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The association between changes in alcohol use and changes in antiretroviral therapy adherence and viral suppression among women living with HIV

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Abstract

Heavy alcohol use has adverse effects in women with HIV. We examined the association between changes in alcohol use (measured with Timeline Followback) and changes in antiretroviral therapy adherence (medication possession ratio) and viral suppression (HIV RNA), measured over 6-month intervals. Among women who were 1) non-adherent or not virologically suppressed and 2) infrequent binge drinkers or non-heavy drinkers at baseline, increasing drinking was significantly associated with lower odds of subsequently improving adherence or viral suppression (OR of becoming adherent of 0.90 in infrequent binge drinkers; OR of becoming suppressed of 0.81 and 0.75 in infrequent binge drinkers and non-heavy drinkers, respectively). Our findings suggest that for these women, increasing drinking may be a barrier to achieving viral suppression. Addressing this barrier by integrating proactive alcohol counseling strategies into routine HIV care may be key to improving viral suppression rates among women retained in HIV care.

Keywords

HIV infection; women; antiretroviral medication adherence; viral load; alcohol

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BACKGROUND

Despite advances in the treatment of HIV, CDC data from 2011 indicate that less than half of women living with HIV in the United States are engaged in care and less than one-third have achieved viral suppression (1). Women with concomitant HIV infection and heavy alcohol use may be particularly vulnerable to worse HIV outcomes (2–8). Data from the Women’s Interagency HIV Study (WIHS) indicate that nearly half of women with HIV infection drink alcohol and between 12 and 24 percent drink 4 drinks/day or > 7 drinks/week (9). Heavy drinking has been associated with multiple harms, including increased burden of other HIV-associated chronic diseases (10), impaired response to antiretroviral therapy (ART) (11–13), decreased medication adherence (14–15), and increased mortality (16). The consequences of heavy drinking for women with HIV infection have significant implications for clinical care and highlight the need to better characterize the relationship between alcohol use, a modifiable risk factor, and ART adherence leading to viral suppression, the single most important mechanism for slowing the progression of HIV infection (17).

Multiple cross-sectional studies have documented a negative association between alcohol use and ART adherence (18–22). Patients who drink heavily are more likely to be non-adherent to ART than patients who do not drink (14–15, 18). Drinking quantity at each drinking episode is also an important predictor of adherence, perhaps more important than drinking frequency (14). Some researchers have found a dose-response relationship between alcohol exposure and medication adherence, putting even moderate drinkers at higher risk of non-adherence than non-drinkers (14, 19–20, 22–23).

Drinking behavior is dynamic and varies over a lifetime, but there are limited longitudinal studies that demonstrate the impact of changes in drinking behavior on changes in ART adherence. There are also few studies that focus on women with HIV, who may be particularly vulnerable to the effects of alcohol (6, 24–25) due to increased rates of psychiatric comorbidity, underdiagnosis of alcohol use disorder compared to men, and greater difficulty accessing substance abuse treatment for a variety of social, economic, and cultural reasons (25, 26).

In a 10-year study of alcohol use among women in the WIHS cohort, 85 percent of women with HIV infection remained non-drinkers or non-heavy drinkers, 3 percent remained heavy drinkers (> 7 drinks per week), and 12 percent changed their drinking trajectory. Eight percent of HIV-infected women increased from non-heavy drinking to heavy drinking, while four percent reduced their heavy drinking to non-heavy drinking (27). These changes in drinking behavior over time suggest that cross-sectional data may not be sufficient to truly capture the relationship between alcohol use and medication adherence. Lucas et al. examined the relationship between substance use, with illicit drug and alcohol use as a combined variable, and medication adherence in men and women over a 30-month period and found that 64 percent of participants who were using heroin, cocaine, or alcohol changed their substance use status at least once. These changes were associated with clinically relevant outcomes with respect to improved adherence, viral load suppression, and increased CD4 count in participants who became non-users (28), thus underscoring the importance of understanding changing patterns of alcohol use in HIV-infected women and

developing interventions that may reduce alcohol use and ultimately improve HIV-associated health outcomes.

This study aims to build upon the existing literature by describing the relationship between changes in alcohol use and ART adherence and viral suppression over 6-month intervals in a clinic-based sample of adult women living with HIV, using longitudinal rather than cross-sectional data. We hypothesized that increased alcohol consumption would be associated with decreased ART adherence and viral suppression.

METHODS

Study Design & Subjects

We performed a secondary analysis of data collected in a randomized control trial (RCT) designed to test the effectiveness of a brief alcohol intervention delivered at an HIV clinic for HIV-infected women who engage in heavy drinking (29). The brief intervention consisted of two 20 minute face-to-face counseling sessions followed by a 5–10 minute booster phone call. In addition to recruiting women for the RCT, we concurrently enrolled women from the same clinic into an observational cohort of women with HIV who did not have heavy drinking behavior at the baseline visit. This combined group of women was included in this analysis. Women were eligible to participate in the study if they had HIV infection, were receiving outpatient care at the Johns Hopkins HIV Clinic, were 18 years of age or older, were not receiving treatment for alcohol use disorder, and were not actively psychotic (29). Women were enrolled between March 2006 and September 2010. Participants were recruited through several methods: clinic flyers advertising a health study, provider referral, waiting room recruitment, and review of drinking data obtained from an audio computer-assisted self-interview (ACASI) routinely administered to Johns Hopkins HIV Clinic patients at six month intervals.

The women in the RCT self-reported at-risk drinking behavior (defined as ≥ 8 drinks/week or ≥ 2 binge drinking episodes, defined as ≥ 4 drinks/occasion) in the past 6 months, or TWEAK score (five-item scale developed originally to screen for risk drinking during pregnancy) ≥ 2 (29). Participants had assessments at study entry (0 months), 3 months, 6 months, and 12 months. Women in the observational cohort were interviewed at 0 months, 6 months, and 12 months. For this purpose of this analysis, we used data from the 0 month, 6 month, and 12 month assessments.

A total of 388 women were recruited into the two groups. To be included in this analysis, participants had to have at least two serial study visits and fill their prescriptions at the Johns Hopkins HIV Clinic Pharmacy. We excluded 25 women who presented for one visit only, 67 participants who did not use the Johns Hopkins HIV Clinic pharmacy, and 62 women who did not have both medication adherence and viral load data available at study visits. The final sample size was 234 women; 186 women participated in all three study visits and were included in the assessments of change between the baseline and 6 month visits, as well as between the 6 month and 12 month visits, and 48 women participated in two study visits and were included in one assessment of change between either the baseline and 6 month visits or the 6 month and 12 month visits. There were no significant differences in age, race, CD4 cell

count at baseline, or heavy versus non heavy drinking status in those excluded (N=154) compared to those included (N=234). There was a significant difference in baseline viral suppression, with women excluded less likely to be suppressed than those included (52% suppressed among those excluded compared to 78% suppressed among those included). One of our inclusion criteria was having pharmacy fill data from the Johns Hopkins HIV Clinic to calculate a medication possession ratio (MPR). The difference in the proportion suppressed between those included and those excluded likely reflects that fewer of the excluded women were using ART. The excluded women who were suppressed were likely using an outside pharmacy.

Independent Variable: Alcohol Use

Alcohol consumption was measured using the 90-day Timeline Followback (TLFB) assessment. The TLFB has been shown to be more reliable than other self-report alcohol use assessment tools and is particularly useful for capturing nuanced information about drinking behaviors (30). The TLFB is a granular measure of drinking, capturing alcohol use over a period of calendar time by querying about daily drinking. TLFB data were summarized into number of drinking days in the 90 days preceding each study visit, number of standard drinks per drinking day, and number of binge drinking days in the 90 days preceding each study visit. Binge drinking was defined as 4 drinks consumed in one day.

Outcome Variables: Antiretroviral Medication Adherence and HIV RNA

The outcome variables were ART adherence, defined as an MPR ≥ 0.8 , and viral suppression, defined as HIV RNA < 400 copies/mL. The MPR reflects the proportion of days in the 180 day period between assessments that a participant had medication in their possession ($\text{MPR} = \text{number of days patient had medication in their possession} / 180 \text{ days}$). We chose to use the MPR as the measure of medication adherence rather than self-reported adherence data, which was also collected as part of the study interviews, because it covered a larger time interval (6 months compared to the 2 week adherence data collected in the study) and because the MPR provides an objective measure of medication adherence. While the MPR has limitations, namely refill compliance may not be congruent with medication compliance, it has been validated as a meaningful proxy for medication adherence in patients with chronic disease (31, 32). MPR data were derived from the Johns Hopkins HIV Clinic Pharmacy refill records and were calculated based on refill data for the backbone drug in each participant's ART regimen: either a protease inhibitor (PI), a non-nucleoside reverse transcriptase inhibitor (NNRTI), or an integrase strand transfer inhibitor (INSTI). HIV RNA was drawn at each study visit. The cutoff of < 400 copies/mL for viral suppression was chosen because that was the lower limit of detection for the assay in a portion of the viral load assessments.

Additional covariates of interest

Additional covariates of interest included age, self-reported race, education, and income. Anxiety and depressive symptoms were captured at each interview with the Hospital Anxiety and Depression Scale (33) and were adjusted for in the analysis because they have been shown to influence both alcohol consumption and ART adherence. Drug use (cocaine,

heroin, and marijuana) were assessed at each interview with the Risk Assessment Battery (34). CD4 count was assessed with a lab draw at each visit.

Analysis

We used the reported number of standard drinks per drinking day and the reported number of drinking days in the past 90 days to calculate the average number of drinks consumed per week at each assessment. Women with an average of >7 drinks/week were categorized as heavy drinkers. Women with ≥ 3 binge drinking episodes in the 90-day interval were classified as frequent binge drinkers. The definitions of heavy drinking and binge drinking were based on the National Institute on Alcohol Abuse and Alcoholism (NIAAA) guidelines (35). We stratified on heavy versus non-heavy drinking at the initial visit (baseline or 6 months) and modeled a unit change in the average number of drinks per week from the initial to subsequent visit (6 months or 12 months, respectively). In an alternate model, we stratified on frequent versus non-frequent binge drinking at the initial visit and modeled a unit change in the number of binge drinking episodes from the initial to subsequent visit. Baseline characteristics were compared using t-test (baseline age) or chi square testing for categorical variables.

To measure the association between changes in alcohol use and ART adherence, we performed logistic regression analysis. To improve interpretation of our results, in models for the probability of being adherent, we stratified by adherence at the initial visit and in models for the probability of achieving viral suppression, we stratified by viral suppression at the initial visit. We further stratified models by heavy drinking at the initial visit when the independent variable of interest was change in drinks per week. We stratified models by frequent binge drinking at the initial visit when the independent variable of interest was change in number of binge days over the prior 90 days. This second level of stratification was used because we believed that the effect of changes in alcohol use might be modified by baseline alcohol use.

We used logistic regression (model form) which was fit using generalized estimating equations rather than maximum likelihood estimation to account for repeated measures (36). Two different sets of regression models were used to look at adherence and viral suppression as outcomes. We adjusted all multivariable models a priori for the following covariates: age, depressive symptoms, and cocaine use. We adjusted for cocaine use since this has consistently been shown to be associated with worse medication adherence, compared with marijuana and heroin, which have not been consistently associated and were not statistically significantly associated with the outcomes in our models. We also included covariates in the multivariable models if the p-value for their univariate association with the outcome was < 0.10.

RESULTS

Sample characteristics

Characteristics of the study population (n = 234 women) are presented in Table 1 stratified by heavy drinking classification at initial assessment. The women included in the analysis

were predominantly African-American, with education level < 12th grade. Women who were heavy drinkers were more likely to report lower annual income, more symptoms of anxiety, and substance use, including heroin, cocaine, and marijuana use, compared to women who were non-heavy drinkers at baseline.

Drinking Behavior

The dataset included 420 intervals during which change in drinking, change in adherence, and change in viral suppression were measured (these intervals include both the 0 to 6 month time period and the 6 to 12 month time period). Heavy drinking was documented at the initial assessment (0 or 6 month assessment) 19% of the time and frequent binge drinking was documented in the initial assessment (0 or 6 month assessment) 26% of the time. Drinking increased in 18% of the intervals in which heavy drinking was initially reported, with a median increase of 14.2 drinks/week (IQR: 5.6, 28.2). Binge drinking increased in 23% of the intervals in which frequent binge drinking was initially reported (median increase = 7 binge episodes, IQR: 4.9, 13.1).

Drinking decreased in 83% of the intervals in which heavy drinking was initially reported (median decrease = -11.6 drinks/week, IQR: -24.4, -5.9) and binge drinking decreased in 74% of the intervals in which frequent binge drinking was initially reported (median decrease = -10.7 binge episodes, IQR: -24, -5). Twenty-five percent of women who were non-heavy drinkers increased their average weekly alcohol consumption (median change 1.0 drink/week; IQR: 0.3, 3.7), and 16% of women who were non-frequent binge drinkers increased their frequency of binge drinking days (median change 2 binge days, IQR: 1, 9).

Changes in alcohol use and association with ART adherence and viral suppression

Women were adherent to ART at 241 of 420 of the initial visits in each interval (57%) and had a suppressed HIV RNA at 336 of 420 (80%) of the initial visits. As shown in Table 2A, among women who were adherent with their medications and frequent binge drinkers at the initial visit, each additional binge drinking day was associated with a 2 percent increase in the odds of becoming non-adherent (OR = 1.02, 95% CI: 1.00, 1.05). There were no statistically significant increases in the odds of becoming unsuppressed or non-adherent among women who were suppressed and frequent binge drinkers, adherent and heavy drinkers, or suppressed and heavy drinkers (OR of 1.01, 1.01, and 0.99, respectively). As shown in Table 2B, among women who were adherent or suppressed at baseline, and were infrequent binge drinkers, the association between an additional binge drinking day and becoming non-adherent or unsuppressed was not statistically significant (OR of 0.65 and 0.94, respectively). Among women who were adherent or suppressed and non-heavy drinkers, increasing drinking by an average of 1 drink per week was associated with increased odds of becoming non-adherent or unsuppressed (OR = 1.05, 95% CI 1.01, 1.08 and OR = 1.03, 95% CI 1.00, 1.07, respectively).

Women were non-adherent to ART at 179 of 420 initial visits (43%) and were unsuppressed at 84 of 420 (20%) of initial visits. As shown in Table 3A, among women who were non-adherent with their medications and frequent binge drinkers at baseline, there was no statistically significant decrease in the odds of becoming adherent with increased drinking

(OR = 1.02, 95% CI 0.99, 1.06). There were no statistically significant decreases in the odds of becoming suppressed or adherent among women who were unsuppressed and frequent binge drinkers, non-adherent and heavy drinkers, and unsuppressed and heavy drinkers (OR = 1.00, 0.99, and 1.00 respectively).

As shown in Table 3B, the pattern was different among the women who were non-adherent or unsuppressed and infrequent binge drinkers or non-heavy drinkers. Among women who were non-adherent and infrequent binge drinkers initially, each additional binge drinking day was significantly associated with decreased odds of becoming adherent (OR = 0.90, 95% CI: 0.82, 0.99). Among women who were unsuppressed and infrequent binge drinkers, each additional binge drinking day was associated with decreased odds of becoming suppressed (OR = 0.81, 95% CI: 0.67, 0.98). Among women who were non-adherent and non-heavy drinkers, there no statistically significant change in odds of becoming adherent with increased drinking. However, among women who were detectable and non-heavy drinkers, an increase in drinking was significantly associated with decreased odds of becoming suppressed (OR = 0.75, 95% CI 0.59, 0.95). No woman who increased her drinking to the point where she changed drinking category (non-heavy to heavy or non-frequent binge to frequent binge) moved from unsuppressed to suppressed.

DISCUSSION

In this study of women living with HIV, women who were non-heavy drinkers at baseline, with either low adherence or unsuppressed viral load, were less likely to become adherent or suppress their viral load over time if they increased their drinking. However, an increase in alcohol use was not associated with poorer outcomes among all groups of women. In fact, women who were heavy or binge drinkers at baseline, with poor adherence or unsuppressed viral load who increased their alcohol use were neither more nor less likely to become adherent or suppressed. Our results suggest that increasing drinking has a more deleterious effect on women who are initially non-heavy drinkers. Our findings have implications for the treatment of women living with HIV engaged in care. In an era where the majority of individuals on ART, in care, achieve viral suppression (37), alcohol remains a barrier to achieving suppression among those with suboptimal HIV control.

We expected that more drinking would consistently lead to worse adherence and viral suppression, as prior studies have found a dose-response relationship between alcohol use and medication adherence (14, 19–20, 22–23). For example, Tucker et. al (19) showed that compared to non-drinkers, moderate, heavy, and frequent heavy drinkers (self-reported alcohol use in the 4 weeks prior to the study interview) had increased odds of being non-adherent (self-report) in the week prior to the study interview. The odds of non-adherence increased as drinking increased. Another study at our institution showed that compared to no drinking, hazardous alcohol use was associated with worse medication adherence in the two weeks prior to assessment (21). Our analysis differs from prior studies as it has both a longer assessment of adherence based on objective measures rather than self-report and more fine-tuned measures of changes in alcohol use, which enhanced our ability to detect the effect of increases in alcohol use in those who are heavy drinkers at baseline.

One reason for the difference between our results and prior studies may be the longitudinal nature of our evaluation, which sought to understand the association between changes in alcohol use and changes in medication adherence and viral suppression over time. Women who engage in heavy or binge drinking at baseline and manage to maintain medication adherence may have developed an organizational strategy that allows them to better cope with increased drinking without a negative impact on self-care activities.

However, our findings among women without heavy or binge drinking may indicate that these women are more sensitive to the effects of alcohol and forget to take their medications or be more worried about potential drug-alcohol interactions when they increase alcohol use. Additionally, it is likely that in women with newly occurring heavy or binge drinking, alcohol may be a proxy for worsening psychiatric or social co-morbidities, such as depression, financial insecurity, or unstable housing, which have all been shown to influence ART adherence (2, 6–7, 38), and ultimately viral suppression.

Another interesting finding in our study was that fewer women were adherent (adherence noted at 57% of the initial visits in each interval) compared to being suppressed (suppression noted at 80% of the initial visits). This may reflect the increased potency of current antiretroviral therapy, allowing for suppression to be maintained despite less-than-perfect adherence (39). It may also reflect that our adherence measure covered a 6-month interval while the viral suppression measure was based only on the viral load value at the study visit.

This study is notable for focusing exclusively on women living with HIV, who are an especially medically and socially vulnerable, but often understudied, population. Women living with HIV are significantly less likely to use HIV primary care services than male patients (8) and are more likely to have psychiatric and social co-morbidities, such as PTSD and intimate partner violence, than women who do not have HIV infection (2). This leaves women living with HIV at high risk for at-risk alcohol use, medication non-adherence, and ultimately progression of disease. Indeed, the relationship between alcohol use and medication adherence and viral suppression demonstrates the very real clinical impact of changes in drinking behavior over time and highlights the importance of integrating proactive counseling strategies into routine HIV care. These strategies should be inclusive of women who do not have a history of heavy or binge drinking.

Implementing alcohol screenings and brief interventions in a primary care setting has been shown to reduce alcohol use in women with hazardous drinking (40,41) and in women with co-occurring alcohol abuse and HIV-infection, namely the RCT from which our study data were derived (29). There has been less emphasis, however, on counseling strategies that may prevent the development of alcohol use disorders all together. The results of this study indicate that it may be beneficial to develop brief preventive intervention strategies that target HIV-infected women without ongoing heavy or binge drinking as they may be particularly sensitive to the negative effects of increased alcohol use.

This study has several limitations. We relied on self-report data for alcohol use, which may be subject to various biases. The TLFB method has been shown to be more reliable than other self-reported methods; however, participants likely underestimated their drinking

behaviors (42). We did not measure phosphatidylethanol (PEth), (43,44), an alcohol biomarker, which forms when a phospholipase enzyme acts in the presence of alcohol, which could potentially provide more accurate information regarding quantity of drinking. It is also difficult to compare our results to other studies due to variable definitions of heavy alcohol use and binge drinking in the literature.

While the MPR has been validated as a measure of medication adherence in chronic disease, it has several limitations. Filling a prescription at the pharmacy does not guarantee that the medications were taken correctly or taken at all. Using the MPR may introduce selection bias by including a more adherent sample as women without pharmacy data were excluded from the study. Additionally, it is not known whether women who chose to use a pharmacy other than the Johns Hopkins HIV Clinic Pharmacy may be more or less likely to be adherent due to factors such as convenience, institutional communication, or differing co-pays. We defined adherence as an MPR of ≥ 0.8 , which has been validated in the literature on chronic disease (32), but the optimal cut off for antiretroviral medications is less clear. Early antiretroviral medications required adherence of > 95 percent to achieve viral suppression (45), while newer antiretroviral medications are more forgiving (46). We chose to use MPR data in our analysis, rather than self-reported adherence data, which was collected as part of the study interviews, because it covered a larger time interval (6 months compared to the 2 week data collected in the study).

This study aimed to understand the impact of changes in drinking behavior on medication adherence and viral suppression, but it is difficult to determine what constitutes a meaningful change in drinking behavior. Our definitions of a clinically significant change in drinking behavior were ultimately arbitrary and may not have been sensitive enough to capture the full impact. Finally, while we did account for many social and psychiatric variables. Future studies would ideally gather even more detailed information about covariates that are known to influence both alcohol use and antiretroviral adherence, such as housing stability, detailed mental health information, and long-term history of substance abuse (47).

The intervention may have affected behaviors other than alcohol use (such as drug use) that influenced medication adherence that we could not account for in this analysis. Finally, the intervention may have affected ART adherence directly because the intervention included discussions of both general health topics and alcohol's effect on medication adherence, which may have influenced health behavior. There was no effect of the intervention on medication adherence detected in the analysis of the RCT data (29), however, the main trial was not fully powered to detect change in adherence. Another potential limitation is that at the time the study was conducted, viral suppression was defined as HIV RNA < 400 copies/mL, which was the lower limit of detection of the assay at that time. The less stringent prior definition of viral suppression (compared with the current definition of < 50 copies/mL) may have allowed women to appear suppressed with lower adherence.

We expected to find a uniformly inverse relationship between alcohol use and medication adherence, as well as viral suppression, but our results tell a more nuanced story. Women without a recent history of high-risk alcohol use may be most vulnerable to the negative

impacts of increased drinking on antiretroviral adherence and viral suppression. These results call for further longitudinal research that examines the relationship between alcohol use and HIV-related health behaviors and outcomes, as well as research that explores the causes of increased alcohol use among women living with HIV and effective prevention strategies. In the meantime, the implications for clinical practice are clear: while clinicians tend to focus alcohol counseling on patients with ongoing hazardous alcohol use, it is important to consider preventive counseling with patients who do not yet have heavy alcohol use as they may be vulnerable to the negative effects of increased drinking.

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References

1. CDC. HIV Among Women. Available at: <http://www.cdc.gov/hiv/group/gender/women/>. Accessed: January 11, 2016
2. Fagbami O, Oluwasanjo A, Fitzpatrick C, Fairchild R, Shin A, Donato A. Factors supporting and inhibiting adherence to HIV medication regimen in women: a qualitative analysis of patient interviews. *Open AIDS J*. 2015; 9:45–50. [PubMed: 26157537]
3. Cohen MH, Cook JA, Grey D, et al. Medically eligible women who do not use HAART: the importance of abuse, drug use, and race. *Am J Public Health*. 2004; 94(7):1147–51. [PubMed: 15226135]
4. Turner BJ, Laine C, Cosler L, Hauck WW. Relationship of gender, depression, and health care delivery with antiretroviral adherence in HIV-infected drug users. *J Gen Intern Med*. 2003; 18(4): 248–57. [PubMed: 12709091]
5. Murphy DA, Greenwell L, Hoffman D. Factors associated with antiretroviral adherence among HIV-infected women with children. *Women Health*. 2002; 36(1):97–111. [PubMed: 12215006]
6. Berg KM, Demas PA, Howard AA, Schoenbaum EE, Gourevitch MN, Arnsten JH. Gender differences in factors associated with adherence to antiretroviral therapy. *J Gen Intern Med*. 2004; 19(11):1111–7. [PubMed: 15566440]
7. Lazo M, Gange SJ, Wilson TE, et al. Patterns and predictors of changes in adherence to highly active antiretroviral therapy: longitudinal study of men and women. *Clin Infect Dis*. 2007; 45(10): 1377–85. [PubMed: 17968839]
8. Sohler NL, Coleman SM, Cabral H, Naar-King S, Tobias C, Cunningham CO. Does self-report data on HIV primary care utilization agree with medical record data for socially marginalized populations in the United States? *AIDS Patient Care STDS*. 2009; 23(10):837–43. [PubMed: 19803677]
9. Cook RL, Zhu F, Belnap BH, et al. Longitudinal trends in hazardous alcohol consumption among women with human immunodeficiency virus infection, 1995–2006. *Am J Epidemiol*. 2009; 169(8): 1025–32. [PubMed: 19270052]
10. Justice A, Sullivan L, Fiellin D, Veterans Aging Cohort Study Project Team. HIV/AIDS, comorbidity, and alcohol: can we make a difference? *Alcohol Res Health*. 2010; 33(3):258. [PubMed: 23584067]
11. Miguez MJ, Shor-Posner GA, Morales G, Rodriguez A, Burbano X. HIV treatment in drug abusers: impact of alcohol use. *Addict Biol*. 2003; 8(1):33–7. [PubMed: 12745413]
12. Samet JH, Horton NJ, Traphagen ET, Lyon SM, Freedberg KA. Alcohol consumption and HIV disease progression: are they related? *Alcohol Clin Exp Res*. 2003; 27(5):862–7. [PubMed: 12766632]
13. Samet JH, Cheng DM, Libman H, Nunes DP, Alperen JK, Saitz R. Alcohol consumption and HIV disease progression. *J Acquir Immun Defic Syndr*. 2007; 46(2):194–99.

14. Hendershot CS, Stoner SA, Pantalone DW, Simoni JM. Alcohol use and antiretroviral adherence: review and meta-analysis. *J Acquir Immune Defic Syndr*. 2009; 52(2):180–202. [PubMed: 19668086]
15. Azar MM, Springer SA, Meyer JP, Altice FL. A systematic review of the impact of alcohol use disorders on HIV treatment outcomes, adherence to antiretroviral therapy and health care utilization. *Drug Alcohol Depend*. 2010; 112(3):178–93. [PubMed: 20705402]
16. Neblett RC, Hutton HE, Lau B, McCaul ME, Moore RD, Chander G. Alcohol consumption among HIV-infected women: impact on time to antiretroviral therapy and survival. *J Womens Health*. 2011; 20(2):279–86.
17. Grossman H. AIDS at 25: a quarter century of medical miracles. *MedGenMed*. 2006; 8(2):57.
18. Cook RL, Sereika SM, Hunt SC, Woodward WC, Erlen JA, Conigliaro J. Problem drinking and medication adherence among persons with HIV infection. *J Gen Intern Med*. 2001; 16(2):83–8. [PubMed: 11251758]
19. Tucker JS, Burnam MA, Sherbourne CD, Kung FY, Gifford AL. Substance use and mental health correlates of nonadherence to antiretroviral medications in a sample of patients with human immunodeficiency virus infection. *Am J Med*. 2003; 114(7):573–80. [PubMed: 12753881]
20. Samet JH, Horton NJ, Meli S, Freedberg KA, Palepu A. Alcohol consumption and antiretroviral adherence among HIV-infected persons with alcohol problems. *Alcohol Clin Exp Res*. 2004; 28(4):572–7. [PubMed: 15100608]
21. Chander G, Lau B, Moore RD. Hazardous alcohol use: a risk factor for non-adherence and lack of suppression in HIV infection. *J Acquir Immune Defic Syndr*. 2006; 43(4):411–7. [PubMed: 17099312]
22. Braithwaite RS, McGinnis KA, Conigliaro J, et al. A temporal and dose-response association between alcohol consumption and medication adherence among veterans in care. *Alcohol Clin Exp Res*. 2005; 29(7):1190–7. [PubMed: 16046874]
23. Braithwaite RS, Conigliaro J, McGinnis KA, Maisto SA, Bryant K, Justice AC. Adjusting alcohol quantity for mean consumption and intoxication threshold improves prediction of nonadherence in HIV patients and HIV-negative controls. *Alcohol Clin Exp Res*. 2008; 32(9):1645–51. [PubMed: 18616666]
24. Schmidt L, Weisner C. The emergence of problem-drinking women as a special population in need of treatment. *Recent Dev Alcohol*. 1995; 12:309–34. [PubMed: 7624551]
25. Ashley OS, Marsden ME, Brady TM. Effectiveness of substance abuse treatment programming for women: a review. *Am J Drug Alcohol Abuse*. 2003; 29(1):19–53. [PubMed: 12731680]
26. Greenfield SF, Pettinati HM, O'Malley S, Randall PK, Randall CL. Gender differences in alcohol treatment: an analysis of outcome from the COMBINE study. *Alcohol Clin Exp Res*. 2010; 34(10):1803–12. [PubMed: 20645934]
27. Cook RL, Zhu F, Belnap BH, et al. Alcohol consumption trajectory patterns in adult women with HIV infection. *AIDS Behav*. 2013; 17(5):1705–12. [PubMed: 22836592]
28. Lucas GM, Gebo KA, Chaisson RE, Moore RD. Longitudinal assessment of the effects of drug and alcohol abuse on HIV-1 treatment outcomes in an urban clinic. *AIDS*. 2002; 16(5):767–74. [PubMed: 11964533]
29. Chander G, Hutton HE, Lau B, Xu X, McCaul ME. Brief intervention decreases drinking frequency in HIV-infected, heavy drinking women: results of a randomized controlled trial. *J Acquir Immune Defic Syndr*. 2015; 70(2):137–45. [PubMed: 25967270]
30. Sobell, LC., Sobell, MB. Timeline follow-back: a technique for assessing self-reported alcohol consumption. In: Litten, RZ., Allen, JP., editors. *Measuring Alcohol Consumption: Psychosocial and Biochemical Methods*. New York, NY: The Humana Press; 1992.
31. Steiner JF, Koepsell TD, Fihn SD, Inui TS. A general method of compliance assessment using centralized pharmacy records: description and validation. *Med care*. 1988; 26:814–23. [PubMed: 3398608]
32. Karve S, Cleves MA, Helm M, Hudson TJ, West DS, Martin BC. Good and poor adherence: optimal cut-point for adherence measures using administrative claims data. *Curr Med Res Opin*. 2009; 25(9):2303–10. [PubMed: 19635045]

33. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand*. 1983; 67(6):361–70. [PubMed: 6880820]
34. Metzger, DS., Nalvaline, HA., Woody, GE. Assessment of substance abuse: HIV risk assessment battery (RAB). In: Carson-DeWitt, R., Macmillan-Thomas, G., editors. *Encyclopedia of Drugs, Alcohol and Addictive Behavior*. New York, NY: Macmillan Reference; 2001.
35. National Institute of Alcohol Abuse and Alcoholism. Helping Patients Who Drink Too Much: A Clinician's Guide. Available at: <http://pubs.niaaa.nih.gov/publications/Practitioner/CliniciansGuide2005/guide.pdf>. January 20, 2016
36. Hanley JA, Negassa A, deB Edwardes MD, Forrester J. Statistical Analysis of Correlated Data Using Generalized Estimating Equations: An Orientation. *Am J Epidemiol*. 2003; 157(4):364–375. [PubMed: 12578807]
37. Moore RD, Bartlett JG. Dramatic Decline in the HIV-1 RNA Level Over Calendar Time in a Large Urban HIV Practice. *Clin Infect Dis*. 2011; 53(6):600–604. [PubMed: 21844006]
38. Noto T, Vecchiet J, Monforte HD, Wu AW. Correlates and predictors of adherence to highly active antiretroviral therapy: overview of published literature. *J Acquir Immune Defic Syndr*. 2002; 31(Suppl 3):S123–7. [PubMed: 12562034]
39. Gordon LL, Gharibian D, Chong K, Chun H. Comparison of HIV Virologic Failure Rates Between Patients with Variable Adherence to Three Antiretroviral Regimen Types. *AIDS Patient Care STDs*. 2015; 29(7):384–388. [PubMed: 26114665]
40. O'Donnell A, Anderson P, Newbury-Birch D, et al. The impact of brief alcohol interventions in primary healthcare: a systematic review of reviews. *Alcohol Alcohol*. 2014; 49(1):66–78. [PubMed: 24232177]
41. Manwell LB, Fleming MF, Mundt MP, Stauffacher EA, Barry KL. Treatment of problem alcohol use in women of childbearing age: results of a brief intervention trial. *Alcohol Clin Exp Res*. 2000; 24(10):1517–24. [PubMed: 11045860]
42. Searles JS, Helzer JE, Rose GL, Badger GJ. Concurrent and retrospective reports of alcohol consumption across 30, 90 and 366 days: interactive voice response compared with the timeline follow back. *J Stud Alcohol*. 2002; 63(3):352–62. [PubMed: 12086136]
43. Bajunirwe F, Haberer JE, Boum Y II, et al. Comparison of self-reported alcohol consumption to phosphatidylethanol measurement among HIV-infected patients initiating antiretroviral treatment in southwestern Uganda. *PloS One*. 2014; 9:e113152. [PubMed: 25436894]
44. Hahn JA, Dobkin LM, Mayanja B, et al. Phosphatidylethanol (PEth) as a Biomarker of Alcohol Consumption in HIV-Positive Patients in Sub-Saharan Africa. *Alcohol Clin Exp Res*. 2012; 36:854–62. [PubMed: 22150449]
45. Paterson DL, Swindells S, Mohr J, et al. Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. *Ann Intern Med*. 2000; 133(1):21–30. [PubMed: 10877736]
46. Bangsberg DR. Less than 95% adherence to nonnucleoside reverse-transcriptase inhibitor therapy can lead to viral suppression. *Clin Infect Dis*. 2006; 43(7):939–41. [PubMed: 16941380]
47. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services; Available at: <http://aidsinfo.nih.gov/contentfiles/lvguidelines/AdultandAdolescentGL.pdf>. Section K. Accessed February 5, 2016

Table 1

Demographic and clinical characteristics of the study sample (n= 234 women)

	Non-heavy Drinker* (N= 181)	Heavy Drinker (N=53)
	Mean or %	Mean or %
Age	46.7	46.6
Race		
African American	89	85
White	9	13
Hispanic	1	0
Other	0	2
Annual Income		
<\$10,000	76	89 **
>\$10,000	24	11
Education Level		
12 grade	81	85
>12 grade	19	15
Baseline CD4 count		
500	45	28
201–499	39	51
200	16	21
Depression		
Not depressed	80	77
Depressed	20	23
Anxiety		
Not anxious	71	53 **
Anxious	28	47
Missing	1	–
Heroin		
No	92	81 **
Yes	8	19
Cocaine		
No	85	51 **
Yes	15	49
Marijuana		
No	79	60 **
Yes	21	37
Initial adherence category		
Nonadherent	489	62

	Non-heavy Drinker* (N= 181)	Heavy Drinker (N=53)
	Mean or %	Mean or %
Adherent	51	38
Initial viral load category		
Unsuppressed	21	23
Suppressed	79	77
Average drinks per week, median	0 drinks/week	21.2 drinks/week
Change in average drinks per week, median	0 drinks/week	-10.1 drinks/week

* Heavy drinker: > average of 7 drinks/week; Non-heavy drinker: average of 7 drinks/week

** p value comparing non-heavy drinkers to heavy drinkers = 0.05 (income category) or <0.05 (all other variables)

Table 2

Association between drinking and becoming nonadherent/unsuppressed (baseline status adherent/suppressed)

A. Hazardous Alcohol Use		
Baseline Status (N observations)	Exposure	Odds Ratio
Adherent, Frequent Binge (54)*	Change in binge drinking (one binge day in 90 day period)	1.02 (1.00, 1.05)
Suppressed, Frequent Binge (81)		1.01 (0.98, 1.05)
Adherent, Heavy Drinker (37)**	Change in drinking (average of 1 drink per week in 90 day period)	1.01 (0.99, 1.02)
Suppressed, Heavy Drinker (58)		0.99 (0.97, 1.01)

B. Non Hazardous Alcohol Use		
Baseline Status (N observations)	Exposure	Odds Ratio
Adherent, Infrequent Binge (183) *	Change in binge drinking (one binge day in 90 day period)	0.65 (0.35, 1.23)
Suppressed, Infrequent Binge (250)		0.94 (0.75, 1.18)
Adherent, Non-heavy Drinker (200) **	Change in drinking (average of 1 drink per week in 90 day period)	1.05 (1.01, 1.08)
Suppressed, Non-heavy Drinker (273)		1.03 (1.00, 1.07)

Table 3

Association between drinking and becoming adherent/suppressed (baseline status nonadherent/unsuppressed)

A. Hazardous Alcohol Use		
Baseline Status (N observations)	Exposure	Odds Ratio
Nonadherent, Frequent Binge (56) *	Change in binge drinking (one binge day in 90 day period)	1.02 (0.99, 1.06)
Unsuppressed, Frequent Binge (29)		1.00 (0.96, 1.04)
Nonadherent, Heavy Drinker (41) **	Change in drinking (average of 1 drink per week in 90 day period)	0.99 (0.98, 1.01)
Unsuppressed, Heavy Drinker (20)		1.00 (0.98, 1.02)

B. Non Hazardous Alcohol Use		
Baseline Status (N observations)	Exposure	Odds Ratio
Nonadherent, Infrequent Binge, (122) *	Change in binge drinking (one binge day in 90 day period)	0.90 (0.82, 0.99)
Unsuppressed, Infrequent Binge (55)		0.81 (0.67, 0.98)
Nonadherent, Non-heavy Drinker (137) **	Change in drinking (average of 1 drink per week in 90 day period)	0.94 (0.87, 1.01)
Unsuppressed, Non-heavy Drinker (64)		0.75 (0.59, 0.95)

* Infrequent binge: < 3 binge days over 90 day period; Frequent binge = 3 binge days

** Non-heavy drinker: average of 7 drinks/week; Heavy drinker: > average of 7 drinks/week