casual partners were defined as those partners with whom the sexual relationship lasted less than 3 months. Clients were defined as those partners with whom sex was traded for drugs or money.

All participants who were HIV-negative at their enrolment and completed at least one follow-up visit were eligible for statistical analysis. The event of interest in this study was HIV seroconversion. The date of seroconversion was estimated using the midpoint between the last negative and the first positive antibody test result. Cumulative incidence rates of HIV infection were calculated using the Kaplan-Meier method. In these analyses, time zero was defined as the date of enrolment. Participants who con-

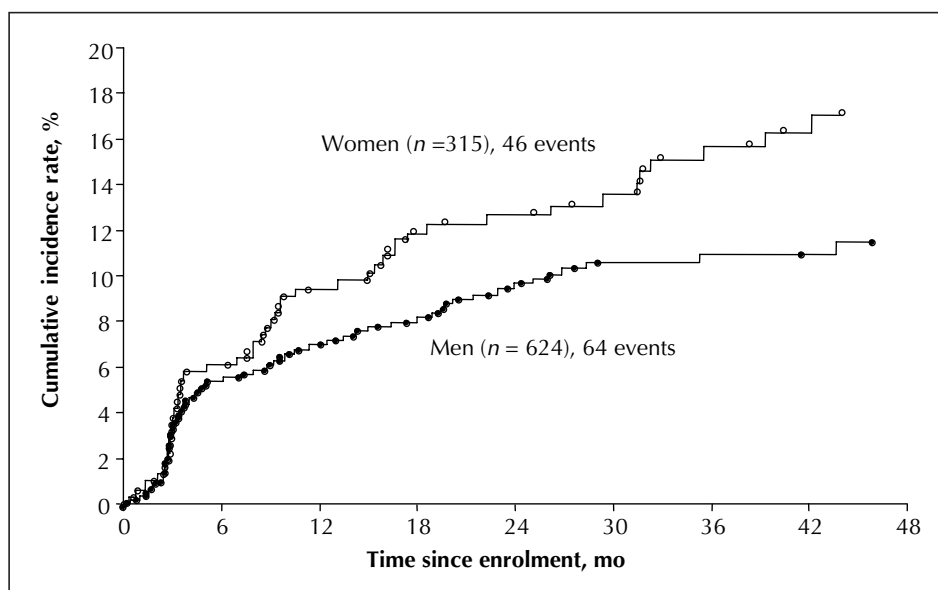


Fig. 1: Comparison of cumulative HIV incidence rates among male and female VIDUS participants (log-rank p value = 0.054). VIDUS = Vancouver Injection Drug User Study.

sistently remained seronegative were considered to be right censored at the time of their most recent test result. Annual rates of HIV seroconversion were calculated using actuarial methods. Relative risks and 95% confidence intervals were obtained for risk factors of interest. The Cox proportional hazards regression model was used to assess the independent effect of fixed and time-dependent covariates on time to HIV seroconversion in 2 separate analyses for men and women. All *p* values were 2-sided.

Results

Overall, 1437 participants completed the enrolment questionnaire. Of those, 939 were HIV-negative at enrolment and completed at least one follow-up visit and were, therefore, eligible for this analysis (624 men, 315 women). In comparison with those participants who did not come for a follow-up visit after January 1999, those who were followed were more likely to be Aboriginal (*p* = 0.001), to be married (*p* = 0.001), to be involved in the sex trade (*p* = 0.010) and to inject heroin (*p* = 0.001). No significant differences were found with regard to the frequency of cocaine use (*p* = 0.39), crack use (*p* = 0.181) or gender (*p* = 0.148).

Seroconversion had occurred in 110 of the 939 participants (64 men, 46 women) by March 2001, yielding a cumulative incidence rate of 13.4% (95% confidence intervals [CI] 11.0–15.8). As seen in Fig. 1, after 48 months of follow-up, incidence was higher among women compared with men (16.6% v. 11.7%, *p* = 0.074), although this difference just failed to reach conventional statistical significance.

There were marked differences between the HIV-negative male and female IDUs in the entire cohort at enrolment into the study (Table 1). Women were more likely to be Aboriginal, younger, to have had nonconsensual sex, to have an IDU sexual partner, to inject heroin, to inject cocaine, to smoke crack and to require assistance injecting (all *p* < 0.05). Of note, women reported shorter injecting careers at baseline (*p* = 0.001)

Table 2 presents the univariate results of the Cox regression analysis of sociodemographic predictors of seroconversion stratified by sex. Aboriginal status was associated with HIV seroconversion in

Table 1: Baseline sociodemographic and behavioural characteristics of male and female VIDUS participants who were HIV-negative at study enrolment

Variable	No. (and %) of men* <i>n</i> = 624	No. (and %) of women* <i>n</i> = 315	<i>p</i> value†
<i>Year of enrolment</i>			
1996	423 (68)	203 (64)	0.331
1997	86 (14)	50 (16)	
1998	65 (10)	29 (9)	
1999	41 (7)	29 (9)	
2000	9 (1)	4 (1)	
<i>Ethnicity</i>			
Non-Aboriginal	521 (83)	186 (59)	0.001
Aboriginal	103 (17)	129 (41)	
<i>Age, yr</i>			
Median	36.6	31.9	< 0.001‡
Interquartile range	29.1–41.8	24.1–38.7	
<i>Housing</i>			
Stable	250 (40)	137 (43)	0.314
Unstable	374 (60)	178 (57)	
<i>Years injecting</i>			
Median	12	9	0.001‡
Interquartile range	4–24	2–1	
<i>Ever had nonconsensual sex</i>			
No	510 (82)	98 (31)	0.001
Yes	114 (18)	217 (69)	
<i>IDU sexual partner</i>			
No	343 (55)	140 (44)	0.002
Yes	281 (45)	175 (56)	
<i>Condom use with regular partners</i>			
No	512 (82)	253 (80)	0.519
Yes	112 (18)	62 (20)	
<i>Frequency of heroin injection</i>			
< once per day	426 (68)	180 (57)	0.001
≥ once per day	198 (32)	135 (43)	
<i>Frequency of cocaine injection</i>			
< once per day	432 (69)	191 (61)	0.008
≥ once per day	192 (31)	124 (39)	
<i>Frequency of speedball (heroin and cocaine) injection</i>			
< once per day	572 (92)	274 (87)	0.023
≥ once per day	52 (8)	41 (13)	
<i>Crack cocaine use</i>			
< once per day	588 (94)	280 (89)	0.003
≥ once per day	36 (6)	35 (11)	
<i>Borrows injection equipment</i>			
No	385 (62)	197 (63)	0.802
Yes	239 (38)	118 (37)	
<i>Requires help injecting</i>			
No	410 (66)	144 (46)	0.001
Yes	214 (34)	171 (54)	

Note: VIDUS = Vancouver Injection Drug User Study, IDU = injection drug user.

*Unless stated otherwise.

†Based on Pearson's χ^2 test (uncorrected).

‡Based on Student's *t*-test for independent samples.

both women (relative risk [RR] 1.7, 95% CI 0.9–3.1) and men (RR 2.2, 95% CI 1.3–3.8), though was of only marginal significance in the former. Incarceration (RR 1.7, 95% CI 0.9–3.2) and unstable housing (RR 1.8, 95% CI 0.98–3.2) were associated with slightly elevated relative risk for women. Among men, there was a trend toward greater age being protective against seroconversion (RR 0.97, 95% CI 0.95–1.00 per year). All other demographic characteristics were not significant.

When risks associated with injection drug use among men were considered, speedball (heroin and cocaine) injection more than once per day (RR 2.2, 95% CI 1.1–4.2), any cocaine use in the last 6 months (RR 1.9, 95% CI 1.0–3.5), cocaine injection more than once per day (RR 3.5, 95% CI 2.1–6.0) and borrowing needles in the last 6 months (RR 2.1, 95% CI 1.2–3.5) were significant predictors of HIV seroconversion in univariate analyses. Current methadone use was marginally protective (RR 0.5, 95% CI 0.2–1.1). Among women, speedball injection more than once per day (RR 2.1, 95% CI 1.1–4.1), any cocaine use in the last 6 months (RR 4.4, 95% CI 1.8–10.5), cocaine injection more than once per day (RR 3.0, 95% CI 1.6–5.4), any heroin use in the last 6 months (RR 2.0, 95% CI 0.97–4.0), heroin use more than once per day (RR 2.0, 95% CI 1.1–3.6) and requiring help injecting in the last 6 months (RR 2.5, 95% CI 1.4–4.5) were associated with seroconversion in univariate analyses. Reporting crack cocaine use in the last 6 months was marginally significant (RR 1.8, 95% CI 0.9–3.3).

With regard to sexual risks, we found no evidence to suggest that having a sexually transmitted infection, being paid for sex or having unsafe sex with clients or casual partners were predictive of seroconversion for men and women. Although it did not achieve statistical significance, having an HIV-positive regular partner was associated with marginally elevated relative risks of seroconversion for both

men (RR 2.3, 95% CI 0.9–5.6) and women (RR 2.7, 95% CI 1.0–7.5). In addition, for men, having sex with another man (RR 2.9, 95% CI 0.9–9.3) was also marginally associated with seroconversion. We also noted a nonsignificant, but elevated, risk associated with having unsafe sex with a regular partner for women (RR 2.6, 95% CI 0.8–8.5).

The variables that were found to be independent predictors of time to HIV seroconversion in the multivariate analysis for women are listed in Table 3. The analysis restricted to women revealed frequent cocaine use (adjusted RR 2.6, 95% CI 1.4–4.8) and requiring assistance with injecting drugs (adjusted RR 2.1, 95% CI 1.1–3.8) to be independent predictors of seroconversion. In addition, unsafe sex with a regular partner (adjusted RR 2.9, 95% CI 0.9–9.5) and having an HIV-positive partner (adjusted RR 2.7, 95% CI 1.0–7.7) were marginally associated with seroconversion after adjustment for Aboriginal ethnicity, which was also marginally significant.

The results of the multivariate analyses of the characteristics of male participants are shown in Table 4. Among male participants, borrowing needles (adjusted RR 2.0, 95% CI 1.1–3.4), Aboriginal ethnicity (adjusted RR 2.5, 95% CI 1.4–4.2) and frequent cocaine injection (adjusted RR 3.3, 95% CI 1.9–5.6) were independent predictors of HIV infection.

Interpretation

The present data confirm that female IDUs in this setting are at higher risk than male IDUs for HIV seroconversion. Although the elevation in incidence rates among women failed to reach conventional statistical significance, we view it as confirmatory in light of the fact that baseline prevalence was statistically higher among women.⁷ Only one other study has reported an elevated HIV incidence rate among female IDUs, but this difference disappeared over

Table 2: Sociodemographic predictors of HIV seroconversion among male and female participants in VIDUS

Characteristic	Men (n = 624)	Women (n = 315)
	RR (and 95% CI)	RR (and 95% CI)
<i>Ethnicity</i>		
(Aboriginal v. non-Aboriginal)	2.2 (1.3–3.8)	1.7 (0.9–3.1)
<i>Housing</i>		
(unstable v. stable)	1.5 (0.9–2.4)	1.8 (0.98–3.2)
<i>Incarceration (during previous 6 mo)</i>		
(yes v. no)	1.4 (0.8–2.3)	1.7 (0.94–3.2)
<i>Married or common-law status</i>		
(yes v. no)	0.7 (0.3–1.4)	0.7 (0.4–1.3)
<i>Attended high school</i>		
(yes v. no)	1.7 (0.9–3.2)	0.9 (0.5–1.8)
<i>Years injecting drugs (per yr)</i>	0.98 (0.96–1.01)	0.98 (0.95–1.02)
<i>Age (per yr)</i>	0.97 (0.95–1.00)	0.98 (0.95–1.02)

Note: RR = relative risk, CI = confidence interval.

time.¹¹ In our data, the incidence curves for male and female IDUs show no sign of convergence in the near future.

What is the explanation for this elevated risk of HIV infection among women in this setting? It is clear from the data that female IDUs in the cohort, although living in the same geographic area as male IDUs, differ significantly in their sociodemographic and risk profiles. Ordinarily, one explanation for this would be differential sampling methods for women and men. However, we know of no method of recruitment for the study that would have selected women differently from the men. Indeed, in our experience, the different profiles seen in Table 1 reflect differences in the underlying populations of female and male IDUs in this area.¹²

Not only did the women in this study differ from the men with regard to their risk behaviours, but it also appears that some risk factors have different etiologic effects in women and men. Previously, the HIV epidemic that has occurred in this setting has been considered to be cocaine driven, and risky behaviours and high rates of seroconversion were believed to be inextricably linked to the chaotic, needle-sharing behaviour of the cocaine binger.^{7,9,13} This analysis does not discount these earlier findings, because frequent cocaine injection was a strong predictor of seroconversion in both men and women. However, needle borrowing was not a risk factor for women but was associated with a markedly elevated risk in men.

The strong association between requiring help injecting and HIV seroconversion appears to be a new finding. Results from a cross-sectional study conducted in San Francisco indicated that women were more likely to be the recipients of injections than men and suggested that women's smaller veins and the fact that men control the administration of drugs might explain this phenomenon.¹⁴ More recently, a study conducted in Scotland confirmed observations by others that being "injection dependent" has much to do with the distribution of power and control in sexual relationships with drug-injecting men.¹⁵ In Canada, we previously identified needing help injecting to be a strong risk factor for syringe sharing,¹⁰ and it is troubling that this risk factor has now been identified as a predictor of HIV seroconversion. The fact that some women have very little control over the drug preparation and injection process presents a very challenging problem for harm reduction initiatives.¹⁶

The extent to which sexual transmission contributes to HIV infection among IDUs is difficult to assess, however, it is generally accepted that having unsafe sex is of greater concern for women,^{4,17} because heterosexual transmission of HIV infection is more efficient from men to women.¹⁸ A recent study from Baltimore provides evidence that sexual behaviour is associated with seroconversion among female IDUs,¹⁹ and working in the sex trade was recently identified as a risk factor in San Francisco.²⁰ Although many studies

Table 3: Multivariate Cox proportional hazards regression model of factors associated with HIV seroconversion for women

Variable	Unadjusted RR (and 95% CI)	Adjusted RR (and 95% CI)
<i>Frequent cocaine injection</i> (≥ once per day v. < once per day)	3.0 (1.6–5.4)	2.6 (1.4–4.8)
<i>Requires help injecting</i> (yes v. no)	2.5 (1.4–4.5)	2.1 (1.1–3.8)
<i>Unsafe sex with a regular partner</i> (yes v. no)	2.5 (0.8–10.0)	2.9 (0.9–9.5)
<i>HIV-positive partner</i> (yes v. no)	2.7 (0.9–7.5)	2.7 (1.0–7.7)
<i>Aboriginal ethnicity</i> (yes v. no)	1.7 (0.9–3.1)	1.8 (1.0–3.2)

Table 4: Multivariate Cox proportional hazards regression model of factors associated with HIV seroconversion for men

Variable	Unadjusted RR (and 95% CI)	Adjusted RR (and 95% CI)
<i>Borrowed needles</i> (yes v. no)	2.1 (1.2–3.5)	2.0 (1.1–3.4)
<i>Aboriginal ethnicity</i> (yes v. no)	2.2 (1.3–3.8)	2.5 (1.4–4.2)
<i>Frequent cocaine injection</i> (≥ once per day v. < once per day)	3.5 (2.1–6.0)	3.3 (1.9–5.6)

emphasize the role of sex trade clients as the source of HIV transmission in female IDUs, it is noteworthy that we did not detect any risk associated with casual partners or clients.²¹ Other studies have similarly suggested that sexual risk in female IDUs may be related more to intimate partnerships than to sex trade clientele.^{22,23}

Several limitations of this study should be acknowledged. First, as with most cohort studies of injection drug users, the study population was not a random sample of all IDUs in this area. Nevertheless, it is noteworthy that our study group contains more than 20% of the estimated 5000 IDUs who reside in the Downtown Eastside. Second, recall bias is always a possibility in such studies, although in most instances individuals with new cases of HIV would not have been aware of their positive HIV status at the time of the interview. Third, as in most studies of injection drug users, our study was based on self-reported behaviours, and it is possible that socially desirable reporting may have had an impact on our study.^{24,25} However, previous studies have shown that self-reporting of injection drug users is valid, and that adjustment for measures of social desirability had only a negligible impact on associations between HIV and risky behaviours.²⁶ A final limitation is that the risk profile of participants who were lost to follow-up in our study was different from that of those who were followed.

Our data demonstrate that an elevated risk of incident HIV infection exists among female IDUs in Vancouver. These findings further demonstrate the urgent need for sex-specific programs involving needle exchanges, safe injection sites and street nurses that can better accommodate the challenges and concerns of female IDUs.²⁷

Competing interests: None declared.

Contributors: Dr. Spittal was responsible for the design of this analysis and its interpretation, for the literature review, and for writing the manuscript. Mr. Craib and Ms. Li conducted the analyses and wrote first drafts of the Methods and Results sections and approved the final version of the article. Ms. Laliberté was responsible for coordinating the collection of the data including the follow-up of the subjects and the interviews and contributed to revisions of the manuscript. Drs. O'Shaughnessy and Tyndall were involved in the interpretation of the findings and in reviewing and revising the final manuscript. Mr. Wood and Dr. Schechter were involved in the data analysis and interpretation of findings and contributed substantively to the final manuscript.

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