Published in final edited form as:

Drug Alcohol Depend. 2017 September 01; 178: 380–385. doi:10.1016/j.drugalcdep.2017.05.021.

Differential effects of perceived stress on alcohol consumption in moderate versus heavy drinking HIV-infected women

Heidi Hutton^{1,*}, Catherine R. Lesko^{2,*}, Geetanjali Chander^{2,3}, Bryan Lau², Gary S. Wand³, and Mary E. McCaul¹

¹Department of Psychiatry and Behavioral Sciences, John Hopkins School of Medicine

²Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health

³Department of Medicine, Johns Hopkins School of Medicine

Abstract

Objective—To examine the association between perceived stress and subsequent alcohol use in women living with HIV.

Methods—Women (n=338) receiving HIV care between April 2006 and July 2010 who enrolled in either a brief intervention for hazardous drinking or a cohort of non-hazardous drinkers completed a 90-day drinking and drug use history, and completed stress, depression and anxiety measures at 0, 6, and 12 months. We examined the association between perceived stress at months 0 or 6 and measures of quantity and frequency of alcohol use in months 3–6 and 9–12, respectively.

Results—The association between perceived stress and subsequent alcohol use depended on whether women were heavy or moderate drinkers at index visit. Among women reporting 7 drinks/week at index visit, high levels of perceived stress were associated with subsequent increased alcohol intake. However, among women reporting >0 but <7 drinks/week at index visit, high levels of perceived stress were associated with a subsequent reduction in drinking.

Correspondence: Heidi E. Hutton, Department of Psychiatry and Behavioral Sciences The John Hopkins University School of Medicine Meyer 3-147 600 N. Wolfe St., Baltimore, MD 21287, hhutton@jhmi.edu, 443-287-2874.

*Denotes first co-authors

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Conflict of Interest

No conflict declared

None

Author Disclosures

Contributors

Dr. Hutton designed the study with Dr. McCaul and the background question. Dr. Lesko designed statistical hypotheses and with Dr. Hutton they were principal in article preparation. Dr. Lesko in consultation with Dr. Lau designed the statistical procedures, data presentation and interpretation. Dr. Chander, Dr. Wand, and Dr. McCaul provided results interpretation, group comparisons, and context. All authors participated in manuscript revisions and reviewed the final manuscript.

Conclusions—Baseline drinking status moderates the relationship between perceived stress and subsequent alcohol use. Perceived stress is an important therapeutic target in women who are heavy drinkers.

Keywords

Alcohol; stress; women; HIV; perceived stress; hazardous alcohol use

1.0 Introduction

Alcohol misuse is prevalent among persons living with HIV (PLWH). Estimates of heavy drinking among PLWH in care range from 8% to 27% (Crane et al., 2017 and Galvan, 2002) compared with 7.0% estimated in the US general population (SAMHSA, 2015). Alcohol misuse is associated with myriad negative HIV-disease outcomes, including delayed initiation of antiretroviral therapy (ART), decreased adherence to ART, and decreased virologic suppression Chander et al., 2006).

The prevalence, frequency and severity of stress and stressful events is also elevated among PLWH, particularly among women living with HIV (WLHIV). The prevalence of post-traumatic stress disorder (PTSD) is estimated to be 30% among WLHIV, more than five times higher than for HIV-uninfected women (Machtiger et al., 2012). Similarly, mental health symptoms including depression, anxiety, and suicidal ideation are 2–4 times more prevalent among WLHIV than in uninfected women (Nanni et al., 2015). Stressors can include compromised health, stigma associated with HIV infection and with behaviors that may have led to infection, low socioeconomic status, minority status, community and interpersonal violence, and mental health concerns (including addiction, depression, trauma, and anxiety) (Tsai et al., 2015 and Whetten et al., 2008). Such stressors have been shown to have deleterious effects on the mental and physical health of PLWH (Weinstein and Li, 2016). Indeed, stress has been associated with HIV disease progression and diminished effectiveness of antiretroviral therapies (Brief et al., 2004).

Among women in general, stress is considered to be a significant contributor to alcohol initiation, misuse and relapse. In US epidemiological surveys, women's alcohol use increases linearly with increases in the number of general life stressors (Keyes et al., 2011). Among women compared with men, traumatic stress is more strongly associated with past year binge drinking (consuming 4/ 5 drinks per occasion women/men) and heavy drinking (consuming >7/>14 drinks per week for women/men). Women who report a past trauma and develop PTSD are 3.5 times more likely to develop alcohol dependence than women who do not report past trauma (Sartor et al., 2010). Thus, heavier alcohol use may be an attempt to cope with stress in the absence of effective and adaptive coping strategies (Corbin et al., 2013).

Among PLWH, cross-sectional observation studies similarly show recent stressful events (e.g., death, assault) and particularly lifetime traumatic experiences (e.g., childhood physical or sexual abuse) are related to an increased frequency of intoxication (Pence et al., 2008). In addition to the number and frequency of stressors, the “perception” of stress too can play an important role in alcohol consumption. Perceived stress is the appraisal that stressful events

exceed one's ability to cope and has been shown to be higher among women than among men (Cohen et al., 1983). Perceived stress is also higher among PLWH than among persons without HIV infection (Williams et al., 2016) and is associated with a higher frequency of drinking days and of days of self-reported intoxication (Scott-Sheldon et al., 2013).

In these HIV studies, as in general population clinical studies, relatively little is known about the direction of the association between stress and alcohol use. Existing studies are largely cross-sectional and individuals vary considerably in their recall of number, type, and perception of stressful events. We examine here the effects of perceived stress on subsequent alcohol consumption patterns in a cohort of HIV-infected women in care. By temporally separating perceived stress and alcohol consumption, we have improved upon prior cross-sectional studies; this approach provides additional clues as to how perceived stress and alcohol consumption may be interrelated. We hypothesized that higher perceived stress would be associated with a subsequent increase in frequency and quantity of alcohol use, and that the relationship between use of alcohol and perceived stress would be cyclical.

2.0 Methods

2.1 Study Sample

All women were receiving care in Johns Hopkins HIV Clinic between April 2006 and July 2010. Two groups of women were enrolled in this study. The first group consisted of 153 women enrolled in a randomized clinical trial (RCT) of a brief alcohol intervention (Chander et al., 2015); RCT drinking inclusion criteria were >7 drinks per week, two or more binge occasions (4 drinks in a day) in the past 6 months, or had a cut-off score of 2 on the TWEAK (Chan et al., 1993). The brief intervention consisted of two 20-minute sessions with a study therapist, approximately one month apart, and a booster phone call within two to three weeks following each session. A second group of 234 women who did not meet RCT drinking inclusion criteria were enrolled in an observational cohort study and underwent the same assessments, but did not receive any intervention. All participants received standard of care, which consisted of access to health care professionals and referrals to an on-site weekly support group or substance abuse treatment as needed.

Women were excluded if they were actively psychotic or if they had other severe mental health symptoms that would prevent participation in the study, or if they were pregnant (due to ethical considerations regarding randomization to the standard of care). All participants signed an informed consent document approved by the Johns Hopkins School of Medicine Institutional Review Board.

2.2 Data Collection

At enrollment (zero months), demographic information was collected via Audio Computer-Assisted Self-Interview (ACASI). At zero, six, and twelve months, women responded via ACASI to validated measures to assess stress, anxiety and depression, including: Perceived Stress Scale (PSS; Cohen et al., 1983); Brief Symptom Inventory (BSI; Derogatis and Melisaratos, 1983), using the anxiety subscale; and Beck Depression Inventory (BDI; Beck et al., 1996). We classified women as anxious if they scored 1.03 on the anxiety subscale of

the BSI; we classified women as depressed if they scored >20 on the BDI. At each visit, women also completed a Timeline Followback (TLFB; Sobell and Sobell, 1992) with a trained interviewer to assess alcohol and illicit drug use patterns over the previous 90 days.

2.3 Analysis

To glean information about the temporal relationship between perceived stress and alcohol use, we examined the association between PSS score reported at one visit and alcohol use from 3 to 6 months subsequent. That is, we examined the association between PSS score at 0/6 months (the index visit) and alcohol use at 3–6 months and 6–12 months, respectively.

2.3.1 Exposure—We dichotomized PSS score into ≤ 14 / >14 . This cut-off score was used to correspond to the mean PSS score among black persons in a community sample (14.7) and to slightly exceed the mean PSS score among women in the same sample (13.7) (Cohen and Williamson, 1998). In a sensitivity analysis we modeled PSS continuously and found comparable results. We report the result of models where PSS score was dichotomized for ease of interpretation and comparability with other samples.

2.3.2 Outcomes—From the TLFB, we examined four separate (but often correlated) measures of alcohol use. In the 90-day TLFB measurement period, we treated each day as a separate observation. (If a woman was in a controlled environment (CE) e.g., hospital, jail, she did not respond to alcohol questions for those days and those days were excluded from analysis.) Outcomes for each daily observation included: 1) any alcohol use; 2) binge use (≥ 4 drinks on one occasion); and 3) number of standard drinks consumed. Finally, we restricted analysis to the subset of daily observations where women reported drinking any alcohol use and examined: 4) number of drinks consumed on drinking days. Using daily observations maximizes the utility of the TLFB to control for days women were not at risk for alcohol use due to CE and allows outcomes to vary unbounded by arbitrary limits (e.g., number of drinking days per week is bounded by 0 and 7). Furthermore, this approach ensures outcomes are better approximated by established distributions (e.g., any drinking on a single day is a binomial random variable) thus allowing our reported parameter and variance estimates to be based on solid statistical theory.

2.3.3 Covariate adjustment—To isolate the association between PSS score and alcohol use, we adjusted analyses using inverse probability weighting, a semiparametric extension of direct standardization (Hernan and Robins, 2016). We estimated the denominator of the weights using logistic regression to obtain the probability of PSS score >14 conditional on age, black race, high school or greater education, income below \$5,000, detectable viral load at baseline visit, cocaine or heroin use in the prior 3 months, depression, anxiety and randomization to the intervention for reducing hazardous drinking. We stabilized weights by the marginal probability of PSS score >14 or PSS score <14 corresponding to the PSS score that women reported in each period.

2.3.4 Statistical model—We modeled the presence or absence of drinking and of binge drinking using log-binomial regression to obtain risk ratios. We modeled the number of drinks per day using negative binomial regression to obtain rate ratios allowing for possible

over-dispersion of the data (both in the set of all days in the follow-up period to estimate drinks/day, and in the restricted set of days where women reported any drinking to estimate drinks/drinking day). We estimated parameters for all models using generalized estimating equations (GEE; Hanley et al., 2003) to account for correlated observations within study participants across index visits and within index visits (women could contribute up to 90 observations per index visit and up to 180 observations overall).

2.3.5 Secondary analyses—Because our hypothesis was that higher perceived stress would be associated with subsequent higher quantity and frequency of drinking, we were concerned that including non-drinkers would potentially wash out some of the associations of interest. That is, we were concerned that women who were nondrinkers during the 90 days prior to the index visit would not be susceptible (or would be much less susceptible) to any effects of stress on drinking. Therefore, in a sensitivity analysis, we repeated analyses above using the same covariates in the subset of women who reported any drinking at their index visit stratified by whether they reported >0 but <7 drinks per week (moderate drinking) or ≥7 drinks per week (heavy drinking). We tested for heterogeneity of associations among moderate versus heavy drinkers using $\alpha=0.20$ given low power to detect heterogeneity (due to smaller sample size) (Gail and Simon, 1985).

Finally, while our primary hypothesis was that higher perceived stress would be associated with heavier drinking in the subsequent 3–6 months, we also theorized that the association between stress and alcohol use may be cyclical. Therefore, we examined the association between alcohol use in the prior 90 days and subsequent reported perceived stress at 0, 6 and 12 month follow-up visits. We standardized estimates using stabilized inverse probability (of the alcohol use exposure in each model) weights, conditional on age, income, high school education or higher, cocaine use in the prior 90 days, heroin use in the prior 90 days, recent depression or anxiety symptoms, detectable viral load and randomization to the intervention for reducing hazardous drinking.

3.0 Results

Of 387 women enrolled in the original trial and cohort study, we excluded four women (3 from the observational cohort study and 1 from the trial) with incomplete baseline data. We further excluded 26 women who did not return after the baseline evaluation, 15 women who did not return for the 6-month visit (and thus were not observed at the beginning and end of any 6-month intervals), and 4 women who were missing drinking quantity or frequency at either the beginning or at the end of all observed 6-month intervals because they were in a controlled environment (CE) or missed a visit. The final study sample included 338 women (87% of the original sample). Had all 338 women been observed for both observation periods (0–6 months and 6–12 months), we would have expected to see 676 observation periods. The final study sample included 661 observation periods (98% of expected); the first observation period was missing for 3 women who were in a CE for all days prior to the 0-month visit and 1 who was missing data on depression and anxiety at 0 months. The second observation period was missing for 6 women who failed to return for their 12-month visit, 4 women who were in a CE for all days prior to their 12-month visit, and 1 woman who was missing a perceived stress score at her 6-month visit.

The majority of women were black (86%), had at least a high school education (54%), a median income of \$8000 (IQR: \$6000, \$9200), and an undetectable viral load (57%). Median age was 47 years, interquartile range (IQR): 41, 52. Enrollment prevalence of depression was 6%, anxiety was 8% and depression with anxiety was 9%. A notable percentage of women reported cocaine (21%) or heroin (9%) use at enrollment (table 1).

The mean PSS score at baseline was 15.1 (median=16, IQR: 10, 20; figure 1) exceeding averages for women and black race in the general population. PSS scores were fairly stable over time. The mean change in PSS score was 0.6 from baseline to 6 months (standard deviation (SD)=6.3), 0.4 from 6 months to 12 months (SD=5.7), and 0.9 from baseline to 12 months (SD=6.2). The Pearson correlation coefficient was 0.63 for PSS scores at baseline and 6 months, 0.66 for PSS scores at 6 months and 12 months, and 0.64 for PSS scores at baseline and 12 months.

During the 3–6 months subsequent to index woman-visits, women reported a mean of 5.6 binge drinking days (SD=15.5), 8.5 drinking days (SD=18.6), 0.8 drinks per day (SD=3.0), and 3.1 drinks per drinking day (SD=5.5). Crude mean measures of alcohol consumption use were all higher for women with high perceived stress at their index visit than for women with low perceived stress. Means (SD) stratified on high/low perceived stress were 7.0 (18.0)/3.8 (11.1) binge drinking days; 9.7 (20.5)/6.8 (15.5) drinking days; 1.1 (3.6)/0.5 (1.7) drinks per day; and 3.6 (6.1)/2.5 (4.5) drinks per drinking day. None of the outcomes were normally distributed.

A high PSS score (>14) was associated with an adjusted risk of binge drinking on any given day in the subsequent 3 to 6 months that was 1.47 (95% CI: 0.89, 2.43) times the risk of binge drinking among women with a low/normal PSS score. A high PSS score was associated with a relative risk of any drinking that was 1.30 (95% CI: 0.88, 1.92) times the risk of any drinking among women with a low/normal PSS score. The number of drinks per day reported by women with high PSS score 2.05 (95% CI: 0.96, 4.38) times the number of drinks per day reported by women with a low/normal PSS score. Finally, the number of drinks per drinking day reported by women with a high PSS score was 1.35 (95% CI: 1.04, 1.74) times the number of drinks per drinking day reported by women with a low/normal PSS score (table 2).

When we restricted the study sample to women who reported at least one drinking day in the 90 days prior to the index assessment (i.e., excluded non-drinkers), the association between high perceived stress and subsequent drinking appeared to be modified by drinking level at the index visit (moderate or heavy) (table 2). Among women drinking moderately at the index visit, high perceived stress was associated with subsequently reporting drinking less frequently, binge drinking less frequently, fewer drinks per day, and fewer drinks per drinking day compared with low perceived stress. Among women drinking heavily at the index visit, high perceived stress was associated with subsequently reporting drinking more frequently, binge drinking more frequently, more drinks per day, and more drinks per drinking day compared with low perceived stress. Differences in the association between perceived stress and subsequent alcohol use among women classified as moderate versus

heavy drinkers at the index visit were significant at $\alpha=0.2$ for all associations except any drinking.

Finally, when we looked at the relationship between alcohol use in the prior 90 days and subsequently reported perceived stress, we found no association between any alcohol consumption measure and subsequent perceived stress (table 3).

4.0 Discussion

In our sample of urban women receiving HIV care, we found high, pervasive and sustained levels of perceived stress that exceed norms established for the general population of women (Cohen and Williamson, 1998). These higher levels of perceived stress are consistent with a recent study examining perceived stress and HIV in a general population survey (Williams et al., 2016) and with the high frequency of stressful events among WLHIV reported in the literature (Tsai et al., 2015 and Whetten et al., 2008). Importantly, perceived stress was associated with increased subsequent alcohol use among women who reported heavy drinking at their index visit, and decreased subsequent alcohol use among women who reported moderate drinking at their index visit. In particular, perceived stress seemed to be most strongly associated with increased binge drinking, number of drinks per drinking day, and number of drinks per day among heavy drinkers. The inverse was true for moderate drinkers. Notably, there was no association between alcohol use in the prior 90 days and subsequent PSS score after adjusting for covariates likely to confound that association.

4.1 “Does stress increase drinking?”

Historically, stress has been cited as an etiological factor in the development of alcohol misuse and alcohol use disorder (AUD) on the assumption that alcohol reduces tension and dampens stress responses (Levenson et al., 1980 and Sher and Levenson, 1982). However, this literature has generally not taken into account baseline drinking behaviors as contributors to the consequences of stress exposure on subsequent drinking. Indeed, a large preclinical literature has shown that chronic stress applied to an animal who was not dependent on alcohol did not reliably induce an increase in alcohol consumption (Becker et al., 2011). In contrast, stress reliably increased alcohol consumption in alcohol dependent animals with histories of intermittent alcohol exposure and withdrawal (Koob, 2014). These findings suggest that cycles of alcohol intoxication and withdrawal are necessary to sensitize the brain so that stress exposure leads to subsequent increased drinking. This is consistent with the Koob model as well as the findings of the Integrative Neuroscience Initiative on Alcoholism (INIA) Stress Consortium (Becker et al., 2011) that chronic alcohol exposure induces durable allostatic changes in brain circuitry that are a prerequisite for stress-induced alcohol consumption. Corroborating the preclinical literature, a recent large review of directly-exposed survivors across 10 disasters found an overall AUD prevalence of 19%, but importantly only 0.3% of the sample developed a new AUD (North et al., 2011). Almost all AUDs in their sample were a continuation of, or relapse to, pre-trauma alcohol misuse. Collectively, these findings and ours underscore the potential effect of preexisting alcohol use patterns on stress-induced changes in alcohol consumption. Indeed, the inconsistent

findings in the literature on stress effects on alcohol use may partially stem from the frequent failure to consider moderation of stress effects by baseline drinking patterns.

4.2 Study Strengths

We were able to examine temporal, rather than cross-sectional associations, between alcohol use and perceived stress. While we are unable to make causal statements about the effect of alcohol consumption on perceived stress or the effect of perceived stress on alcohol consumption, these results do suggest that any link between the two variables is most likely to extend from stress to alcohol more strongly than from alcohol to stress. We used inverse probability weights to control for possible confounders, which allows us to report marginal estimates of association (risk ratios and rate ratios are not dependent on the other variables in the model) (Greenland et al., 1999). We used a well-validated, detailed measure of alcohol consumption (TLFB) to examine the effect of perceived stress on alcohol use patterns and our analyses retained the richness of these data. We also adjusted for illicit drug use, depression and anxiety, all of which could influence the stress-alcohol association. Finally, we believe our findings in heavy drinking women to be particularly robust because we detected increases in their alcohol use even though they were in an ongoing clinical trial that was effective in significantly reducing alcohol use (Chander et al., 2015).

4.3 Study Limitations

Our sample was urban WLHIV, predominantly African American and low-income, and thus our results may not apply to the general population of WLHIV or of women regardless of HIV-serostatus if the associations we observed vary by disease, race, socio-economic or urban status. Second, we did not measure type and severity of actual stress exposure. Finally, our sample was exclusively women; it would be of interest to learn whether a similar perceived stress-alcohol relationship would be observed in men. We encourage future studies to examine baseline drinking status as a moderator of the relationship between perceived stress and subsequent alcohol use.

4.4 Study Implications

Exposure to stress from compromised health, stigma associated with HIV infection, low socioeconomic status, minority status, and community and interpersonal violence are difficult to control. However, 'perceived stress' offers two potential therapeutic targets. One goal is to change the patient's perception of the frequency and magnitude of stressful episodes. Therapeutic interventions could include relaxation training, mindfulness, and other well-validated stress reduction strategies (Goyl et al., 2013 and Gu et al., 2015). A second goal is to improve coping skills to enable the patient to better manage response to stressful events. Common therapeutic approaches would include coping skills training and cognitive behavioral therapy including stress inoculation training (Cusack, 2016).

Our findings highlight that baseline drinking patterns modulate the relationship between perceived stress and future alcohol consumption, highlighting the importance of targeting treatment resources to the subset of women who engage in heavy drinking as a means of coping with their life stressors. This is especially important in women with HIV in whom it has been clearly established that heavy drinking negatively influences treatment adherence

and disease progression. Findings emphasize the importance of evaluating baseline drinking patterns in future studies examining stress/alcohol interactions.

Acknowledgments

None

Role of Funding Source

This research was supported by NIH R01 AA014500 (McCaul, PI), K23 AA015313 (Chander, PI), U01AA020890 (Wand/McCaul, co-PI) and U24 AA020801 (McCaul, PI). The sponsors had no role in: design, collection, analysis or interpretation of data; in the writing of the report; and in the decision to submit the article for publication.

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Highlights

- Women with the human immunodeficiency virus (HIV) have high levels of perceived stress
- Influence of stress on alcohol use depends on preexisting drinking patterns
- Alcohol use increases with stress only if women were already heavy/binge drinkers
- Alcohol use decreases with stress if women were already moderate drinkers
- Following stress exposure, treatment should target subset of heavy drinkers

Figure 1. Distribution of Perceived Stress Scale (PSS) scores at baseline for 338 HIV-infected women, overlaid with kernel density plot. Reference lines are provided for average perceived stress scores among women and among black respondents in a probability sample in the United States (Cohen and Williamson, 1988)

Table 1

Characteristics [Number (percent) or median (interquartile range)^a where noted] of 338 women enrolled in the study sample at baseline, over 661 6-month person-periods of follow-up

	Women	6-month person-periods		
	(at enrollment)	PSS 14	PSS >14	Total
N	338	281	380	661
Age, years ^a	47 (41, 52)	48 (42, 53)	46 (40, 51)	47 (41, 52)
Black race	290 (86)	246 (88)	320 (84)	566 (86)
HS education	184 (54)	179 (64)	181 (48)	360 (54)
Income (1,000 USD) ^a	8.0 (6.0, 9.2)	8.1 (7.2, 12.0)	7.7 (4.3, 8.3)	8.0 (6.0, 9.2)
Detectable viral load	152 (45)	99 (35)	180 (49)	287 (43)
Recent cocaine use ^b	70 (21)	35 (12)	97 (26)	132 (20)
Recent heroin use ^b	32 (9)	14 (5)	45 (12)	59 (9)
Depressed only (BDI)	20 (6)	3 (1)	32 (8)	35 (5)
Anxious only (BSI)	28 (8)	5 (2)	53 (14)	58 (9)
Depressed+anxious	29 (9)	0 (0)	44 (12)	44 (7)

* Values presented are N (%) unless otherwise noted.

^a Median (interquartile range)

^b Any use in the prior 3 months, based on Time-Line Follow-Back

Table 2

Crude and adjusted^a associations between high PSS score (>14) at baseline/6 months and alcohol use reported at 3–6/9–12 months, respectively, overall and stratified by report of moderate (>0 but ≤6 drinks/week) or heavy (>7 drinks/week) alcohol use at baseline excluding nondrinkers

Risk Ratios	Crude, Overall	Adjusted ^a , Overall	Moderate Drinkers ^a	Heavy Drinkers ^b	p-value for heterogeneity ^c
Binge drinking	1.83 (1.19, 2.80)	1.47 (0.89, 2.43)	0.57 (0.23, 1.42)	1.55 (0.71, 3.36)	0.05
Any drinking	1.43 (1.02, 2.01)	1.30 (0.88, 1.92)	0.85 (0.46, 1.57)	1.31 (0.65, 2.63)	0.22
Rate Ratios	Crude, Overall	Adjusted ^a , Overall	Moderate Drinkers ^a	Heavy Drinkers ^b	
Drinks/day	1.96 (1.20, 3.20)	2.05 (0.96, 4.38)	0.59 (0.19, 1.78)	3.96 (1.03, 15.21)	0.001
Drinks/drinking day	1.30 (1.05, 1.62)	1.35 (1.04, 1.74)	0.66 (0.42, 1.03)	1.82 (1.14, 2.90)	0.001

^a Adjusted for age, income<\$5000, high school education, cocaine use, heroin use, depression or anxiety, detectable viral load and randomization to hazardous alcohol reduction intervention.

^b There were not enough women who reported heroin use among women with low perceived stress for proper adjustment; Adjusted for age, income<\$5000, high school education, cocaine use, depression or anxiety, detectable viral load, and randomization to hazardous alcohol reduction intervention.

^c P-value for heterogeneity comparing associations among moderate and among heavy drinkers to one another

Table 3

Association between alcohol use in prior 90 days and subsequent high PSS score (>14) at 0/6/12 month assessments

	Crude Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI) ^a
Binge drinking (yes/no)	1.29 (0.91, 1.83)	0.96 (0.62, 1.47)
Any drinking (yes/no)	1.24 (0.91, 1.70)	0.97 (0.63, 1.50)
Per (7) drinks/days	1.01 (1.00, 1.02)	0.99 (0.93, 1.07)
Per drink/drinking day	1.04 (1.01, 1.07)	1.01 (0.97, 1.05)

^a Adjusted for age, income, high school education, cocaine use, heroin use, anxiety, depression, detectable viral load, and randomization to hazardous alcohol reduction intervention.