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Determinants of alcohol consumption in HIV-uninfected injection drug users

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Abstract

We assess the association between time fixed and time varying participant characteristics and subsequent alcohol consumption in 1,968 injection drug users (median age 37 years, 28% female, 90% African-American) followed semi-annually from 1988 to 2008. Median alcohol consumption was seven drinks per week at study entry (first and third quartile: 1, 26) with 36% reporting binge drinking. Alcohol consumption and binge drinking decreased over follow-up. Older individuals and women reported consuming fewer drinks per week. Higher typical alcohol consumption was reported by those participants who reported in the prior six months: non-injection cocaine use, injection drug use, having one or more sex partners, or among men, a same sex partner. Associations were generally similar for drinks per week and binge drinking. This study demonstrates that in a large urban cohort of persons with a history of injection drug use, risky drug use and sexual risk behavior are associated with subsequent alcohol consumption.

Keywords

Alcohol; Bias; Cohort study; HIV/AIDS

1. Introduction

Alcohol consumption is considered an indirect cause of sexually transmitted infections mediated through subsequent risk behaviors, such as illicit drug use and sexual activity (Cook and Clark, 2005; Lauchli et al., 1996; Robertson and Plant, 1988; Van Tieu and Koblin, 2009). The standard quantitative approach used to investigate the association between alcohol

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consumption and subsequent sexually transmitted infections in longitudinal data is statistical adjustment to control for confounding by other risk behaviors (Howe et al., 2010). Wang et al. (2005) report that alcohol consumption did not predict HIV seroconversion after adjustment for time varying behavioral factors including injection drug use and male sex with men (adjusted hazard ratio = 1.15; 95% confidence limits: 0.82, 1.62) in the AIDS Link to Intravenous Experience (ALIVE) cohort of injection drug users. However, this approach adjusted for risk behaviors, which might themselves be determinants of *subsequent* alcohol consumption. If alcohol consumption affects subsequent risk behaviors and is affected by prior risk behaviors, then standard quantitative approaches may provide biased estimates of the effects of alcohol consumption on downstream consequences, such as sexually transmitted infections (Cole et al., 2003; Cook et al., 2002; Robins et al., 2000). We assess the association between time varying risk behaviors and subsequent alcohol consumption in a prospective cohort of HIV-uninfected injection drug users. We hypothesized that prior risk behaviors are associated with subsequent alcohol consumption.

2. Methods

2.1 Study Cohort

The purpose of the ALIVE cohort is to assess risk factors associated with HIV seroconversion and study the natural history of HIV infection among injection drug users. 3,627 adult injection drug users were recruited through community outreach efforts in Baltimore, MD (Vlahov et al., 1991) and followed between 1988 and 2008. At a first follow-up visit within two years of initial visit, 1,969 of 3,627 remained HIV uninfected. One participant was excluded due to incomplete demographic data. Participants attended visits every six months at a University-affiliated clinic, yielding a maximum possible 40 study visits. At visits, all participants completed both an interviewer-administered medical history questionnaire and an audio-computer assisted structured behavioral interview, and provided blood specimens. Selected participants underwent physical examination. A Johns Hopkins University committee on human research approved study protocols and informed consent forms, which were completed by all participants.

Participants were followed through their last study visit before 1 January 2008, death or HIV seroconversion. Dates of death were ascertained by the National Death Index or death certificates. Dates of HIV seroconversion were determined from blood specimens tested at each visit. Participants were classified as lost to follow-up at their last study visit when they were not observed subsequently for a period of more than two years.

2.2 Study measurements

Alcohol consumption was defined as the typical number of drinks per week in the prior six months and was obtained as the product of the reported number of drinking-days per week and the number of drinks per drinking-day. Reports of more than 20 drinks per drinking-day (<2%) were set to 20. Binge drinking was constructed as five or more drinks per typical drinking-day for one or more days per week over the prior six months. Number of male and female sexual partners, an indicator for men who had sex with men, number of sexually transmitted infections (i.e., herpes simplex virus, genital warts, gonorrhea), cocaine use (including crack cocaine), and number of drug injections per day, all for the prior six months, were obtained at each study visit. Reports of more than three sexual partners (<9%) were set to three due to the small percentage reporting four (3%), five (2%), six (1%), seven (<1%), or eight or more (3%) sexual partners. Chlamydia infections were not assessed at all study visits and were excluded from the total number of sexually transmitted infections. Time varying covariates were lagged one visit to ensure values were temporally prior to reported alcohol consumption. Missing data (2, 7, <1, <1 and <1% of alcohol consumption, sexual partners, cocaine, injections per day, and

sexually transmitted infections, respectively) were set to median values. Results were similar if missing data were set to zero although adjusted estimates for the association between both injection drug use and cocaine use with alcohol consumption were somewhat further from the null under the latter approach.

2.3 Statistical analysis

Box plots and smoothing splines provided graphic depictions of unadjusted associations between discrete and continuous characteristics and drinks per week, respectively. The ratio of median alcohol consumption (i.e., median ratio) and relative odds of binge drinking were used to measure the association between participant characteristics and alcohol consumption. Median ratios were obtained from log-normal regression models where the log of drinks per week at each visit was the outcome variable (Tien et al., 2007). We added 0.1 to all drinks per week to allow inclusion of participants who reported 0 drinks. Odds ratios were obtained from logistic regression models where binge drinking at each visit was the outcome variable. 95 percent confidence limits (CL) were used to quantify precision for both models. The CLs were constructed using robust variance estimates (White, 1982) to account for the dependence incurred by multiple visits by each participant. Such robust variance estimates are equivalent to generalized estimating equations (Zeger and Liang, 1986) with a diagonal/independent working covariance matrix (Pepe and Anderson, 1994). Time-on-study and drinks per week reported at the initial visit were included in regression models as restricted cubic splines with knots at the 5, 35, 65 and 95 percentiles (Harrell et al., 1988). All analyses were conducted using SAS (SAS Institute; Cary, NC).

3. Results

At entry, the 1,968 participants were a median of 37 years of age (quartiles: 31, 42), with 10 years of education (quartiles: 10, 12), 28% female, 90% African-American and 2% Hispanic. Participants were followed for a median of 3.9 years (quartiles: 1.2, 10.1). 356 participants died during follow-up, 242 seroconverted with HIV, and 752 participants were lost to follow-up.

Over follow-up, 0, 1, 2, and 3 or more sexual partners were reported at 23%, 45%, 16%, and 16% of 23,579 visits respectively. Men having sex with men and any sexually transmitted infection were reported at 1% of 23,579 visits. Cocaine use (irrespective of injection behavior) was reported at 54%, cocaine use without injection was reported at 12% and daily injections (with or without cocaine use) at 46% of visits. Median daily number of injections for those injecting was one (quartiles: 0.5, 2.5).

Median alcohol consumption at study entry was eight drinks per week, although this was highly variable (quartiles: 1, 26). At study entry, 32% of participants were binge drinkers. As with other risk behaviors, both measures of alcohol use decreased during follow-up: median consumption at last visit was two drinks per week (quartiles: 0, 14) and 21% of participants were binge drinkers. Alcohol consumption in the 752 visits prior to drop out was similar to the remaining visits (median drinks/week: 2.5 prior to drop out; 4 at all others; Wilcoxon $p = 0.19$).

Figure 1 depicts *unadjusted* box plots and smoothed scatter plots for alcohol consumption. Adjusted median ratios for alcohol consumption and odds ratios for binge drinking by characteristics are presented in Table 1. For example, median number of drinks per week was 1.54-fold (95% CL: 1.38, 1.71) and odds of binge drinking were 1.59-fold (95% CL: 1.32, 1.90) among visits where cocaine use without injection was reported. There was consistency between unadjusted (Figure 1) and adjusted (Table 1) results. There was also consistency between models for consumption and binge drinking with the exception of education.

Education was not associated with consumption but higher education was associated with lower odds of binge drinking.

4. Discussion

In a large urban cohort of persons with a history of injection drug use, we observed substantial alcohol consumption and frequent binge drinking at study entry. During subsequent follow-up, the level of alcohol consumption and proportion of binge drinking declined. Even after adjustment for alcohol consumption at study entry and other characteristics, time fixed and time varying participant characteristics were associated with subsequent alcohol consumption. Older age and female gender were both associated with lower alcohol consumption. Risk behaviors including non-injecting cocaine use, injecting drugs, males having sex with men and increased numbers of sexual partners were associated with higher subsequent alcohol consumption.

We observed that associations of risk characteristics with alcohol consumption were generally similar to those for binge drinking, with the exception of higher educational attainment, which was associated with reduced binge drinking but did not substantially influence consumption (Table 1). Application of a zero-inflated log-normal model (Chu et al., 2006), which can distinguish determinants of any alcohol use from determinants of the quantity of alcohol consumed, indicated both cocaine use and drug injection were stronger determinants of any alcohol use rather than of alcohol consumption among drinkers (data not shown).

Our results are consistent with some associations from cross-sectional studies of injection drug users and clarify the time order of observed unadjusted associations between time varying behavioral factors and alcohol consumption. For example, in a cohort of 6,341 injection drug users entering detoxification or methadone maintenance treatment in New York City, at-risk drinkers were of older age, more likely to be male, to inject cocaine or have multiple sex partners (Arasteh et al., 2008). Similarly in a cohort of Hispanic, community-dwelling injection drug users, drinking to the point of intoxication was associated with needle-sharing and transactional sex partnerships (Matos et al., 2004). Our findings suggest that these associations are likely not only the result of alcohol consumption increasing risk behaviors, but also of risk behaviors influencing subsequent alcohol consumption.

Our approach and interpretation assumes no unmeasured confounding, information bias or selection bias. Given long-term alcohol consumption cannot be randomized, longitudinal observational data provides the best source of evidence even though such data is subject to possible confounding. Reports of alcohol consumption and other characteristics are subject to measurement error. In this prospective study, we expect such measurement error to be non-differential and likely bias measures of association towards the null. Future investigations should consider alcohol consumption patterns over longer periods such as 12-36 months to assess whether predictors of long-term alcohol consumption differ from short-term consumption as observed here. Although efforts to account for drop out using inverse probability-of-censoring weights (Cain and Cole, 2009; Robins and Finkelstein, 2000) provided similar results (data not shown), drop out was not rare (i.e., 752 of 1,968) and may have been differential due to unmeasured participant characteristics, but was non-differential with respect to alcohol consumption.

We presented evidence of associations of participant characteristics with subsequent alcohol consumption in a large, well-defined prospective cohort of injection drug users. As hypothesized, alcohol consumption appears to be affected by prior risk behaviors. In such a setting standard quantitative methods may provide biased estimates of alcohol effects on downstream consequences. This bias is due to standard methods for covariate adjustment

blocking the effects of alcohol that are mediated through time varying characteristics (e.g. cocaine use), as well as inducing possible selection bias (Cole and Hernan, 2002). Based on these findings, future investigations should pursue methods for causal inference (Cole et al., 2003; Cook et al., 2002; Robins et al., 2000) to examine the effect of alcohol consumption on HIV acquisition.

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FIGURE 1.

Box plots of alcohol consumption by gender (A), cocaine use (B), sexually transmitted infections (STI) (C) and male sex with men (D) and smoothed scatter plots of alcohol consumption by age (E), injections per day (F), education (G) and number of sexual partners (H) for 1968 HIV-negative participants seen at 23579 study visits (percentages are of visits) between 1988 and 2008. The Tukey box plot gives a visual summary of the data distribution. The box shows the middle 50% of the distribution, split with a line at the median; whiskers extend from the box to 1.5 times the interquartile range; and dots represent outliers.

TABLE 1

Alcohol consumption by characteristics for 1,968 HIV-negative participants seen at 23,579 study visits between 1988 and 2008

Characteristic:	Consumption (drinks per week)		Binge drinking ^b	
	Median Ratio ^a	95% Confidence Limits	Odds Ratio ^a	95% Confidence Limits
Time fixed				
Age, per 10 years	0.88	0.82, 0.94	0.81	0.72, 0.91
Female gender	0.87	0.78, 0.98	0.76	0.61, 0.94
African-American race	0.99	0.82, 1.20	0.87	0.62, 1.22
Education, per 4 years	0.96	0.88, 1.05	0.78	0.68, 0.90
Time varying				
Non-injection cocaine use	1.54	1.38, 1.71	1.59	1.32, 1.90
Any injection drug use ^c	1.39	1.27, 1.51	1.39	1.18, 1.64
No. of sexual partners ^d	1.08	1.04, 1.12	1.13	1.06, 1.20
Male sex with men	1.83	1.23, 2.71	2.24	1.21, 4.13
Sexually transmitted infection	1.03	0.86, 1.24	1.41	1.02, 1.93

^a Adjusted for characteristics in table, time-on-study and baseline drinks per week (as restricted cubic splines)

^b Defined as ≥ 5 drinks per drinking-day for ≥ 1 drinking-day per week

^c With or without cocaine use

^d Categorized as 0, 1, 2 or 3+ partners