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Impact of length of injecting career on HIV incidence among people who inject drugs

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HIGHLIGHTS

- The duration of injection drug use career on HIV seroconversion is examined.
- Kaplan–Meier methods and Cox regression are applied to data from a prospective cohort study.
- Results indicate length of injection drug use is negatively associated with HIV seroconversion.
- Interventions are needed for PWID with shorter duration of injection drug use careers.

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ABSTRACT

We examined the relationship between duration of injecting career and HIV seroconversion among people who inject drugs (PWID) in Vancouver, Canada. Data were derived from HIV-negative PWID enrolled in a prospective cohort study. We employed Kaplan–Meier methods and Cox regression to investigate the effect of length of time since injection drug use initiation on time to HIV seroconversion. In multivariable Cox analysis, duration of injecting career was negatively associated with time to HIV seroconversion (adjusted hazard ratio = 0.82; 95% confidence interval [CI]: 0.69–0.97). Our findings highlight the need for interventions that target individuals who participate in high-risk drug use behaviors.

1. Introduction

Injection drug use is associated with a multitude of health risks, including soft tissue infections (e.g., abscesses and cellulitis) and blood-borne infections (e.g., Human Immunodeficiency Virus [HIV] and Hepatitis C Virus [HCV]) (Binswanger et al., 2000; Wood et al., 2003). The prevalence of HIV infection is at least 22 times greater among people who inject drugs (PWID) than among the general population based upon available data from 49 countries worldwide; and at least 50 times greater for PWID in 11 countries (HIV/AIDS, J.U.N.P.o., 2012). It is well known that, unlike other high-risk populations (e.g., men who have sex with men, sex workers), where HIV transmission is mainly driven by unprotected sexual intercourse, HIV infection among PWID is mainly transmitted via the sharing of unsterile syringes.

With evidence suggesting that conventional drug-control and enforcement policies, including punitive mandatory minimum sentencing and compulsory drug detention are not adequate in reducing injection drug use and the high prevalence of HIV infection among PWID (Beyrer et al., 2010; Degenhardt et al., 2010; Hankins, 2013; Strang et al., 2012; Vlahov, Robertson, & Strathdee, 2010; Wood et al., 2003), world leading public health and medical bodies are strongly recommending comprehensive strategies that include interventions to reduce the number of people injecting drugs, reduce transmission of HIV among PWID, and provide treatment for those who are HIV positive (Ball, 2007; Ball et al., 2005; Piot & Quinn, 2013; Strang et al., 2012; Vlahov et al., 2010; WHO, 1974, 2004, 2008, 2012; Wood et al., 2003). In the interest of minimizing risk of HIV infection in the most cost-effective manner, it has been shown that HIV interventions are best targeted toward the most vulnerable subgroups of PWID (Degenhardt et al., 2010; Piot et al., 2008; Vlahov et al., 2010).

Early studies of HIV prevalence and incidence among PWID provided equivocal evidence concerning the complex relationship between potential changes in risk-taking behavior over time and HIV infection (Fennema et al., 1997; Nicolosi et al., 1992; Rezza et al., 1994; Van

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Ameijden et al., 1992). While increasing rates of HIV infection over time have been observed, they were associated strictly with current chronological age of the drug user or the age at initiation of injection drug use, leaving increasing rates to be interpreted as a result of any or all of escalating network risk, behavioral risk, or cumulative exposure over time (Bautista et al., 2010). More recent cross-sectional studies specifically investigated duration ('shorter duration' vs. 'more experienced' drug users) as a variable of interest, although inconsistent definitions of 'short duration' and/or the use of chronological age as a proxy for actual duration of drug use itself make the interpretation difficult (Des Jarlais et al., 1999; Rezza et al., 1994; Vlahov et al., 2011). Additionally, the research to date was also limited by the inherent disadvantage in cross-sectional studies such that actual time of infection remains unknown, and specific behavior around time of infection therefore only roughly measurable (Van Ameijden et al., 1992). In order to assess if PWID with different durations of drug use should be targeted with more intensive prevention strategies, we undertook this study to identify the impact of duration of injection drug use career on HIV incidence rates among individuals participating in an open prospective cohort study of PWID in Vancouver, Canada (HIV/AIDS, J.U.N.P.o., 2009).

We hypothesized that risk-taking behaviors of PWID vary according to the length of time that study participants had been injecting drugs, contributing to differences in rates of HIV seroconversion between PWID with shorter duration and longer duration injecting careers. Thus, the primary explanatory variable of interest was length of injecting career, defined as the number of years since initiation of injecting drugs.

2. Methods

2.1. Participant recruitment

The Vancouver Injection Drug User Study (VIDUS) is a prospective cohort study of PWID who have been recruited through self-referral and street outreach from Vancouver's Downtown Eastside since May 1996. The cohort has been described in detail previously (Wood et al., 2005). In brief, persons were eligible to enroll in the VIDUS study if they had injected illicit drugs at least once in the previous month and resided in the Greater Vancouver region at enrollment. All participants complete an interviewer-administered questionnaire and provide a blood sample at baseline and semiannual follow-up visits. All study participants provided informed consent, and participants were given a stipend ($20) at each study visit. The study has been reviewed and approved by Providence Health Care/University of British Columbia's Research Ethics Board. The present study was conducted between May 1996 and May 2013.

2.2. Measures

The primary outcome of interest in this analysis was time to HIV seroconversion. The date of HIV seroconversion was estimated using the midpoint between the last negative and first positive antibody test result dates. Analyses were restricted to study participants who were HIV negative at time of enrollment and had at least one follow-up visit during the study. Consistent with the large body of previous research in this area, and given that risk of HIV seroconversion is known to be shaped by an array of individual and contextual variables, a range of potential covariates were considered for inclusion in the model. Based on previous literature (Clarke et al., 2001; Craib et al., 2003; Lamothe et al., 1993; Patrick et al., 1997; Spittal et al., 2002; Strathdee & Sherman, 2003; Tyndall et al., 2003), demographic and environmental secondary variables for this analysis included: gender (male vs. female); age (per 10 years older); Indigenous ancestry (yes vs. no); incarceration in the last 6 months (yes vs. no); participation in sex work in the last 6 months (yes vs. no); and practice of unprotected sex in the last 6 months (yes vs. no). In addition, secondary drug use variables included: syringe borrowing in the last 6 months (yes vs. no); daily use of each of crack smoking, cocaine injection and heroin injection in the last 6 months (yes vs. no); requiring help injecting drugs in the last 6 months (yes vs. no); and enrollment in methadone maintenance therapy (MMT) in the last 6 months (yes vs. no). It was hypothesized that being male (Ahamad et al., 2014), age (per 10 years older) (Broz et al., 2014) and enrollment in methadone maintenance therapy (MMT) in the last 6 months (Ahamad et al., 2015) were negatively associated with HIV seroconversion; while having Indigenous ancestry (Bingham et al., 2014), being incarcerated in the last 6 months (Milloy et al., 2013), and participating in sex work (Shannon & Csete, 2010; Shannon et al., 2015), unprotected sex (Dosekun & Fox, 2010; Patel et al., 2014; Varghese et al., 2002), syringe borrowing (Kerr et al., 2010), requiring help injecting drugs (Cheng et al., 2015), or daily use of cocaine, crack or heroin in the last 6 months (Tavitian-Exley et al., 2015) were positively associated with HIV seroconversion.

2.3. Statistical analyses

As an initial step, Kaplan–Meier methods were employed to estimate the cumulative incidence of HIV seroconversion, stratified by the median length of time injecting drugs at baseline. The log-rank test was used to compare the cumulative incidence curves of both groups. As the next step, using bivariable and multivariable Cox regression analyses, the hazard ratios were calculated to assess the independent effect of length of injecting career on time to HIV seroconversion. We constructed the multivariable confounding model using a variable selection process described previously by Maldonado and Greenland (1993). While there can be limitations to conventional stepwise approaches to model selection including the potential for low sensitivity in screening for confounders (Greenland, 1989), we aimed to find the most parsimonious model that describes the data. Given that age and length of time injecting were highly collinear variables, we excluded age from the multivariable analysis before proceeding with this process. We first fitted a full model containing all variables with $p < 0.05$ in the bivariable analyses, and then proceeded to fit a series of reduced models, noting the value of the coefficient associated with the primary variable of interest. After comparing the value of the coefficient associated with the primary variable of interest in the full model to the value of the coefficient in each of the reduced models, we removed the secondary variable associated with the smallest relative change from further consideration. We continued this iterative process until the minimum change of the value of the coefficient for length of time injecting exceeded 5%. Remaining variables were considered confounders in the multivariable analysis. All statistical analyses were performed using the SAS software version 9.3 (SAS, Cary, NC). All p-values were from two-sided statistical tests.

3. Results

Among 1639 baseline HIV-negative PWID recruited into the VIDUS cohort, the median age at baseline was 36 years (interquartile range, or difference between the third (75th percentile) and first quartile (25th percentile) accordingly, was [IQR]: 28–42). The median length of time injecting at baseline was 13 years (IQR: 5–23). After 5 years of follow-up, the cumulative incidence of HIV seroconversion for this entire sample was 8.27% (95% confidence interval [CI]: 6.96%–9.81%). After 5 years of follow-up, the cumulative incidence among PWID who reported a history of <13 years of injecting drugs at baseline was 10.13% (95% CI: 8.08%–12.66%) while those with a history of ≥13 years of injecting was 6.64% (95% CI: 5.09%–8.64%). After 10 years of follow-up, the cumulative incidence of HIV seroconversion for the entire sample was 10.04% (95% CI: 8.46%–11.90%); while the cumulative incidence among PWID who reported a history of <13 years of injecting drugs at baseline was 11.88% (95% CI: 9.54%–14.76%) while those with a history of ≥13 years of injecting was 8.47% (95% CI: 6.44%–11.09%. As shown in