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A prospective study of alcohol consumption and HIV acquisition among injection drug users

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Abstract

Objective—Estimate the effect of alcohol consumption on HIV acquisition while appropriately accounting for confounding by time-varying risk factors.

Design—African American injection drug users in the AIDS Link to Intravenous Experience cohort study. Participants were recruited and followed with semiannual visits in Baltimore, Maryland between 1988 and 2008.

Methods—Marginal structural models were used to estimate the effect of alcohol consumption on HIV acquisition.

Results—At entry, 28% of 1,525 participants were female with a median (quartiles) age of 37 (32; 42) years and 10 (10; 12) years of formal education. During follow up, 155 participants acquired HIV and alcohol consumption was 24%, 24%, 26%, 17%, and 9% for 0, 1–5, 6–20, 21–50 and 51–140 drinks/week over the prior two years, respectively. In analyses accounting for socio-demographic factors, drug use, and sexual activity, hazard ratios for participants reporting 1–5, 6–20, 21–50, and 51–140 drinks/week in the prior two years compared to participants who reported 0 drinks/week were 1.09 (0.60, 1.98), 1.18 (0.66, 2.09), 1.66 (0.94, 2.93) and 2.12 (1.15, 3.90), respectively. A trend test indicated a dose-response relationship between alcohol consumption and HIV acquisition (P value for trend = 9.7×10^{-4}).

Conclusion—A dose-response relationship between alcohol consumption and subsequent HIV acquisition is indicated, independent of measured known risk factors.

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All authors contributed to the design of the study. CJH and SRC undertook the analysis and drafted the manuscript. All authors provided feedback on drafts and approved the final version.

There are no conflicts of interest.

Keywords

Alcohol consumption; HIV infection; Bias; Cohort studies; Injection drug users

Introduction

Alcohol consumption is generally believed to be a determinant of sexual risk behaviors and other drug use, and therefore an indirect determinant of HIV acquisition [1–2]. Alcohol consumption is also hypothesized to compromise the immune system, which in turn could allow for increased risk of HIV infection [3–5]. However, more than two decades after the onset of the HIV epidemic, the extant literature [3,6–8] regarding the association between alcohol consumption and HIV acquisition remains inadequate to inform public health policy or preventive interventions. Lack of definitive evidence for a link between alcohol consumption and HIV acquisition is of great concern in part because many populations at highest risk for HIV infection also consume high levels of alcohol, such as injection drug users [9], men who have sex with men [7,10], and Sub-Saharan Africans [8,11].

Most existing studies using prospective data to examine whether alcohol consumption increases the risk of HIV infection have not accounted for expected confounding by sexual activity and drug use [8,12–13]. Studies [14–16] that have accounted for time-updated reports of these potential confounders by standard adjustment ignore the fact that alcohol consumption may affect subsequent sexual activity and drug use [17–18]. If sexual activity and drug use are time-varying confounders that are affected by prior alcohol consumption, then standard adjustment for time-updated sexual activity and drug use is flawed. Specifically, such an approach may remove the indirect effect of alcohol consumption on HIV acquisition mediated through these behaviors [19–21], as well as induce a selection bias [22–23]. Therefore, appropriate statistical methods are needed to obtain unbiased estimates of the effect of alcohol consumption on HIV acquisition. Marginal structural models allow for estimation of total (direct and indirect) effects while appropriately accounting for time-varying confounding without inducing selection bias [12].

Here we use rich, prospective data on over 1,500 African American injection drug users from the AIDS Link to Intravenous Experience (ALIVE) cohort study [24] and marginal structural models to characterize the association between alcohol consumption and risk of HIV infection.

Methods

Study Population

The ALIVE cohort enrolled 3,627 adults in Baltimore, Maryland between 1988 and 2008. Potential participants were recruited through extensive community outreach and were screened for inclusion based on a history of active or recent injection drug use. Among the 3,627 enrollees, 1,683 were seronegative at entry and had at least one seronegative follow up visit subsequent to baseline. One enrollee was excluded due to a lack of demographic information. The remaining 157 non-African Americans were excluded from the analysis due to small numbers, leaving 1,525 African American participants.

The committee on human research at the Johns Hopkins Bloomberg School of Public Health approved study protocols and informed consent forms, which were completed by all study participants. Participants attended a study visit every six months at a University-affiliated, freestanding clinic. At visits, participants provided blood and completed an interviewer-administered questionnaire.

Ascertainment of HIV infection

The outcome of interest was incident infection with HIV. Participants were followed from their first visit through HIV seroconversion, death, or their last follow up visit before 1 January 2008. HIV seroconversion was determined from participants' blood specimens which were tested for HIV antibodies by enzyme-linked immunoassay at each visit: reactive specimens were confirmed by Western blot. Dates of death were ascertained from death certificates. Participants not observed for any period of more than one year were censored at the minimum of their date of death (if applicable), one year after their last visit prior to nonattendance, and 1 January 2008. Censored participants were classified as lost to follow up if they were lost prior to 1 January 2007 and not seen at a subsequent ALIVE visit.

Assessment of Alcohol Consumption and Covariates

The study questionnaire elicited information on demographic characteristics, drug and alcohol use history and practices, and sexual behaviors within the prior six months. Alcohol consumption, as the number of drinks/week, was obtained as the product of the reported number of drinking-days in a typical week and the usual number of drinks/drinking-day. A drink was defined to be a can, bottle or glass of beer, a glass of wine, a shot of liquor, a mixed drink with a shot of liquor, or any other kind of alcoholic beverage. Less than 3% of alcohol consumption reports were >20 drinks/drinking-day, and were set to 20 drinks/drinking-day. For analysis, alcohol consumption is quantified as the number of drinks/week averaged over the prior four visits (approximately two years), as well as binge drinking in the prior six months. We averaged the prior four visits to reduce random error and capture both short- and moderate-term alcohol effects. Average drinks/week over the prior two years was categorized as: 0, 1–5, 6–20, 21–50, and 51–140 to divide the distribution of HIV cases into approximate quintiles. Binge drinking was considered to be drinking at least once a week and consuming more than five drinks on a given drinking day. In secondary analyses, we explored a 4-level composite measure of drinks/week and binge drinking with categories defined as: 0 drinks/week, 1–20 drinks/week with no binge drinking, 1–20 drinks/week with binge drinking, and 21–140 drinks/week. We also explored alternate exposure windows, namely: drinks/week in the most recent six months and cumulatively averaged over the entire follow up.

Gender, age, and years of formal education were obtained at the first visit for all participants. Number of male and female sexual partners, self-reported sexually transmitted infections (STI) (i.e., genital herpes simplex virus, genital warts, gonorrhea, and syphilis), cocaine use, shooting gallery attendance, and number of drug injections per day were obtained at each visit with reference to the prior six months, based on prior research [25]. Less than 3% of the number of sexual partner reports were >8, and were set to eight partners. Relatively rare missing data (2%, 7%, <1%, <1%, <1% and <1% on alcohol consumption, sexual partners, cocaine, shooting gallery attendance, injections/day, and STIs, respectively) were set to zero. Inferences were invariant if missing data were set to observed medians or modes.

Statistical Analysis

Characteristics of participants at study entry and averaged over follow up are presented as percentages or medians and quartiles, as appropriate. The association between drinks/week and binge drinking was assessed using Spearman's rank correlation. Incidence rates were calculated as the number of HIV cases divided by the number of person-years at risk.

Hazard ratios (HR) were used to quantify associations between alcohol consumption and HIV incidence; 95% confidence limits (CL) were used to quantify precision. HRs were obtained from Cox proportional hazards models [26] with time-on-study as the time scale.

CLs were obtained using the standard large-sample approximation for the variance in crude and adjusted data, and the robust variance [20] for weighted data (details below). Drinks/week was included in the Cox model as either indicator variables for categories or a restricted quadratic spline with knots at the 5^{th}, 35^{th}, 65^{th}, and 95^{th} percentiles. Wald chi-square trend tests were used across groups with the median assigned for categories. The complement of the weighted Kaplan-Meier [27] curve is presented by categories of drinks/week. Proportional hazards was assessed by a statistical test of the product term between the indicator for the highest drinks/week category and time (P value = 0.932) as well as log time (P value = 0.567); there was no evidence of non-proportionality.

Observed data were weighted by the product of stabilized inverse probability-of-exposure-and-censoring weights to account for confounding and selection biases by measured characteristics. Weights were multiplied over time to account for histories of exposure and censoring. Drinks/week at each visit, as described previously, was modeled using a cumulative logistic regression model [28] while death and drop out were modeled using logistic regression models. All logistic models were pooled over visits [29]. Covariates included: age at entry, gender, years of education, time-varying drug use (i.e., cocaine use, shooting gallery attendance, and injections/day) and sexual activity (i.e., sexual partners and STIs). Time-varying covariates were lagged one visit. Continuous covariates were fit using splines as defined previously. Weights were stabilized to improve efficiency by a function of drinks/week, age, and education. The resultant weights had a mean (SD) of 1.02 (0.33) with a range from 0.21 to 7.33. To estimate incidence rates and assess non-linearity in the association between alcohol consumption and HIV acquisition, weights were stabilized solely by a function of drinks/week. These latter weights had a mean (SD) of 1.03 (0.43) with a range from 0.12 to 9.17. An adjusted model is provided for comparison and accounts for the same confounders as the weighted model as well as concurrent values of time-varying confounders to reflect practices in the existing literature [8].

Based on the observed number of HIV cases and distribution of drinks/week, we had 80% statistical power to detect a crude HR of 1.58 comparing drinkers to non-drinkers for a sample size of 1,525 where 25% of the sample population is non-drinkers, the cumulative incidence of HIV at the end of follow up among non-drinkers is 0.15, and the 2-sided type I error is 0.05. All analyses were conducted using SAS (SAS Institute; Cary, NC).

Results

Among the 1,525 participants followed for 8,181 person years, 155 acquired HIV. Among the remaining 1,370 HIV seronegative participants who were censored; 127 died, 559 were censored due to an interval of one year or more without a study visit, 362 were lost to follow up, and 322 completed follow up alive. Loss to follow up and censoring due to missed visits were greater among participants who did not report cocaine use (HR=1.22; 95% CL: 1.02, 1.45) as well as those who reported more than one sexual partner (1.25; 1.02, 1.53) and injecting more than once a day (1.56; 1.30, 1.88). Although non-significant, there was a trend towards poorer follow-up among participants with less alcohol consumption (e.g., 1.25; (0.95 1.64) for 0 drinks/week versus 51–140 drinks/week) (Appendix Table A1). Such observed differences in loss to follow up and censoring due to missed visits were accounted for in the analysis.

Table 1 describes the characteristics of participants at study entry and over follow up. At entry, 28% of 1,525 participants were female with a median (quartiles) age of 37 (32; 42) years and 10 (10; 12) years of education. Consumption of alcohol and use of illicit drugs was heavy at entry and during follow up, albeit less so during follow up. Male sex with men and reported STIs were rare, but multiple sex partners were common.

Figure 1 depicts alcohol consumption by years of follow up. Alcohol consumption decreased with increasing time since enrollment. Seventy-six and 23% of the person years occurred while participants were consuming any alcohol in the prior two years or binge drinking in the prior six months, respectively. At entry and over follow up participants who had a higher number of drinks/week in the prior two years also tended to be binge drinkers. Specifically, among those reporting 0 drinks/week, 1–5 drinks/week, 6–20 drinks/week, 21–50 drinks/week, and 51–140 drinks/week in the prior two years over follow up, 0%, 2%, 21%, 55%, and 87% reported binge drinking in the prior six months, respectively. The rank correlation for number of drinks/week in the prior two years and binge drinking in the prior six months was 0.60.

Figure 2 shows the weighted HR of HIV acquisition with 95% CLs by number of drinks/week in the prior two years. The HR appears to non-linearly increase with the number of drinks/week. Crude and weighted HRs with 95% CL for alcohol consumption on HIV acquisition are shown in Table 2. In crude analyses, HRs for participants reporting 1–5, 6–20, 21–50, and 51–140 drinks/week in the prior two years compared to participants who reported 0 drinks/week were 1.22 (95% CL: 0.69, 2.15), 1.41 (0.82, 2.42), 2.06 (1.20, 3.54) and 2.96 (1.67, 5.23), respectively. The weighted marginal structural Cox model resulted in HRs of 1.09 (0.60, 1.98), 1.18 (0.66, 2.09), 1.66 (0.94, 2.93) and 2.12 (1.15, 3.90), respectively. The P values for the Wald tests-of-trend are also shown in Table 2: the P values for the crude and weighted tests were 8.2×10^{-6} and 9.7×10^{-4}, respectively. Figure 3 illustrates cumulative proportions of HIV positive participants over years of follow up stratified by alcohol consumption categories for the number of drinks/week in the prior two years. The cumulative proportion of HIV positive participants increased with greater alcohol consumption.

As also shown in Table 2, the weighted HR for binge drinking was 1.70 (1.22, 2.37). For the composite metric, light to moderate drinking (i.e., 1–20 drinks/week) in the absence of binge drinking did not demonstrate an elevated hazard of HIV acquisition in the weighted analysis. Despite not achieving statistical significance, light to moderate drinking in the presence of binge drinking did appear to elevate the hazard of HIV acquisition. As shown in both the crude and weighted analyses in Appendix Table A2, the association between alcohol consumption in the prior six months and HIV acquisition was similar to that of consumption in the prior two years and cumulative over follow up.

For comparison, standard adjusted analysis did not demonstrate a statistically significant association for the highest drinks/week category compared to the lowest, while the weighted analysis did. Adjustment diminished the crude HRs for drinks/week in the prior two years to 1.00 (0.56, 1.79), 1.07 (0.61, 1.87) 1.36 (0.76, 2.41) and 1.70 (0.92, 3.14), respectively. The P value for the Wald test-of-trend for the standard adjusted analysis was 0.02.

Discussion

During 20 years of follow up 155 of 1,525 African American injection drug users in the ALIVE cohort acquired HIV. Alcohol consumption was highly prevalent and heavy in this cohort, but lessened with time. The marginal structural model analysis indicated a strong dose-response relationship between alcohol consumption and subsequent HIV acquisition, independent of prior drug use and sexual activity. The hazard ratios for alcohol consumption were on par with some prior identified risk factors for HIV acquisition in this cohort such as younger age, not completing high school, shooting gallery attendance, self-reported STIs, and cocaine use; but weaker than frequent injections and male homosexual behavior [25].

Weaker evidence for a dose-response relationship of alcohol on HIV acquisition was obtained from standard adjusted analysis. Specifically, the excess hazard from the weighted analysis was 38% (=1–0.70/1.12) stronger than results from the standard adjusted model. In standard analysis, indirect effects of alcohol use on HIV infection mediated through sexual activity and drug use were likely blocked with adjustment for these time-varying confounders affected by prior alcohol use.

The role of binge drinking in HIV infection remains unclear, particularly in the setting of an injection drug using population. Given the strong correlation between number of drinks/week and binge drinking, the observed association between number of drinks/week and HIV acquisition may be partially explained by binge drinking. The fact that the independent association between number of drinks/week in the prior two years and HIV acquisition was muted in the presence of binge drinking in the prior six months provides evidence for a role of binge drinking. However, given that binge drinking is likely to have acute effects and in this analysis the strength of the observed association between number of drinks/week and HIV acquisition was independent of the exposure window, the effect of number of drinks/week may not be explained entirely by binge drinking.

As suggested by Dingle and Oei [2] alcohol consumption may lead to lowered inhibition and in turn increase risky sexual and drug use behaviors. Steel and Joseph [1] similarly suggest alcohol may impair decision making and in turn hinder risk reduction techniques. The low observed prevalence of STIs may be due to underreporting. However, if the STI prevalence is indeed low, alcohol consumption may not be working primarily through risky sexual behavior to increase the hazard of HIV infection in this population of injection drug users. Instead, high risk drug use practices may be the primary mediating factor. Alcohol may also work to compromise the immune system and in turn allow for increased risk of HIV infection [3–5]. In a series of studies, Bagasra and colleagues showed alcohol to increase HIV-1 replication in human peripheral blood mononuclear cells. This increase in HIV-1 replication coincided with lower production of soluble immune response suppressor activity and interleukin-2 attributed to functional impairment of both suppressor (CD8+) and helper (CD4+) T lymphocytes. CD4+ and CD8+ T-lymphocytes regulate the immune response. CD8+ T lymphocytes have been shown to inhibit HIV-1 replication [30–32]

There are limitations to the present research. For valid inference we must assume the absence of unmeasured confounding as well as no informative censoring by unmeasured factors. If unmeasured factors for confounding or informative censoring exist then the reported incidence rates and hazard ratios will be biased. Admittedly the indicators of high risk sexual activity and drug use behaviors such as number of sexual partners, any sexually transmitted infections, as well as attendance at a shooting gallery may not fully capture the extent of risk behaviors in this population of injection drugs users. Therefore, residual confounding of effect estimates may still be present. If sexually transmitted infections were more underreported in heavy drinkers or heavy drinkers were more likely to share drug injection equipment then this residual confounding would bias effect estimates away from the null. Bias can also occur in the presence of non-positivity, model misspecification, or lack of consistency [33]. We do not account for the fact that variables as assessed are typically imperfect measures of the true underlying characteristic. In addition, many heavy drinkers were HIV infected at entry. If heavy drinkers who were HIV negative at entry were less prone to risky sex and drug use activities as compared to heavy drinkers who seroconverted prior to entry, then the association between heavy drinking and HIV acquisition would be muted.

There are several strengths to the present work. Use of prospective data helps ensure temporal order between alcohol consumption and HIV infection. Lagging covariates further

facilitates temporal order for confounders, and in turn proper causal inference. Use of time-updated reports minimizes systematic bias due to measurement error [34]. Use of marginal structural models avoids bias associated with standard adjustment techniques in the presence of time-varying confounders affected by prior exposure [20,22]. Finally, randomized evidence is not feasible due to ethical concerns, or lack of compliance in the case of risk reduction trials [35–36]. Without randomized evidence, thorough analysis of prospective observational studies with repeated assessments of exposures and outcomes provides the best evidence for estimation of etiologic effects.

Our findings provide compelling evidence for a dose-response relationship between alcohol consumption and HIV acquisition *in populo*. This evidence lends support for the enhancement of HIV risk reduction strategies with alcohol-specific interventions, including incorporation of alcohol-related prevention into programs tailored for substance users and for prevention programs among HIV positives [37]. It is estimated that lowering drinking from the highest drinks/week category (i.e., 51–140) to the lowest (i.e., 0) for 2/3 of the person years contributed in the highest category would reduce HIV incidence in this population of injection drug users by 29%. Future work should thoroughly explore the pathways by which alcohol consumption increases risk of HIV infection. Identifying mediating factors will be central to identifying new targets for HIV prevention interventions. In addition, marginal structural models should be used to examine the association between alcohol consumption and HIV acquisition in other high-risk populations such as men who have sex with men and Sub-Saharan Africans.

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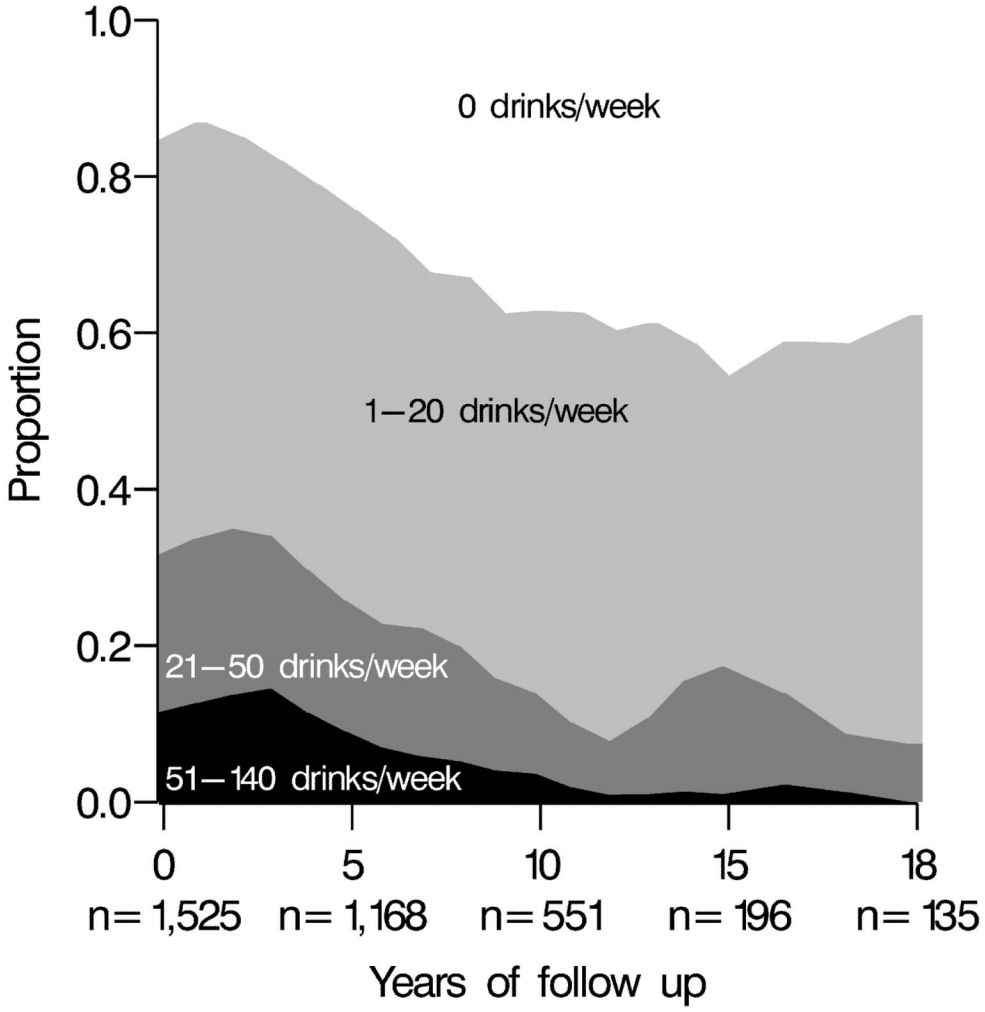

Figure 1.
Alcohol consumption by years of follow up among 1,525 African American injection drug users with 8,181 person-years of follow up, ALIVE cohort, 1988 – 2008.

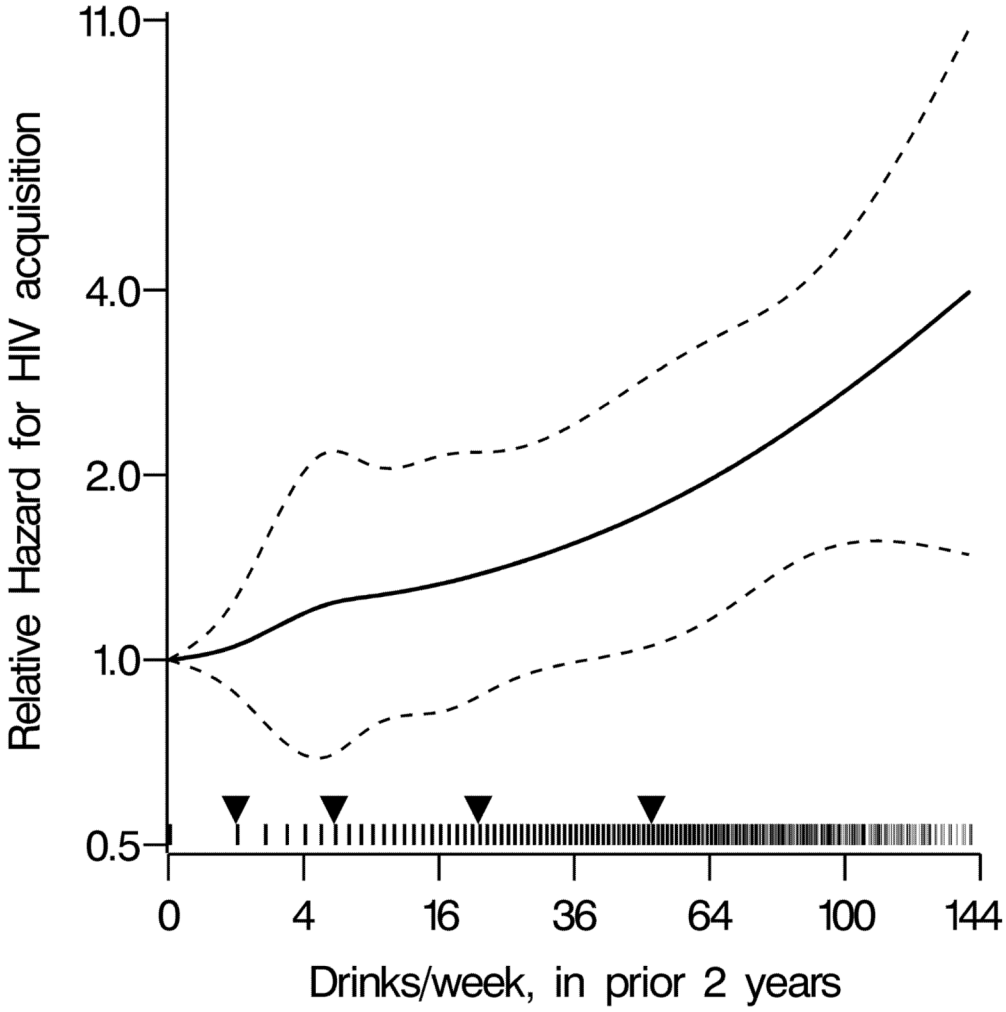

Figure 2.

Weighted relative hazard of HIV acquisition by alcohol consumption among 1,525 African American injection drug users with 8,181 person-years of follow up, ALIVE cohort, 1988 – 2008. Hash marks represent participants who reported a given number of drinks/week in the prior two years. Arrow heads are located at 1, 6, 21, and 51 drinks/week which are at the lower bounds of the average drink/weeks categories. Knots are placed at: 1, 7, 20, and 78 drinks/week. Dash lines are point-wise 95% confidence bands.

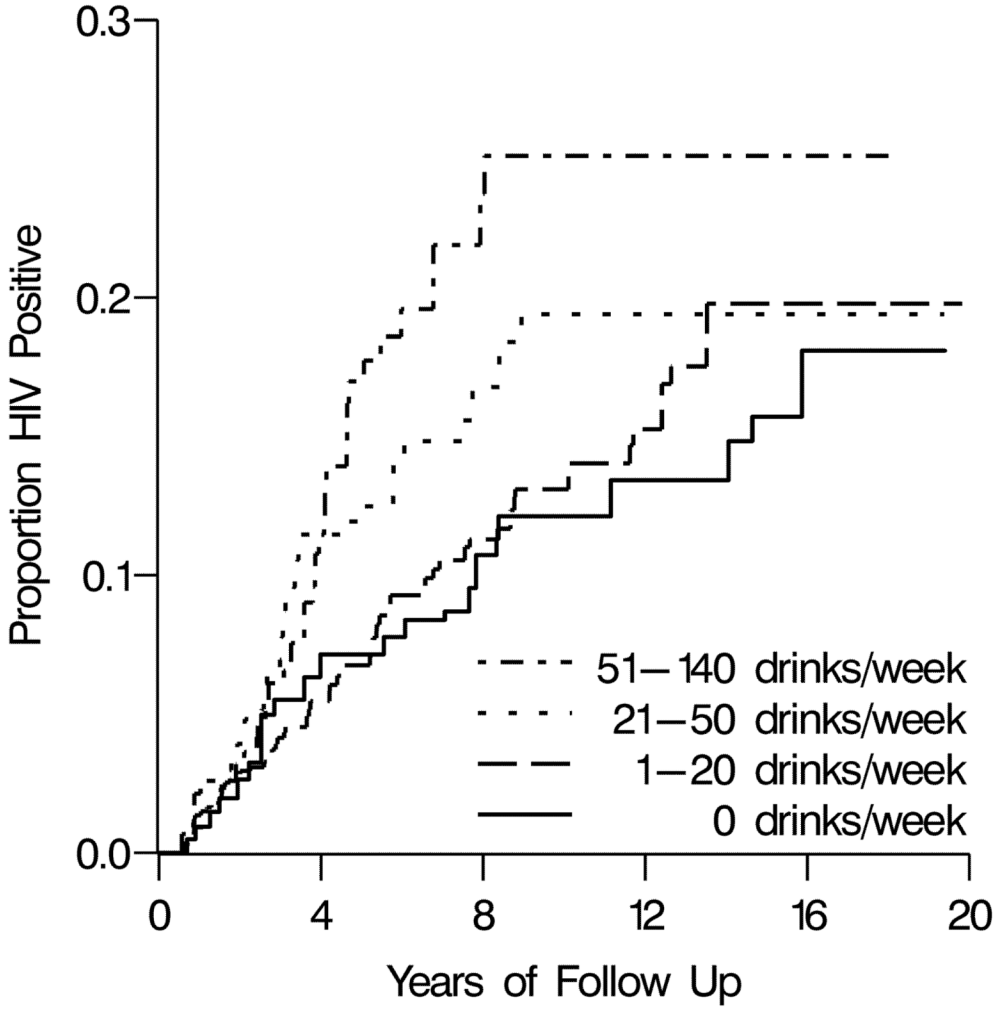

Figure 3.
Proportion HIV positive by alcohol consumption among 1,525 African American injection drug users with 8,181 person-years of follow up, ALIVE cohort, 1988 – 2008.

Table 1

Characteristics of 1,525 African American injection drug users at study entry and over 8,181 person-years of follow up, ALIVE cohort, 1988 – 2008.

Characteristic: [a]	Entry N = 1,525 participants	Follow up N = 8,181 person-years
Age, years	37 (32; 42)	42 (36; 48)
Older than 37 years, % (n)	48 (736)	73 (5,972)
Female sex, % (n)	28 (428)	28 (2,291)
Education, years	10 (10; 12)	10 (10; 12)
More than 10 years of education, % (n)	43 (662)	44 (3,599)
Cocaine [b], % (n)	78 (1,184)	58 (4,745)
Number of sexual partners, % (n)		
>1	40 (604)	28 (2,291)
1	43 (661)	47 (3,845)
0	17 (260)	25 (2,045)
Male having sex with a man, % (n)	1 (16	0.7 (57)
Any sexually transmitted infections [c], % (n)	3 (52)	2 (164)
Number of drug injections/day	0.7 (0.0; 2.0)	0.1 (0; 1.0)
Number of drug injections/day, % (n)		
>1	35 (525)	21 (1,718)
1	21 (327)	18 (1,473)
0	44 (673)	61 (4,990)
Attended shooting gallery, % (n)	13 (199)	6 (491)
Median number of drinks/week in prior 2 years	11 (2; 28)	6 (1; 22)
Number of drinks/week in prior 2 years, % (n)		
51–140	13 (193)	9 (736)
21–50	21 (322)	17 (1,390)
6–20	28 (430)	26 (2,127)
1–5	23 (356)	24 (1,964)
0	15 (224)	24 (1,964)
Binge drinking [d], % (n)	34 (514)	23 (1,882)
Composite, % (n)		
21–140	34 (515)	26 (2,127)
1–20, binge	8 (118)	6 (491)
1–20, no binge	43 (668)	44 (3,599)
0	15 (224)	24 (1,964)

[a] Median (quartiles), for prior six months unless noted otherwise.

[b] Crack, snort cocaine, inject cocaine alone, and speedball.

[c] Genital herpes simplex virus, genital warts, gonorrhea, or syphilis.

[d] Drinking at least once a week and consuming more than five drinks on a given drinking day.

Table 2

Association between alcohol consumption in the prior two years and binge drinking in the prior six months with HIV acquisition among 1,525 African American injection drug users with 8,181 person-years of follow up, ALIVE cohort, 1988 – 2008.

	Crude		Weighted [b]	
	Incidence Rate / 100 PY [a]	**Hazard Ratio (95% CL[a])**	**Incidence Rate / 100 PY [a]**	**Hazard Ratio (95% CL[a])**
Drinks/week, prior 2 years:				
51–140	4.00	2.96 (1.67, 5.23)	3.25	2.12 (1.15, 3.90)
21–50	2.64	2.06 (1.20, 3.54)	2.65	1.66 (0.94, 2.93)
6–20	1.73	1.41 (0.82, 2.42)	1.77	1.18 (0.66, 2.09)
1–5	1.46	1.22 (0.69, 2.15)	1.65	1.09 (0.60, 1.98)
0	1.10	1.	1.25	1.
P value for trend		8.2×10^{-6}		9.7×10^{-4}
Binge drinking, prior 6 months: [c]				
Yes	3.33	2.04 (1.47, 2.83)	3.03	1.70 (1.22, 2.37)
No	1.44	1.	1.57	1.
Composite:				
21–140 drinks/week	3.12	2.38 (1.44, 3.92)	2.87	1.83 (1.07, 3.12)
1–20 drinks/week and binge drinking	2.84	2.23 (1.13, 4.41)	2.90	1.80 (0.88, 3.66)
1–20 drinks/week and no binge drinking	1.43	1.18 (0.71, 1.98)	1.55	1.03 (0.60, 1.78)
0 drinks/week	1.10	1.	1.25	1.
Overall	1.89		1.92	

[a] PY, person-years; CL, confidence limits.

[b] Accounting for: cocaine use, shooting gallery attendance, gender, age at entry, years of formal education, number of sexual partners, being a male having sex with a male, history of sexually transmitted infections, and daily frequency of drug injections; value at prior visit used for time-varying covariates.

[c] Drinking at least once a week and having more than five drinks on a given drinking day in prior six months.

Table A1

Predictors of loss to follow up and censoring due to missed visits among 1,525 African American injection drug users with 8,181 person-years of follow up, ALIVE cohort, 1988 – 2008.

Characteristic:[a]	Crude Hazard Ratio (95% CL[b])	Adjusted [c] Hazard Ratio (95% CL[b])
Age, years		
>37	0.86 (0.76, 0.99)	0.88 (0.76, 1.01)
≤37	1.	1.
Gender		
Female	1.00 (0.86, 1.16)	1.00 (0.86, 1.17)
Male	1.	1.
Education, years		
>10	1.02 (0.89, 1.16)	1.02 (0.89, 1.17)
≤10	1.	1.
Cocaine [d]		
Yes	0.98 (0.85, 1.13)	0.82 (0.69, 0.98)
No	1.	1.
Number of sexual partners		
>1	1.24 (1.02, 1.50)	1.25 (1.02, 1.53)
1	1.06 (0.88, 1.27)	1.08 (0.90, 1.29)
0	1.	1.
Male having sex with a man		
Yes	1.44 (0.72, 2.89)	1.33 (0.66, 2.69)
No	1.	1.
Any sexually transmitted infections [e]		
Yes	0.79 (0.47, 1.34)	0.72 (0.43, 1.23)
No	1.	1.
Number of drug injections/day		
>1	1.44 (1.23, 1.69)	1.56 (1.30, 1.88)
1	1.09 (0.91, 1.31)	1.18 (0.97, 1.44)
0	1.	1.
Attended shooting gallery		
Yes	1.41 (1.10, 1.80)	1.29 (1.00, 1.67)
No	1.	1.
Number of drinks/week in prior 2 years		
51–140	0.90 (0.70, 1.17)	0.80 (0.61, 1.05)
21–50	0.92 (0.74, 1.14)	0.87 (0.69, 1.09)
6–20	0.84 (0.69, 1.02)	0.83 (0.68, 1.02)
1–5	0.92 (0.76, 1.12)	0.92 (0.76, 1.13)
0	1.	1.

[a] For prior visit unless noted otherwise.

[b] CL, confidence limits.

[c] Adjusted for all covariates included in table.

[d] Crack, snort cocaine, inject cocaine alone, and speedball.

[e] Genital herpes simplex virus, genital warts, gonorrhea, or syphilis.

Table A2

Association between alcohol consumption in the prior six months and throughout follow up with HIV acquisition among 1,525 African American injection drug users with 8,181 person-years of follow up, ALIVE cohort, 1988 – 2008.

	Crude		Weighted [b]	
	Incidence Rate /100 PY [a]	**Hazard Ratio (95% CL[a])**	**Incidence Rate /100 PY [a]**	**Hazard Ratio (95% CL[a])**
Drinks/week, prior 6 months:				
51–140	3.99	2.76 (1.69, 4.51)	3.52	2.10 (1.25, 3.53)
21–50	2.59	1.85 (1.14, 3.02)	2.38	1.45 (0.88, 2.40)
6–20	1.86	1.42 (0.88, 2.27)	1.88	1.22 (0.74, 2.01)
1–5	1.71	1.32 (0.79, 2.20)	1.87	1.12 (0.66, 1.88)
0	1.22	1.	1.38	1.
P value for trend		3.4×10^{-5}		1.9×10^{-3}
Drinks/week, prior follow up:				
51–140	3.63	3.33 (1.63, 6.79)	3.10	2.25 (1.06, 4.80)
21–50	2.19	2.22 (1.11, 4.44)	2.18	1.63 (0.78, 3.41)
6–20	1.95	1.97 (0.99, 3.90)	2.00	1.42 (0.70, 2.89)
1–5	1.29	1.33 (0.65, 2.75)	1.43	1.10 (0.52, 2.35)
0	1.01	1.	1.26	1.
P value for trend		5.1×10^{-5}		2.4×10^{-3}

[a] PY, person-years; CL, confidence limits.

[b] Accounting for: cocaine use, shooting gallery attendance, gender, age at entry, years of formal education, number of sexual partners, being a male having sex with a male, history of sexually transmitted infections, and daily frequency of drug injections; value at prior visit used for time-varying covariates.