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Daily Alcohol Use as an Independent Risk Factor for HIV Seroconversion Among People Who Inject Drugs

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Abstract

Aims—To estimate the relationship between daily alcohol use and HIV seroconversion among people who inject drugs (PWID) in a Canadian setting.

Design and Setting—Data from an open prospective cohort study of PWID in Vancouver, Canada, recruited via snowball sampling and street outreach between May 1996 and November 2013. An interviewer-administered questionnaire including standardized behavioural assessment, and HIV antibody testing were conducted semiannually. Baseline HIV-seronegative participants completing 1 follow-up visits were eligible for the present analysis.

Participants—1683 eligible participants, including 564 (33.5%) women, were followed for a median of 79.8 (interquartile range [IQR]: 33.3 – 119.1) months.

Measurements—The primary endpoint was time to HIV seroconversion, with the date of HIV seroconversion estimated as the midpoint between the last negative and the first positive antibody test results. The primary explanatory variable was self-reported daily alcohol use in the previous 6 months assessed semiannually. Other covariates considered included demographic, behavioural, social/structural, and environmental risk factors for HIV infection among PWID (e.g. daily cocaine injection, methadone use, etc.).

Findings—Of 1683 PWID, there were 176 HIV seroconversions during follow-up with an incidence density of 1.5 (95% confidence interval [CI]: 1.3 – 1.7) cases per 100 person-years. At baseline, 339 (20.1%) consumed alcohol at least daily in the previous six months. In multivariable extended Cox regression analyses, daily alcohol use remained independently associated with HIV seroconversion (Adjusted Hazard Ratio: 1.48; 95% CI: 1.00–2.17).

Conclusions—Daily alcohol use appears to be an independent risk factor for HIV seroconversion among our cohort of PWID.

Keywords

alcohol; HIV; injection drug use; Canada

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CONFLICT OF INTEREST:

None declared.

INTRODUCTION

It has been well established that people who inject drugs (PWID) are at an increased risk of acquiring HIV. While PWID make up only an estimated 0.2–0.5% of the world's population, they account for approximately 5–10% of all people living with HIV infection (1). Similarly, in Canada, PWID comprise 0.4% of the population yet 16% of all new HIV infections (2). The increased rate of HIV transmission among PWID is known to be multifactorial including sexual risk as well as mediated, in large part, by direct needle-sharing as well as indirect sharing behaviours such as multi-person use of cookers, cotton and rinse water (3).

An estimated 43% of adults globally consume alcohol, with 4.9% meeting criteria for alcohol use disorder, making it one of the most commonly abused substances (4). High rates of alcohol consumption have also been reported among PWID (5–7); a large study of PWID in the United States found 66% reported consuming alcohol and 28% reported heavy alcohol use in the previous 30 days (8). Alcohol has been shown to increase transmission of HIV through its effect on sexual risk behaviour and has even been implicated in increased viral replication and shedding (9). Therefore, there has been substantial interest in exploring the link between alcohol use and increased risk of HIV infection.

Among men who have sex with men, the population making up the highest proportion of new HIV infections in North America, several studies have shown increased rates of HIV seroconversion associated with alcohol use, primarily through high-risk sexual risk behaviour such as unprotected anal intercourse (10, 11). Similarly, in PWID, alcohol has been shown to increase both high-risk sexual behaviour and injection drug use behaviours, such as needle-sharing, which should theoretically lead to higher rates of HIV infection (12, 13). However, to our knowledge, no study has examined the impact of alcohol use on HIV incidence in this population. Therefore, the aim of this study was to estimate the relationship between daily alcohol use and HIV seroconversion among PWID in Vancouver, Canada.

METHODS

Participants and Design

Data for this study was obtained as part of the Vancouver Injection Drug Users Study (VIDUS), an open prospective cohort study of PWID that has been ongoing since May 1996. Details of the study are described in a previous publication (14). In brief, eligibility for enrollment required that participants to be 18 years of age or older, reside in the Greater Vancouver area, have used illicit injection drugs at least once in the past month and provide written informed consent at the time of enrolment. At baseline and semi-annually thereafter, participants complete an interviewer-administered questionnaire, and venous blood samples are drawn to test for HIV and hepatitis C virus. The questionnaire is designed to elicit demographic data and information about patterns of drug use, risk behaviours for HIV infection, health status, and exposures to health care, addiction treatment services and criminal justice system. At each study visit, participants are given an honorarium (\$30 CDN) for their time and transportation. VIDUS has been approved by the University of British Columbia/Providence Healthcare Research Ethics Board. For the present study, participants

were eligible if they were recruited between May 1, 1996 and November 30, 2013, were HIV negative at baseline and had had at least one follow-up visit to assess for HIV incidence.

Measures

The primary endpoint in the analysis was time to HIV seroconversion. As in previous studies (14, 15), the date of HIV seroconversion was estimated using the midpoint between the last negative and the first positive antibody test results. The primary explanatory variable of interest was self-reported daily alcohol use during the previous six months (daily vs. < daily). In a sub-analysis, we changed the definition to binge alcohol use during the previous six months, defined as consuming alcohol at least daily and having > 4 drinks per day on average vs. consuming alcohol less than daily or having ≤ 4 drinks per day on average). Potential confounders were selected based on previously known risk factors for HIV infection among PWID and included as secondary explanatory variables: gender (male vs. female); age; ancestry (Caucasian vs. non-Caucasian); homelessness; enrolment in a methadone maintenance program; daily heroin injection; daily cocaine injection; daily crack smoking; daily methamphetamine injection; benzodiazepine use; unprotected sex, defined as vaginal or anal sex without a condom; and involvement in sex work, defined as exchange of sex for gifts, food, shelter, drugs, or clothing. All variable definitions were identical to those used in earlier studies (16, 17). All behavioural variables were treated as time-updated covariates and referred to the previous six months.

Statistical Analysis

First, the baseline characteristics of those who did and did not report at least daily alcohol use during the previous six months at baseline were compared using the Chi-square test for binary measures and Wilcoxon rank sum test for continuous measures. The cumulative probabilities of remaining HIV negative were estimated using the Kaplan-Meier product limit method, and compared based on the baseline reports of at least daily alcohol use using the two-sample log-rank test.

Then, extended Cox regression was used to examine univariable associations between each explanatory variable and the time to HIV seroconversion. To fit the multivariable model, a conservative stepwise backward selection approach was employed using *a priori*-defined confounder-selection modelling strategy suggested by Maldonado and Greenland (18). This modeling strategy has been employed in previous studies pursuing similar enquires (19, 20). Briefly, along with the primary explanatory variable, all secondary explanatory variables (shown in Table 2) were included in a full multivariable model, and a stepwise approach was used to fit a series of reduced models. After comparing the value of the coefficient associated with daily alcohol use in the full model to the value of the coefficient in each of the reduced models, the secondary explanatory variable associated with the smallest relative change was dropped. This iterative process was continued until the minimum change exceeded 5%. Remaining variables that would result in >5% change in the value of the coefficient for daily alcohol use when removed from the final multivariable model were considered as potential confounders. These included: gender, daily heroin injection, daily cocaine injection, benzodiazepine use, and enrolment in a methadone maintenance

program. We repeated the same modelling procedure in a sub-analysis, in which we changed the primary explanatory variable from at least daily alcohol use to binge alcohol use. Analyses were conducted using SAS 9.3 (SAS, Cary, NC, USA); the threshold for statistical significance was set at $p < 0.05$. All p -values were two-sided.

RESULTS

In total, 1931 HIV seronegative participants were enrolled in VIDUS. Among these, 1683 (87.2%) had at least one follow-up visit and were therefore included in the analysis. Compared to those who were eligible, the 248 HIV-negative participants excluded from the analysis were more likely to be younger (median 32.0 vs. 36.6 years for included participants, $p < 0.001$) and engage in unprotected sex ($p = 0.013$) and daily methamphetamine injection ($p = 0.004$), but were less likely to engage in daily cocaine injection ($p = 0.045$) at baseline. Otherwise, there was no significant difference between the two groups, including in terms of daily alcohol use or binge alcohol use (all $p > 0.05$).

The 1683 participants included in this study were followed for a median of 79.8 (interquartile range [IQR]: 33.3 – 119.1) months. The median number of study visits per participant was 11 (IQR: 5–17) visits. The total person-years of follow-up was 11,941.8. The baseline characteristics of the study participants stratified by daily alcohol use are presented in Table 1. As shown, 339 (20.1%) individuals reported at least daily alcohol use at baseline; of those, 282 (16.8%) reported binge alcohol use, defined as daily drinking of greater than 4 drinks per day. Those who consumed alcohol daily were younger, less likely to be Caucasian, homeless, inject heroin at least daily, inject methamphetamine at least daily, smoke crack at least daily, or be enrolled in methadone program, while being more likely to use benzodiazepines and have unprotected sex (all $p < 0.05$).

Of the 1683 initially HIV negative study participants, there were 176 HIV seroconversions for an incidence density of 1.5 (95% CI: 1.3 – 1.7) cases per 100 person-years. Of the 176 HIV seroconversion cases, the median time to HIV seroconversion was 15.4 (IQR: 4.2 – 37.6) months. Those who consumed alcohol at least daily at baseline were significantly less likely to remain HIV negative during the follow-up period, as evidenced in the Kaplan Meier curve (Figure 1). The cumulative probability of remaining HIV negative by 5 years after study enrolment among those who did not consume daily alcohol was 91.6% compared with 83.3% among those who consumed alcohol at least daily (log-rank $p < 0.001$).

The results of univariable and multivariable extended Cox regression analyses are shown in Table 2. As shown, in the final multivariable model adjusting for gender, daily cocaine injection, daily heroin injection, benzodiazepine use and enrolment in a methadone program, daily alcohol use remained independently and positively associated with time to HIV seroconversion (Adjusted Hazard Ratio: 1.48; 95% confidence interval [CI]: 1.00–2.17). In the sub-analysis, binge alcohol use was not significantly associated with time to HIV seroconversion (Hazard Ratio: 1.10; 95% CI: 0.64 – 1.92) in the univariable analysis, and therefore no multivariable model was constructed using this alternative explanatory variable.

DISCUSSION

Our results indicate that alcohol use was prevalent among this cohort of PWID, with 20% of participants consuming alcohol at least daily during the previous six months at baseline. Further, daily alcohol use was independently associated with a nearly 1.5 fold increase in a hazard of HIV infection compared to less than daily alcohol use, even after adjusting for confounding demographic, behavioural, social/structural, and environmental risk factors. To our knowledge, this is the first study to quantify an increased hazard of HIV seroconversion due to alcohol use among PWID.

Several studies have explored the effect of alcohol use on increased sexual and injection-related risk factors for HIV infection. Under the influence of alcohol, PWID have been shown to be more likely to engage in sex with multiple partners and have intercourse without a condom, increasing the probability of HIV transmission (21, 22). Similarly, alcohol use has been linked with an increased likelihood of sharing needles or other injecting paraphernalia (12, 13). The increased risk of HIV seroconversion with daily alcohol use shown in this study may also potentially be mediated through these behaviours. However, as shown in our analyses, unprotected sex was not significantly associated with HIV seroconversion in this study; higher rates of condom use have been shown among casual or new sexual partners compared to regular partners (23). Other known sexual risk behaviours such as multiple partners were not formally assessed in the VIDUS questionnaire throughout the study period but may be implicated in the increased risk of seroconversion seen with daily alcohol use.

Interestingly, while use of alcohol at least daily was associated with a significantly increased risk of HIV seroconversion, binge alcohol behaviour was not. Prior studies examining the relationship of alcohol use with HIV risk behaviour among PWID have been heterogeneous in reporting and quantifying alcohol use, making comparison difficult. However, Booth *et al.* have shown increased days of alcohol use among PWID to be independently associated with increased HIV sexual risk behaviour (24). There is also evidence to suggest a decreased incidence of condom use on days when drinking occurs (22). Taken together, our findings suggest that the frequency, rather than the quantity, of alcohol use may confer increased risk of HIV infection among PWID. Unfortunately, we were unable to assess the effect of non-daily binge drinking behaviour in the present analysis because such variable was unavailable in our data set. It is important to consider these patterns of drinking given the known yet complex health and social consequences of high risk alcohol consumption (25); this represents an area for future research in order to fully understand the effect of alcohol use on HIV seroconversion.

This study has other limitations we wish to acknowledge. As VIDUS is a non-random sample, our findings may not be generalizable to all PWID in Vancouver or other settings. With respect to the applicability of these results to other populations of PWID, it is notable that this study is based out of Vancouver's Downtown Eastside, a neighbourhood estimated to have among the highest HIV prevalence in the Western world (17). It is therefore possible that participants in our study have higher rates of contact with HIV-positive individuals, increasing the potential for infection. As the data is derived from self-reports, it may be

subject to recall and social desirability bias although previous studies have shown a negligible confounding effect of social desirability on the strength of association between HIV status and risk behaviours (26). As with all observational research, the estimated relationship between alcohol use and HIV seroconversion may be under the influence of unmeasured confounding, although we sought to address this bias with multivariable adjustment involving key potential demographic, behavioural, social/structural, and environmental confounders.

In summary, daily alcohol use has been shown to be an independent risk factor for HIV seroconversion among our sample of PWID in Vancouver. Given the high prevalence of daily alcohol use in this population, our findings have important implications for preventing HIV transmission going forward. Great strides have been made in the treatment and prevention of HIV among PWID including needle exchange and opioid substitution. Findings from this study highlight the importance of incorporating treatment and education related to alcohol use within HIV prevention strategies in the PWID community.

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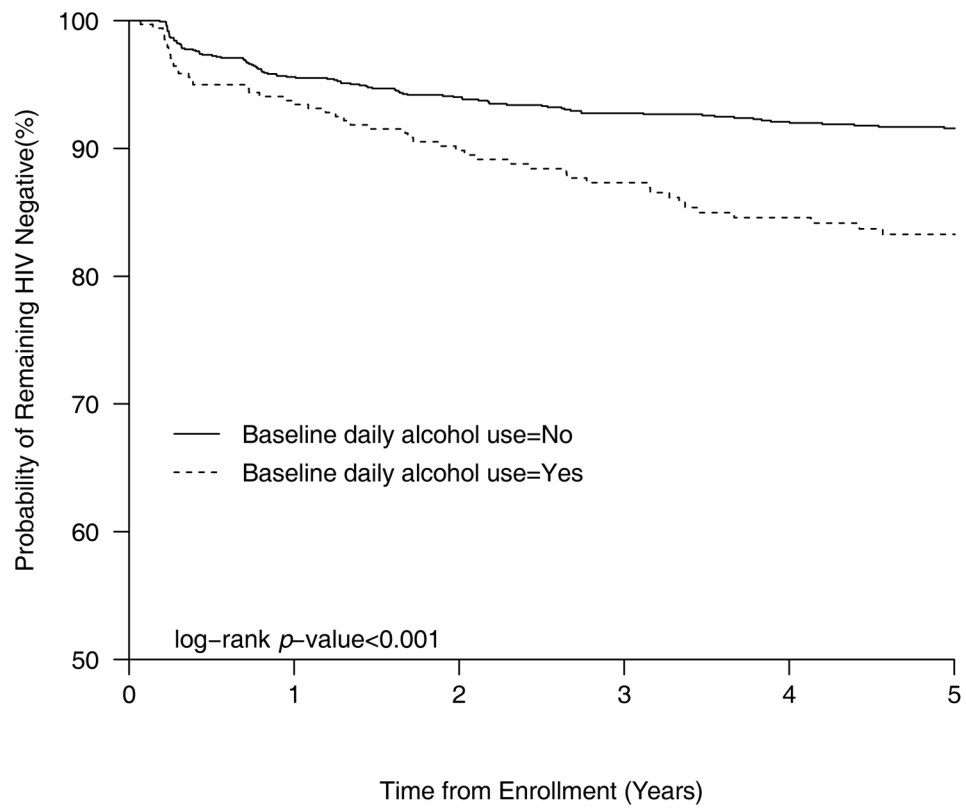


Figure 1. Kaplan-Meier survival curve showing cumulative probability of remaining HIV-negative during five years after study enrolment, stratified by daily alcohol use at baseline.

Table 1

Baseline characteristics of PWID stratified by daily alcohol use in the previous six months.

Characteristic	Daily Alcohol Use [*]		Odds Ratio(95% CI)	P-value
	Yes n (%) 339 (20.1)	No n (%) 1343 (79.8)		
Gender				
Male	215 (63.4)	903 (67.2)	0.84 (0.66, 1.08)	0.184
Female	124 (36.6)	440 (32.8)		
Age				
Median (IQR)	34.3 (26.2–41.2)	37.0 (28.9–43.4)		<0.001
Ancestry				
Caucasian	167 (49.3)	879 (65.5)	0.51 (0.40, 0.65)	<0.001
Other	172 (50.7)	464 (34.5)		
Homeless[*]				
Yes	41 (12.1)	347 (25.8)	0.39 (0.28, 0.56)	<0.001
No	298 (87.9)	996 (74.2)		
Heroin Injection[*]				
Daily	102 (30.1)	629 (46.8)	0.49 (0.38, 0.63)	<0.001
< Daily	236 (69.6)	710 (52.9)		
Cocaine Injection[*]				
Daily	113 (33.3)	399 (29.7)	1.19 (0.92, 1.53)	0.186
< Daily	223 (65.8)	935 (69.6)		
Methamphetamine Injection[*]				
Daily	0 (0.0)	24 (1.8)		0.013
< Daily	339 (100.0)	1314 (97.8)		
Crack Smoking[*]				
Daily	47 (13.9)	355 (26.4)	0.45 (0.32, 0.62)	<0.001
< Daily	292 (86.1)	986 (73.4)		
Benzodiazepine Use[*]				
Yes	166 (49.0)	334 (24.9)	2.90 (2.27, 3.71)	<0.001
No	173 (51.0)	1009 (75.1)		
Methadone Program Enrollment[*]				
Yes	23 (6.8)	320 (23.8)	0.23 (0.15, 0.36)	<0.001
No	315 (92.9)	1017 (75.7)		
Unprotected Sex^{**}				
Yes	194 (57.2)	431 (32.1)	2.85 (2.24, 3.65)	<0.001
No	143 (42.2)	907 (67.5)		
Sex Work[*]				
Yes	82 (24.2)	298 (22.2)	1.12 (0.85, 1.49)	0.420
No	255 (75.2)	1040 (77.4)		

Note: PWID=people who inject drugs.

* Indicates behaviour during the six-month period prior to interviews.

** Unprotected sex was defined as vaginal or anal sex without a condom at least once.

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Table 2

Univariable and multivariable extended Cox regression analyses of the time to HIV infection among 1682 PWID.

Variable	Unadjusted HR (95% CI)	P-value	Adjusted HR (95% CI)	P-value
Daily Alcohol Use [*]	1.65 (1.13, 2.41)	0.010	1.48 (1.00, 2.17)	0.048
Binge Alcohol Use [*]	1.10 (0.64, 1.92)	0.725		
Male gender	0.59 (0.44, 0.79)	<0.001	0.63 (0.47, 0.85)	0.002
Age (per 10 years older)	0.97 (0.95, 0.98)	<0.001		
Caucasian (versus other)	0.71 (0.53, 0.96)	0.025		
Homeless [*]	0.81 (0.55, 1.18)	0.278		
Daily Heroin Injection [*]	1.72 (1.27, 2.33)	<0.001	1.26 (0.92, 1.73)	0.153
Daily Cocaine Injection [*]	3.88 (2.85, 5.28)	<0.001	3.38 (2.43, 4.71)	<0.001
Daily Methamphetamine Injection [*]	0.84 (0.22, 3.26)	0.797		
Daily Crack Smoking [*]	1.07 (0.77, 1.48)	0.698		
Benzodiazepine Use [*]	1.60 (1.08, 2.36)	0.019	1.32 (0.88, 1.97)	0.183
Methadone Program Enrollment [*]	0.58 (0.41, 0.83)	0.003	0.67 (0.47, 0.96)	0.030
Unprotected Sex ^{**}	1.14 (0.82, 1.57)	0.433		
Sex Work [*]	1.82 (1.28, 2.58)	<0.001		

Note: PWID=people who inject drugs. HR=hazard ratio.

^{*} Indicates behaviour during the six-month period prior to interviews.

^{**} Unprotected sex was defined as vaginal or anal sex without a condom at least once.