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ORIGINAL PAPER

Number of Drinks to "Feel a Buzz" by HIV Status and Viral Load in Men

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Abstract The impact of HIV and its treatment on the effects of alcohol remain unclear. Blood alcohol concentrations have been noted to be higher in HIV infected individuals prior to antiretroviral initiation. Our goal was to compare number of drinks to "feel a buzz or high" among HIV infected and uninfected men, stratified by viral load (VL) suppression. Data includes 1478 HIV infected and 1170 uninfected men in the veterans aging cohort study who endorsed current drinking. Mean (SD) number of drinks to feel a buzz was 3.1 (1.7) overall. In multivariable analyses, HIV infected men reported a lower mean number of drinks to feel a buzz compared to uninfected men (coef $= -14$ for VL < 500; -34 for VL ≥ 500; $p \leq .05$). Men with HIV, especially those with a detectable VL, reported fewer drinks to feel a buzz. Future research on the relationship between alcohol and HIV should consider the role of VL suppression.

Keywords HIV · Alcohol intoxication · Alcohol use · Alcohol-related disorders · Buzz

List of Abbreviations

VACS	Veteran Aging Cohort Study
ART	Antiretroviral therapy
VL	HIV RNA viral load
AUDIT-C	Alcohol use disorder identification test-consumption
HED	Heavy episodic drinking
ICD-9	International classification of diseases, ninth revision
BMI	Body mass index
SD	Standard deviation
Haz	Hazardous
Alc Rel Dx	Alcohol related ICD-9 diagnosis

Introduction

Unhealthy alcohol use [1] has been associated with worse disease progression in individuals with HIV [2–5]. Among other effects, alcohol use, even use below standard drinking limits, contributes to non-adherence to antiretroviral

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therapy (ART) [4, 6, 7], liver fibrosis [8] and intoxication can increase risky sexual behavior [9]. To prevent such consequences, some suggest that recommended drinking limits in the HIV infected should be lower than limits used in the uninfected populations [5, 6]. In laboratory studies, upon exposure to the same amount of alcohol, HIV infected individuals achieve higher blood alcohol concentrations prior to receiving ART compared to after initiating ART [10]. The impact of HIV infection and ART treatment on alcohol metabolism and sensitivity to alcohol's effects is unclear [11].

Understanding the differential effects of alcohol on blood alcohol concentration and intoxication in HIV infected individuals is important in informing thresholds for healthy drinking limits, which may differ from those who are uninfected. In addition, given the profound impact of ART on immune and inflammatory processes, the effects of alcohol among HIV infected individuals both on and off ART and by HIV-RNA viral load (VL) status (detectable versus suppressed) need to be better understood. Self-reported sensitivity to the intoxicating effects of alcohol can be a useful metric to compare populations of subjects and reflects drink size along with a number of genetic, pharmacokinetic, and pharmacodynamics factors [12–14]. Since VL suppression is an indicator of effective ART, the primary aim of this research is to examine the sensitivity to alcohol's effects by HIV status and VL suppression.

Methods

Data

We included HIV infected and uninfected male participants enrolled in the Veterans Aging Cohort Study (VACS), an ongoing 9 site cohort study of HIV infected and uninfected veterans [2, 15, 16] in care in infectious disease and general medicine clinics in the Veterans Affairs (VA) Healthcare System. Women were excluded because they represent only 5 % of VACS subjects and sensitivity to the effects of alcohol varies by gender [12].

There were 3631 HIV infected and 3693 uninfected participants enrolled in VACS between 2002 and 2010. Follow-up surveys assessing a range of health behaviors, including alcohol use, are administered annually. In addition to self-reported survey data, laboratory, medication, and comorbidity data from the VA Clinical Case Registry, Pharmacy Benefits Management, and inpatient and outpatient treatment files were utilized. Participants who reported no alcohol consumption in the past year or did not answer the questionnaire items regarding the number of drinks to feel a buzz were excluded.

Main Outcome

Participants were asked on self-completed surveys at follow-up 1, 4, and 5: "How many drinks of alcohol does it take for you to begin to feel a "buzz" or high?" This item assessing alcohol's subjective effects is similar to an item from the National Alcohol Survey ("How many drinks do you think you would have to have before you would feel high?") [12] that has been used in multiple national surveys assessing alcohol use [12, 17, 18]. The use of the term "buzz" has been validated using factor analysis [13]. For each participant, the first survey in which they reported a response for this item was used for the analysis.

Main Predictor

HIV status was determined at the time of enrollment into the study. Of those with HIV infection, HIV-RNA viral load (VL) at the time of the survey was categorized as detectable (>500 copies/mL) or suppressed (≤500 copies/mL). For comparisons, three categories were created: uninfected, HIV infected with a detectable VL, and HIV infected with a suppressed VL.

Covariates

The Alcohol Use Disorder Identification Test-Consumption (AUDIT-C) [19] was included on all of the VACS surveys. We used the AUDIT-C reported on the same survey on which number of drinks to feel a buzz was reported. Alcohol related diagnosis was considered positive if an International Classification of Diseases, Ninth Revision (ICD-9) diagnosis was present prior to the survey (specific ICD-9 codes used are available at vacohort.org). Alcohol use categories were based on the AUDIT-C, heavy episodic drinking (HED) which was defined as ever having 6 or more drinks on one occasion based on the 3rd item of the AUDIT-C, and the presence/absence of an alcohol related ICD-9 diagnosis code [20]. Six mutually exclusive alcohol use categories were created to reflect increasing severity of use: (1) non-hazardous comprised of non-hazardous drinking and no alcohol related diagnosis; (2) alcohol related diagnosis only; (3) hazardous with AUDIT-C 4+ criteria only; (4) hazardous with HED criteria only; (5) hazardous with AUDIT-C 4+ and HED criteria; (6) both hazardous and an alcohol related diagnosis present.

The VACS Index, a validated measure of overall health and mortality risk among HIV infected individuals, was included as a covariate. The VACS index is composed of age, CD4 count, VL, hemoglobin, FIB4, eGFR, Hepatitis C infection, and is described in detail elsewhere [21–23]. Whether the participant was receiving ART at the time of survey was determined using a previously validated

algorithm using pharmacy refill data from the Veterans Affairs National Pharmacy Benefits Management database [24].

Potential Mediating Variable

Because HIV is associated with lower body mass index (BMI) [20, 25], and blood alcohol concentrations are impacted by volume of distribution and inversely associated with BMI, we examined whether BMI mediates the relationship between HIV and number of drinks to feel a buzz [26]. BMI was calculated based on height and weight measurements collected as part of routine clinical care and documented in the electronic medical record during the clinic visit closest to the corresponding survey. BMI was calculated as the ratio of weight (kilograms) over height (meters) squared and was categorized as less than 18.5, 18.5–29.9, and 30 or greater.

Analysis

Demographic characteristics were summarized for HIV infected and uninfected participants. Because sensitivity to alcohol's effects is impacted by age and level of tolerance, we examined graphs of number of drinks to feel a buzz by uninfected, HIV infected with a detectable VL, and HIV infected with a suppressed VL, by both age and alcohol use categories. Tests for trend were conducted for each age and alcohol use category to determine whether a statistically significant difference exists within each group. To assess the association of HIV status and VL suppression with number of drinks to feel a buzz, we generated univariate and multivariable linear regression models adjusted for age, race/ethnicity, VACS Index, and alcohol use categories. In our data, number of drinks to feel a buzz resembles a normal distribution and linear regression is robust to departures from the normal distribution assumption. To account for the non-linear association of age with number of drinks to feel a buzz that was identified in preliminary analyses, piece-wise regression models with age knots set at 40 and 50 years were used for the multivariable models [27, 28].

To determine the role of BMI in potentially influencing the relationship between HIV infection/VL suppression and number of drinks to feel a buzz, BMI was examined as a possible mediator using Baron and Kenny mediation analysis [29]. This is a three-step process to determine whether: [1] HIV infection/VL suppression is associated with number of drinks to feel a buzz, [2] HIV infection/VL suppression is associated with the potential mediator, BMI, and [3] the association between HIV infection/VL suppression and number of drinks to feel a buzz is attenuated after adjustment for BMI [30]. Sobel's test was run to determine whether the HIV and VL status coefficients were statistically significantly different in the models with and without BMI [28, 31, 32]. Collinearity was assessed using variance inflation factors. Goodness of fit was assessed using r-squared values and by examining residual and residual-versus-fitted value and observed-versus-fitted value plots.

As a sensitivity analysis, we ran the two multivariate models with the VACS Index components in place of the VACS Index. As a second sensitivity analysis, instead of running linear regression models, we ran logistic regression models with the dichotomous outcome of less than 4 versus 4 or more drinks to feel a buzz.

Results

Demographic and Clinical Characteristics

There were 1478 HIV infected men (607 with a detectable VL; 871 with a suppressed VL) and 1170 uninfected men identified who reported a number of drinks to feel a buzz on follow-up surveys 1, 4 or 5. The mean age of the HIV infected group with a detectable VL (48.8 years) was younger than those with a suppressed VL (52.2 years) and in the uninfected group (53.3 years, $p < .001$). Race/ethnicity was similar between groups with approximately 63 % being African-American and 9 % Hispanic. Hepatitis C infection was more prevalent among HIV infected with a detectable VL (46.8 %) and among those with a suppressed VL (45.5 %) compared to those uninfected (28.1 %). Obesity (defined as a BMI greater than 30) was less prevalent among those with a detectable VL (14.3 %) and among those with a suppressed VL (15.0) compared to the uninfected men (38.7 %). A greater percentage of those with HIV infection were non-hazardous drinkers (44.8 % of those with a detectable VL and 49.0 % of those with a suppressed VL) compared to those who were uninfected (38.9 %). A lower percentage of those with HIV infection met criteria for both an alcohol related diagnosis and hazardous drinking (14.3 % of those with a detectable VL and 12.7 % of those with a suppressed VL) compared to the uninfected group (22.1 %). The VACS index score was higher, indicating worse heath, in the HIV infected groups. Of those with HIV infection, a lower percentage of those with a detectable VL were receiving ART (67.3 %) compared to those with a suppressed VL (90.7 %), and a lower percent of those with a detectable VL had a CD4 of 200 cells/mm^3 or greater (72.3 %) compared to those with a suppressed VL (89.9 %) (Table 1).

Drinks to Feel a Buzz

The mean number of drinks to feel a buzz was lower among those with HIV infection (2.8 for those with a

Table 1 Description of analytic sample of VACS participants by HIV status

	HIV+ detectable VL (n = 607)	HIV+ suppressed VL (n = 871)	Uninfected (n = 1170)	p value
Mean age (SD)	48.8 (8.4)	52.2 (8.8)	53.3 (9.0)	<.001
Race/ethnicity (%)				
White	21.4	25.5	24.0	
African-American	64.6	61.4	62.5	
Hispanic	8.4	9.1	10.0	
Other	5.6	4.0	3.5	.2
Alcohol use (%)				
Non-hazardous	44.8	49.0	38.9	
Alcohol related Dx only	8.1	6.4	8.2	
Haz-AUDIT-C 4+ only	4.0	4.3	4.1	
Haz-HED Only	5.9	7.1	6.2	
Haz-AUDIT-C 4+ and HED	22.9	20.4	20.6	
Alc Rel Dx and Haz	14.3	12.7	22.1	<.001
Drinks to feel a buzz				
Mean (SD)	2.8 (1.6)	2.9 (1.6)	3.2 (1.7)	
Median (interquartile range)	3 (2, 3)	3 (2–4)	3 (2-4)	
4+ (%)	24.1 %	28.3 %	35.6 %	<.001
Hepatitis C (%)	46.8	45.5	28.1	<.001
BMI (%)				
<18.5	3.1	2.5	.6	
18.5–29	82.5	82.4	60.7	
>30	14.3	15.0	38.7	<.001
Mean VACS index (SD)	36.6 (20.7)	25.7 (15.1)	18.1 (15.3)	<.001
On ART (%)	67.3	90.7	–	<.001
CD4 200 + (%)	72.3	89.9	–	<.001

VACS veteran aging cohort study, *SD* standard deviation, *VL* HIVRNA viral load, *Haz* hazardous, *HED* heavy episodic drinking, *Alc Rel Dx* alcohol related international classification of diseases, ninth revision diagnosis

detectable VL and 2.9 for those with a suppressed VL), compared to those uninfected (3.2, $p < .001$) (Table 1). The percentage who reported four or more drinks to feel a buzz was lower among those with HIV (24.1 % for those with a detectable VL and 28.3 % for those with a suppressed VL) compared to those uninfected (35.6 %). Based on univariate models, compared to uninfected men, HIV infected men report a lower number of drinks to feel a buzz (coefficient = −.38 for those with a detectable VL and coefficient = −.25 for those with a suppressed VL) (Table 2).

Analyses by Alcohol Use Groups and Age

When stratified by alcohol use groups, the pattern of a lower number of drinks to feel a buzz for HIV infected compared to uninfected (and HIV infected with a detectable VL compared to a suppressed VL) was statistically significant for the following alcohol use categories: non-hazardous, hazardous—HED only, and hazardous—both AUDIT-C 4+ and HED (Fig. 1). Additionally, Fig. 1 shows that as severity of alcohol use category increased, the number of drinks to feel a buzz also increased. Based on the multivariable model without BMI, compared to non-hazardous drinkers, those with hazardous drinking reported from .7 to 1.2 more drinks to feel a buzz ($p < .001$). Those with both an alcohol related diagnosis and hazardous drinking reported consuming 1.4 more drinks to feel a buzz (coefficient = 1.39; $p < .001$) (Table 2). When stratified by age groups, the trend of a lower number of drinks to feel a buzz for HIV infected compared to uninfected (and HIV infected with a detectable VL compared to a suppressed VL) was statistically significant for all age groups under 60 years (Fig. 2).

Multivariable and Mediation Analyses

In multivariable analyses without BMI, both HIV infected groups reported a lower number of drinks to feel a buzz compared to those uninfected (coefficient = −.34, $p < .001$ for those with a detectable VL and coefficient = −.14, $p = .05$ for those with a suppressed VL)

Table 2 Association of HIV/VL status with drinks to feel a buzz (n = 2648)

	Univariate model		Multivariable model		Multivariable model with BMI	
	Coef	p value	Coef	p value	Coef	p value
HIV status						
HIV− (referent)						
HIV+ VL < 500[a]	−.25	.001	−.14	.05	−.07	.3
HIV+ VL 500+[a]	−.38	<.001	−.34	<.001	−.27	.004
Race/ethnicity						
White (referent)						
African-American			−.02	.8	−.01	.9
Hispanic			.27	.02	.28	.017
Other/unknown			.04	.8	.03	.9
Alcohol use						
Non-hazardous (referent)						
Alcohol related Dx only			.16	.20	.18	.13
Haz-AUDIT-C 4+ only			.71	<.001	.75	<.001
Haz-HED only			.82	<.001	.81	<.001
Haz-AUDIT-C 4+ and HED			1.17	<.001	1.17	<.001
Alc Rel Dx and Haz			1.39	<.001	1.41	<.001
VACS Index			.015	.15	.019	.07
Age <40			−.04	.036	−.05	.03
Age 40–50			.03	.007	.03	.009
Age 50+			−.005	.4	−.005	.4
BMI			–	–		
18.5–30.0 (referent)						
<18.5					−.12	.57
>30.0					.30	<.001
Intercept	3.18	<.001	3.97	<.001	3.93	<.001

VL HIVRNA Viral load, *Haz* hazardous, *HED* heavy episodic drinking, *Alc Rel Dx* alcohol related international classification of diseases, ninth revision diagnosis; *coef* coefficient

[a] For HIV infected VL suppressed versus detectable comparison, p = .14 in univariate model; p = .027 in multivariate model w/out BMI; p = .018 in multivariable model with BMI

(Table 2). Also, the coefficient for HIV infected with a detectable VL was statistically significantly lower than the coefficient for HIV infected with a suppressed VL (p = .027), indicating that fewer drinks are needed to feel a buzz in those with a detectable VL compared to those with a suppressed VL.

Compared to having a BMI between 18.5 and 30, having a BMI of greater than 30 was associated with a higher number of drinks to feel a buzz in multivariable analyses (coefficient = .30, p < .001). With BMI added to the multivariable model, the association between HIV infection/VL suppression and number of drinks to feel a buzz was attenuated. The difference in number of drinks to feel a buzz between those with a suppressed VL and uninfected individuals was no longer statistically significant (coefficient = −.07, p = .3) in the model adjusted for BMI. The difference between those with a detectable VL and those who were uninfected remained statistically significantly (coefficient = −.27, p = .004). The coefficient for HIV infected with a detectable VL remained statistically significantly lower than the coefficient for those with a suppressed VL (p = .018). Comparing HIV infected with a suppressed VL to the uninfected, the Sobel test was statistically significant (p < .004) and the proportion of the total effect that is mediated by BMI was 44 %. Comparing HIV infected with a detectable VL to uninfected individuals, the Sobel test was statistically significant (p < .004) and the total effect that is mediated by BMI was 15 %. The attenuated results indicate that BMI plays a mediating role in the association between HIV infection and number of drinks to feel a buzz (Table 2).

Based on variance inflation factors, collinearity was not an issue in the multivariate models. The adjusted r-squared in the unadjusted model was .08. In the adjusted models, the r-squared was .14 in the model without BMI and .15 with BMI included, indicating an improvement in model

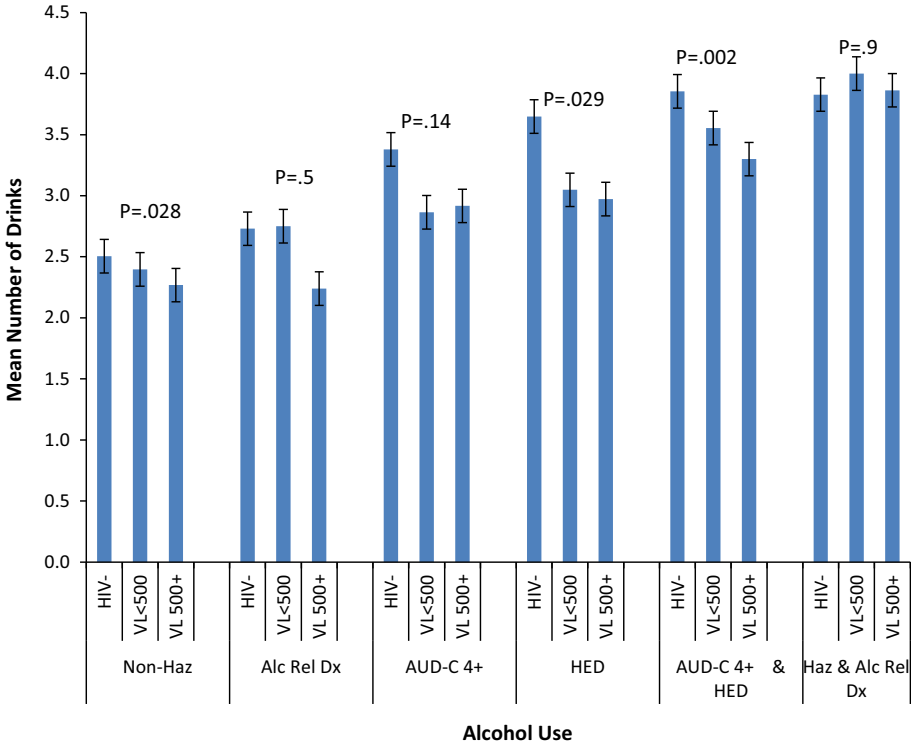

Fig. 1 Number of drinks to feel a buzz by HIV, viral load, and alcohol use

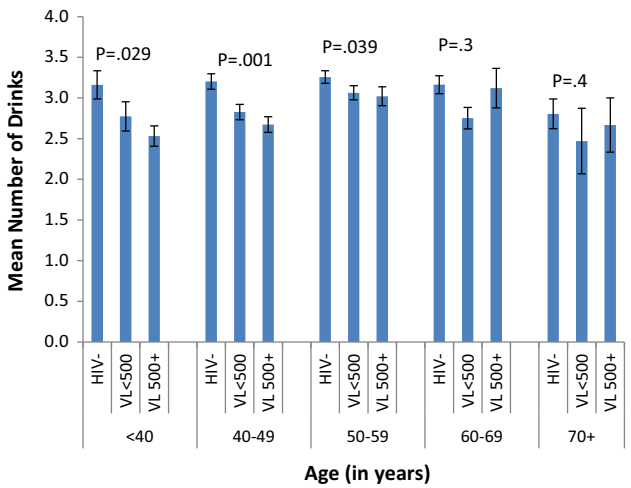

Fig. 2 Number of drinks to feel a buzz by HIV, viral load, and age

fit. Residuals were approximately normally distributed with a mean of 0. Based on residual-versus-fitted and observed-versus-fitted value plots, we determined that the model fit was adequate. In the sensitivity analysis in which the two multivariate models were run including the components of the VACS index in place of the VACS index, results were similar to those shown in Table 2. In the second sensitivity analysis, in which logistic regression models predicting 4 or more drinks to feel a buzz (versus less than 4 drinks to feel a buzz) were run, the odds ratio (OR) for reporting 4 or more drinks to feel a buzz was .76 ($p = .010$) for HIV infected with a suppressed VL and OR = .53 ($p < .001$) for those with a detectable VL (referent group uninfected) for the model without BMI. For the model with BMI, OR = .82 ($p = .071$) for those HIV infected with a suppressed VL and OR = .57 ($p < .001$) for those with a detectable VL. Findings are similar to those from the linear regression models, as they also suggest that those with HIV infection require a lower number of drinks to feel a buzz compared to those who are uninfected, and of those who are HIV infected, those with a detectable VL require a lower number of drinks to feel a buzz compared to those with a suppressed VL.

Discussion

HIV infected participants with a detectable VL were more sensitive to alcohol's effects compared to HIV infected with suppressed VL and compared to those uninfected. After adjustment, HIV infected individuals with a detectable VL required greater than one quarter of a drink less to feel a buzz compared to uninfected. One potential reason for this finding could be that there is greater alcohol absorption in those with a detectable VL or untreated HIV disease due to the intestinal barrier dysfunction associated with HIV disease [29].

Although few participants had very low BMIs, a statistically significantly lower percent of those with HIV

infection are obese (BMI of greater than 30) compared to those who are uninfected. Using Baron and Kenny methods [30], we determined that BMI mediates the association between HIV status and number of drinks to feel intoxicated. This finding indicates that thresholds for alcohol consumption should perhaps be lower for those with HIV infection and that BMI should also be included when considering thresholds for hazardous alcohol consumption.

Previous research has reported that blood alcohol concentration was reduced by 10–15 % after start of ART but participants reported "no significant changes in perception of intoxication" [10] before and after start of ART. However the sample size was relatively small and the amount of alcohol consumed was modest. Additionally, the amount of alcohol administered was based on weight (1 g/kg).

There are limitations to the current study. We excluded women due to their relatively small numbers in our sample and the known association between gender and sensitivity to alcohol's effects. Future research should include samples of HIV infected and uninfected women. Results are based only on reports of number of drinks to feel a buzz, and there could be variation in what a person considers feeling a "buzz". While potentially subjective and retrospective in nature, self-report remains an essential component of research on alcohol [33–36]. Self-report of alcohol consumption, for instance, has been validated against collateral reports, and is considered reliable, especially when the respondent is not intoxicated [33, 34]. Specifically self-reported sensitivity to alcohol's effects has been widely used in the field and recent work has supported the use of terms such as "buzz" in assessing levels of intoxication [12, 13, 18, 37]. While conceptions of what constitutes a drink of alcohol may vary, we attempted to mitigate this variation by providing subjects with instructions that "one "drink" was equal to 12 oz of beer (1 can), or 4 oz of wine (1 glass), or 1 oz of liquor (1 shot). The r-squared values indicate that 14 and 15 % of the variation was explained by the multivariate models. The multivariate linear models demonstrate that there is a statistically significant association between HIV status and number of drinks to feel a buzz and this association is also apparent in the sensitivity analysis using logistic regression models with less than 4 versus 4 or more drinks as a bivariate outcome. Given the limitations of this study, these results should be considered preliminary and future research should also examine the association between number of drinks to feel the effects of alcohol, BMI, and HIV.

There are strengths to this study. We have a relatively large sample of both HIV infected and uninfected men who are racially and ethnically diverse. We were able to examine the impact of VL suppression on the subjective effects of alcohol. We were also able to adjust for and assess important factors which may affect the impact of alcohol, such as health using the VACS Index, alcohol use category, and BMI. Understanding the impact that BMI could have on sensitivity to the effects of alcohol is important to consider because in the current analysis it mediated these effects and it is usually not considered in standard assessments of alcohol consumption.

We were surprised that those with an alcohol related diagnosis but not hazardous drinking did not report a greater number of drinks to feel the effects of alcohol than non-hazardous drinkers. Because our determination of alcohol related diagnosis was based on ICD-9 codes, it is possible that some individuals had an ICD-9 code that reflected a remote history of an alcohol related diagnosis rather than a current diagnosis.

Conclusions

In multivariate analyses not including BMI, compared to uninfected individuals, those with HIV infection reported a greater sensitivity to alcohol's effects based on number of drinks to feel a buzz or high. This greater sensitivity was present among HIV infected individuals both with a detectable VL and a suppressed VL. However, in the model adjusted for BMI, these effects are only seen in those with a detectable VL. Efforts to address the adverse impact of alcohol on HIV disease and transmission should consider this greater sensitivity to alcohol's effects and consider the role of a detectable VL and BMI. Future research should examine whether this increased sensitivity is due to increased blood alcohol concentrations or decreased tolerance for similar levels. Providers should consider these findings as they screen for alcohol use and counsel patients regarding the impact of alcohol on HIV infection.

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