



Published in final edited form as:

J Acquir Immune Defic Syndr. 2006 December 1; 43(4): 411–417. doi:10.1097/01.qai.0000243121.44659.a4.

Hazardous Alcohol Use: A Risk Factor for Non-Adherence and Lack of Suppression in HIV Infection

Geetanjali Chander, MD, MPH, Bryan Lau, PhD, MHS, ScM, and Richard D. Moore, MD, MHS
Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD

Abstract

Objective—We examined the independent effect of alcohol and combined effects of drug and alcohol use on antiretroviral (ART) utilization, adherence, and viral suppression in an urban cohort of HIV-infected individuals.

Methods—In an observational clinical cohort, alcohol use, active drug use, and adherence were prospectively assessed at 6-month intervals. We classified hazardous alcohol use as >7 drinks/week or >3 drinks/occasion in women, and >14 drinks/week or >4 drinks/occasion in men and active drug use as any use in the previous 6 months. Our outcomes included ART utilization, 2-week adherence, and viral suppression. We used generalized estimating equations to analyze the association between independent variables and outcomes. Analyses were adjusted for age, sex, race, years on ART, and clinic enrollment time.

Results—Between 1998 and 2003, 1711 individuals participated in 5028 interviews. 1433 of these individuals received ART accounting for 3761 interviews. The prevalence of any alcohol use at the first interview was 45%, with 10% classified as hazardous drinkers. One-third of the sample used illicit drugs. In multivariate analyses adjusting for age, sex, race, active drug use, years on ART, and clinic enrollment time, hazardous alcohol use was independently associated with decreased ART utilization (AOR, 0.65; 95% CI: 0.51 to 0.82), 2-week adherence (AOR, 0.46; 95% CI: 0.34 to 0.63), and viral suppression (AOR, 0.76; 95% CI: 0.57 to 0.99) compared to no alcohol use. Concurrent injection drug use (IDU) exacerbated this negative effect on ART use, adherence, and suppression.

Conclusions—Hazardous alcohol use alone and combined with IDU was associated with decreased ART uptake, adherence, and viral suppression. Interventions targeting alcohol use may improve HIV outcomes in individuals with hazardous alcohol use.

Keywords

alcohol; HIV; viral suppression; adherence; illicit drug use

Alcohol use is common among HIV-infected individuals and is associated with decreased adherence to antiretroviral medication.^{1–8} In the United States, a nationally representative sample reported a 1-month prevalence of current alcohol use among HIV-infected individuals of 53%, with 8% classified as heavy drinkers.⁹ In the same sample, moderate, heavy, and frequent heavy drinkers were significantly more likely to be nonadherent compared to nondrinkers.¹⁰

Despite its prevalence and known association with decreased medication adherence, alcohol use and its effect on HIV disease outcomes have been overshadowed by illicit drug use. Indeed, few studies have examined the relationship between alcohol use and viral suppression, and

those studies that have evaluated this association have included small samples, or have combined drugs and alcohol into a single variable, rather than evaluating them independently.^{5,11,12} Importantly, studies examining the role of alcohol on HIV disease progression, either alone or in combination with active drug use, have used varying definitions of alcohol use. The National Institute on Alcohol Abuse and Alcoholism defines hazardous alcohol use as >7 drinks per week or >3 drinks per occasion for women and >14 drinks per week or >4 drinks per occasion in men.¹³ Yet, few studies have used a consistent measure of alcohol use. Finally, alcohol and drug use do frequently co-occur, but studies have not explicitly examined their independent and joint effects on HIV disease outcomes.

Illicit drugs and alcohol are used alone and concurrently by HIV-infected individuals and may have different independent and joint effects on HIV outcomes. Importantly, these different effects on HIV treatment outcomes could have implications for HIV treatment and interventions. Thus, we sought to determine the independent effect of alcohol use and combined effects of active drug and alcohol use on antiretroviral utilization, adherence, and viral suppression in an urban cohort of HIV-infected individuals.

METHODS

Clinical Setting and Survey

The Johns Hopkins AIDS Service provides care for a large proportion of the HIV-1-infected individuals in the Baltimore area. This is a dynamic, clinical cohort that captures information on those HIV-infected individuals in care. An ongoing series of patient surveys was initiated in the clinic in November 1998. Surveys were conducted daily, and all patients attending the clinic were eligible to participate. Surveys were offered longitudinally to participants at approximately 6-month intervals. The methods of this longitudinal assessment are described in earlier studies.¹⁴

The survey took approximately 15 minutes to complete and addressed 3 areas: antiretroviral therapy (ART) use, adherence to therapy, and use of alcohol and illicit drugs. Participants were asked to estimate, for each antiretroviral medication they reported taking, the number of doses missed in the preceding 2 weeks. In survey participants, information from clinical records was reviewed and abstracted by trained technicians onto structured data collection forms and then entered into an automated database. The clinic medical records, the main hospital medical record, and various institutional automated databases (eg, laboratory, radiology, pathology, discharge summaries) were abstracted. Comprehensive demographic, clinical, laboratory, pharmaceutical, and psychosocial data were collected at times corresponding to enrollment in the clinic and updated at 6-month intervals thereafter.¹⁵ This study was approved by the Johns Hopkins Hospital Institutional Review Board.

Study Inclusion

For analyses examining ART use, we included all HIV-infected individuals participating in the survey between January 1998 and November 2003, who were either on therapy or were considered eligible for ART (because they had a CD4 cell count ≤ 350 cells/ μ L, as suggested by the therapeutic guidelines set forth by the Department of Health and Human Services).¹⁶ We then examined ART utilization using more stringent criteria, including those either on ART or with a CD4 cell count ≤ 200 cells/ μ L. To assess medication adherence and viral suppression, we limited analyses to only those persons on antiretroviral therapy.

Outcome Variables

Our outcome variables of interest included antiretroviral use, adherence, and viral suppression. We categorized antiretroviral use if participants reported use of any available antiretroviral

preparation at the time of survey. We defined ART non-adherence as ≥ 2 missed doses of an antiretroviral regimen in the 2 weeks preceding survey, as this has correlated with viral suppression in previous analyses.¹⁷ Viral suppression was defined as an HIV-1 RNA count at ≤ 400 copies/mL. The HIV-1 RNA level closest in time to each survey was used for analysis of this parameter. All outcomes were dichotomous.

Primary Independent Variables

Our primary independent variables included level of alcohol use (hazardous, moderate, or none) and active drug use. We assessed the level of alcohol consumption through quantity and frequency questions. Per NIAAA guidelines, we defined hazardous alcohol use as >7 drinks per week or >3 drinks per occasion for women and as >14 drinks per week or >4 drinks per occasion for men.¹³ Moderate alcohol use was defined as any alcohol use at less than hazardous levels. We defined active drug use as illicit drug use in the 6 months before the interview. This included heroin, cocaine, marijuana, and other illicit drugs. Marijuana use only, without other concurrent drugs, was examined separately, and did not differ from nondrug use with respect to our outcomes. Thus, those with marijuana use alone were categorized with nondrug users. Both active drug use and level of alcohol use varied over time. After examining alcohol and drug use independently, these variables were combined into 6 categories: (1) neither alcohol nor drug use; (2) moderate alcohol use without drug use; (3) hazardous alcohol use without drug use; (4) drug use, without alcohol use; (5) drug use with moderate alcohol use; and (6) drug use and hazardous alcohol use.

Covariates

Other covariates included sex, age, race, CD4 nadir, clinic enrollment time, and years on ART. These variables were chosen a priori and either were demonstrated to be associated with ART use, adherence, or viral suppression in previous literature or were thought to be clinically important.

Analysis

To account for multiple measurements on participants, generalized estimating equation (GEE) methods were utilized. The multiple measurements on individuals create a correlation structure within the data that must be accounted for in analyses. The GEE methods account for this correlation within participants, giving proper estimation of regression coefficients and standard errors.¹⁸ These methods were applied to each of the dichotomous outcomes (ART utilization, adherence, and viral suppression) in separate models utilizing the logit-link and an exchangeable correlation matrix. To adjust for age, race, sex, enrollment time, and years on ART, these variables were included in the models. Because enrollment time and years on ART were found to be correlated (correlation coefficient, 0.73), we used enrollment time for analyses of ART utilization and years on ART for analyses of adherence and viral suppression, because time on ART was more clinically relevant to the latter 2 outcomes than enrollment time. An interaction term was created for drug and alcohol use and was assessed for each outcome. In addition, interaction was assessed between our independent variables and age, race, sex, years on ART, and enrollment time. The data were analyzed using STATA, version 8.0 (StataCorp, College Station, TX).

RESULTS

Between November 4, 1998, and December 3, 2003, 1957 HIV-infected individuals completed 6045 surveys. Of those interviewed, 1711 were either on antiretroviral therapy (ART), or ART eligible, accounting for 5028 interviews. 1433 individuals received ART, accounting for 3761 interviews. Table 1 describes the characteristics of the entire study cohort at their first interview. The population was primarily African American (80.9%), with the largest proportion acquiring

HIV through injection drug use (47.9%). The mean age was 38. The overall prevalence of alcohol use at the time of the first survey was 45.8%, with 10.7% classified as hazardous drinkers. Approximately one-third of the sample had used illicit drugs in the 6 months preceding their baseline interview. Of those who used illicit drugs, 75% used heroin or cocaine, 22% used marijuana alone, and 3% used other drugs. Forty percent of individuals used neither drugs nor alcohol. Individuals ART eligible or on ART were similar to the entire cohort with respect to age, sex, race, HIV risk factor, enrollment time, and number of visits. However, those on ART had a lower CD4 nadir (106 cells/mm³ (IQR: 26 to 256) vs. 153 cells/mm³ (IQR: 38 to 313)) were less likely to drink at hazardous levels (7.4% vs. 10.7%) or use illicit drugs (27.6% vs. 32.6) compared to the overall cohort. Of those on ART or ART eligible, 10% to 12% used marijuana alone compared to 22% of the entire cohort. The median duration of antiretroviral therapy for individuals on ART was 3 years (IQR: 1.3 to 5.4).

Bivariate and Multivariate Analysis

Bivariate and multivariate analyses of the effects of drug and alcohol use on antiretroviral therapy use, adherence, and viral suppression are presented in Table 2.

Antiretroviral Therapy

In bivariate and multivariate analyses, hazardous drinking and active drug use were both associated with decreased antiretroviral therapy use compared to nonuse of these substances, while moderate alcohol use was not. In adjusted analyses, active drug users had a 42% decrease in their odds of receiving therapy compared to nondrug users (AOR, 0.58; 95% CI: 0.49 to 0.70). Hazardous drinkers had a 35% decrease in their odds of receiving therapy compared to nondrinkers (AOR, 0.65; 95% CI: 0.51 to 0.82). Factors associated with increased antiretroviral therapy included older age, male sex, white race, and moderate alcohol use. There was no evidence of interaction between level of drinking and drug use, nor was there interaction between either alcohol or drug use and other variables in the model.

When multivariate analysis was limited to individuals on ART or with a CD4 count <200 cells/mm³, both hazardous alcohol use (AOR, 0.58; 95% CI: 0.44 to 0.77), and active drug use (AOR, 0.55; 95% CI: 0.45 to 0.68) continued to be associated with a decreased odds of antiretroviral utilization.

Adherence

On both bivariate and multivariate analysis, both moderate and hazardous levels of alcohol use were associated with decreased antiretroviral adherence compared to no alcohol use (Table 2). Hazardous drinkers had a lower odds of adherence (AOR, 0.46; 95% CI: 0.34 to 0.63) than moderate drinkers (AOR, 0.78; 95% CI: 0.64 to 0.95). Active drug users were 45% less adherent than nonusers (AOR, 0.55; 95% CI: 0.44 to 0.68). There was no evidence of interaction between level of drinking and drug use, nor was there interaction between either alcohol or drug use and the other variables in the model.

Virological Suppression

On bivariate analysis, both hazardous drinking and active drug use were associated with decreased viral suppression (Table 2). After multivariate analysis was adjusted for age, race, sex, nadir CD4, and years on ART, we found that hazardous drinkers were 25% less likely to suppress their viral load compared to nondrinkers (AOR, 0.75; 95% CI: 0.57 to 0.99), and active drug users were 38% less likely to suppress their viral load compared to nondrug users (AOR, 0.62; 95% CI: 0.52 to 0.76). Moderate alcohol use was not associated with decreased viral suppression. There were no interactions among the variables in the model.

After the factors associated with viral suppression were examined, adherence was added to the model to assess if this accounted for the decreased odds of suppression among active drug users and hazardous drinkers (Table 3). Self-reported adherence attenuated the effect of active drug use (AOR, 0.65; 95% CI: 0.54 to 0.78) and hazardous drinking (AOR, 0.83; 95% CI: 0.63 to 1.08) on viral suppression.

Independent and Joint Effects of Drugs and Alcohol on HIV Outcomes

Drug and alcohol use were then combined into categories to evaluate the effects of both drug and alcohol use, of alcohol use alone, and of drug use alone on HIV outcomes. Compared to those who used neither drugs nor alcohol, both hazardous drinking and active drug use alone were negatively associated with antiretroviral therapy use, adherence, and viral suppression (Table 4). Concurrent hazardous alcohol and drug use was associated with the lowest odds of ART use (AOR, 0.40; 95% CI: 0.29 to 0.57), adherence (AOR, 0.32; 95% CI: 0.21 to 0.51), and viral suppression (AOR, 0.50; 95% CI: 0.32 to 0.77). Moderate alcohol use plus drug use was also associated with decreased antiretroviral therapy, adherence, and viral suppression.

DISCUSSION

Among this urban HIV-infected cohort, hazardous alcohol use and active drug use were each independently associated with decreased antiretroviral therapy uptake, adherence, and viral suppression. Concurrent drug and alcohol use exacerbated this negative association; their combined effect on HIV outcomes was greater than their independent effects. However, these variables did not interact to provide an association different from what one would expect from the independent effects. Self-reported antiretroviral adherence attenuated the effects of hazardous alcohol on HIV RNA suppression. Although the association between active drug use remained significantly associated with viral suppression, this is likely due to residual confounding.

This study differs from previous literature on substance abuse and HIV in that it (1) focuses specifically on the association between alcohol use and HIV outcomes, (2) examines alcohol and active drug use independently and jointly, thus acknowledging that these behaviors occur both independently and concurrently, and (3) assesses the outcome of viral suppression among HIV-infected individuals who consume alcohol.

Several cohort and cross-sectional studies have evaluated the association between drug use and HIV medication uptake, adherence, and virologic and immunologic outcomes.^{2,8,14,17,19–23} One study, examining data from 10 HIV primary care sites in the United States, found that individuals with injection drug use (IDU) as their risk factor had decreased odds of receiving HAART (AOR, 0.86; 95% CI: 0.76 to 0.99) compared to patients who did not have IDU as a risk factor.²⁴ Lucas and colleagues, using earlier data from the Johns Hopkins AIDS service, found that active drug users were more likely to report HAART nonadherence than either former drug users or those who had never injected drugs.¹⁷ In addition, they later reported that changing from nonuse to active substance abuse was associated with decreased adherence and poorer virological outcomes.¹⁴ Other studies have examined specific drugs of abuse, including cocaine and marijuana. Studies by Arnsten and Tucker reported an association between active cocaine use and antiretroviral nonadherence.^{25,26} The literature on marijuana, however, is mixed with studies demonstrating an association between marijuana use and poorer adherence²⁶ and others demonstrating improved adherence among HIV-infected individuals using marijuana for nausea.²⁷ Although our analysis did not examine individual illicit substances of abuse, our findings are consistent with the current literature on drug use and HIV outcomes.

Alcohol consumption among HIV-infected individuals has previously been shown to be associated with decreased antiretroviral adherence. Studies report a range of adherence ($\geq 95\%$ adherence) between 25% and 57% among those with varying levels of alcohol use (current, moderate, at-risk, heavy), compared to 56% and 76% in nondrinkers.^{1–8} Our study, similar to a recently published study of adherence among an HIV-infected sample with a history of alcohol dependence, found that both hazardous and moderate levels of alcohol use were associated with decreased adherence.⁴ We also found that hazardous alcohol use (compared to abstinence) was associated with lower odds of adherence than moderate alcohol use (compared to abstinence). This lends support to recent findings among a Veterans Administration cohort of a dose-response relationship between alcohol use and medication adherence.³

Concurrent drug and alcohol use has been associated with decreased viral suppression.^{11,12} One study examined the effect of alcohol use on viral suppression among 220 drug users and found that heavy alcohol users were less likely to achieve viral suppression compared to light or nondrinkers.¹² Another study found that changing from nonuse to active drug and alcohol use was associated with decreased adherence and poorer virological outcomes.¹⁴ In contrast, Fabris and colleagues examined 94 HIV-positive individuals on HAART found no difference in viral suppression among nondrinkers, moderate drinkers, and heavy drinkers.¹¹ We found that hazardous levels of alcohol use were associated with decreased viral suppression independent of active drug use. Our results differ from those of Fabris and others and may be explained by the significantly larger sample size.

The effect of hazardous alcohol use on viral suppression was attenuated after adjusting for adherence on multivariate analysis, suggesting that adherence may be a mediator between alcohol use and lack of suppression among HIV-infected individuals with a history of hazardous alcohol use. The persistent association between hazardous alcohol use and viral suppression after adjustment for adherence may be due to residual confounding; however, animal models have suggested an association between chronic alcohol consumption and simian immunodeficiency virus (SIV) viral replication in Macaques, suggesting a possible direct effect of alcohol on viral replication.^{28–30}

Our study has potential limitations. First, we used self-reported 2-week adherence. Although, in this cohort, this measure has correlated with viral suppression in previous analyses, self-report over a 2-week period may be subject to recall inaccuracies, resulting in residual confounding. In addition, in our study, we were unable to adjust for depressive symptoms. Depression and depressive symptoms are prevalent among HIV-infected individuals and frequently co-occur with alcohol and drug use. They are also associated with decreased medication adherence,³¹ ART discontinuation,³² and virologic failure³³ among HIV-infected persons. The absence of this variable does not permit us to examine either its interactive effects with drug and alcohol use or potential confounding. Furthermore, our definition of active drug use included multiple illicit substances, including heroin, cocaine, and marijuana. The current literature on marijuana and HIV outcomes is mixed, and there is evidence to suggest that marijuana use is not always associated with poor HIV outcomes. The inclusion of these individuals in our definition of active drug use may have biased our outcomes toward the null; however, we specifically did not categorize marijuana use alone as active drug use, which may have decreased this potential source of bias. Finally, in this study, we did not distinguish between different patterns of alcohol consumption, such as binge drinking or chronic daily drinking. We chose to use the standard NIAAA definition for hazardous alcohol use, which can encompass a range of alcohol consumption patterns based on weekly quantity and frequency. Thus, we were unable to determine the differential effects of binge drinking only versus daily consumption on HIV treatment outcomes.

Our study has several implications. First, it demonstrates that hazardous alcohol use alone affects ART utilization, adherence, and viral suppression. The effect of hazardous drinking on these outcomes is similar to illicit drugs. This underscores the importance of screening not only for illicit drugs among HIV-infected individuals but also alcohol use. Furthermore, the independent effect of alcohol on HIV outcomes may have practical implications for HIV-infected individuals with a history of hazardous drinking only. Brief alcohol interventions have been successful in primary care settings in decreasing alcohol consumption among individuals with hazardous alcohol use.³⁴ This intervention strategy may be effective in decreasing alcohol use and improving outcomes among HIV-infected persons who have a history of hazardous alcohol use. However, in those individuals who use both illicit drugs and alcohol, interventions targeting only one substance of abuse may prove to be inadequate as both independently affect HIV treatment outcomes.

In summary, we found that hazardous levels of alcohol use were associated with decreased antiretroviral utilization, adherence, and viral suppression independent of active drug use. Combined alcohol and drug use was associated with lower odds of adherence and viral suppression than either drugs or alcohol alone. Regular screening for alcohol use, brief alcohol interventions, and treatment referral may improve antiretroviral uptake, adherence, and viral suppression in this group. Future studies examining the relationship between different patterns of alcohol use and HIV outcomes may further clarify the role of alcohol in HIV disease progression.

Acknowledgments

This research is funded by the National Institute of Alcohol Abuse and Alcoholism (R21 AA105032, to Moore, and K23 AA015313, to Chander) and The National Institute of Drug Abuse (R01 DA11602, to Moore and Lau, and K24 DA00432, to Moore).

The funding organizations had no role in the design and conduct of the study; in the collection, management, analysis, and interpretation of the data; or in the preparation, review, or approval of the manuscript. Dr. Geetanjali Chander had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

References

1. Howard AA, Arnsten JH, Lo Y, et al. A prospective study of adherence and viral load in a large multi-center cohort of HIV-infected women. *AIDS* 2002;16:2175–2182. [PubMed: 12409739]
2. Arnsten JH, Demas PA, Grant RW, et al. Impact of active drug use on antiretroviral therapy adherence and viral suppression in HIV-infected drug users. *J Gen Intern Med* 2002;17:377–381. [PubMed: 12047736]
3. 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;29:1190–1197. [PubMed: 16046874]
4. Samet JH, Horton NJ, Meli S, et al. Alcohol consumption and antiretroviral adherence among HIV-infected persons with alcohol problems. *Alcohol Clin Exp Res* 2004;28:572–577. [PubMed: 15100608]
5. Palepu A, Tyndall MW, Li K, et al. Alcohol use and incarceration adversely affect HIV-1 RNA suppression among injection drug users starting antiretroviral therapy. *J Urban Health* 2003;80:667–675. [PubMed: 14709714]
6. Cook RL, Sereika SM, Hunt SC, et al. Problem drinking and medication adherence among persons with HIV infection. *J Gen Intern Med* 2001;16:83–88. [PubMed: 11251758]
7. Golin CE, Liu H, Hays RD, et al. A prospective study of predictors of adherence to combination antiretroviral medication. *J Gen Intern Med* 2002;17:756–765. [PubMed: 12390551]
8. Berg KM, Demas PA, Howard AA, et al. Gender differences in factors associated with adherence to antiretroviral therapy. *J Gen Intern Med* 2004;19:1111–1117. [PubMed: 15566440]

9. Galvan FH, Bing EG, Fleishman JA, et al. The prevalence of alcohol consumption and heavy drinking among people with HIV in the United States: results from the HIV Cost and Services Utilization Study. *J Stud Alcohol* 2002;63:179–186. [PubMed: 12033694]
10. Tucker JS, Burnam MA, Sherbourne CD, et 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;114:573–580. [PubMed: 12753881]
11. Fabris P, Tositti G, Manfrin V, et al. Does alcohol intake affect highly active antiretroviral therapy (HAART) response in HIV-positive patients? *J Acquir Immune Defic Syndr* 2000;25:92–93. [PubMed: 11064510]
12. Miguez MJ, Shor-Posner G, Morales G, et al. HIV treatment in drug abusers: impact of alcohol use. *Addict Biol* 2003;8:33–37. [PubMed: 12745413]
13. NIAAA. Alcoholism: The Physician's Guide to Helping Patients With Alcohol Problems. Washington, DC: National Institutes of Health; 1995.
14. Lucas GM, Gebo KA, Chaisson RE, et al. Longitudinal assessment of the effects of drug and alcohol abuse on HIV-1 treatment outcomes in an urban clinic. *AIDS* 2002;16:767–774. [PubMed: 11964533]
15. Moore RD. Understanding the clinical and economic outcomes of HIV therapy: the Johns Hopkins HIV clinical practice cohort. *J Acquir Immune Defic Syndr Hum Retrovirol* 1998;17(Suppl 1):S38–S41. [PubMed: 9586651]
16. Department of Health and Human Services. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. DHHS guidelines. [Accessed October 10, 2005]. Available at: <http://www.Aidsinfo.NIH.gov>
17. Lucas GM, Cheever LW, Chaisson RE, et al. Detrimental effects of continued illicit drug use on the treatment of HIV-1 infection. *J Acquir Immune Defic Syndr* 2001;27:251–259. [PubMed: 11464144]
18. Zeger SL, Liang KY. Longitudinal data analysis for discrete and continuous outcomes. *Biometrics* 1986;42:121–130. [PubMed: 3719049]
19. Wood E, Montaner JS, Yip B, et al. Adherence to antiretroviral therapy and CD4 T-cell count responses among HIV-infected injection drug users. *Antivir Ther* 2004;9:229–235. [PubMed: 15134185]
20. Palepu A, Tyndall M, Yip B, et al. Impaired virologic response to highly active antiretroviral therapy associated with ongoing injection drug use. *J Acquir Immune Defic Syndr* 2003;32:522–526. [PubMed: 12679704]
21. Anastos K, Schneider MF, Gange SJ, et al. The association of race, sociodemographic, and behavioral characteristics with response to highly active antiretroviral therapy in women. *J Acquir Immune Defic Syndr* 2005;39:537–544. [PubMed: 16044004]
22. Lucas GM, Chaisson RE, Moore RD. Highly active antiretroviral therapy in a large urban clinic: risk factors for virologic failure and adverse drug reactions. *Ann Intern Med* 1999;131:81–87. [PubMed: 10419445]
23. Howard AA, Arnsten JH, Lo Y, et al. A prospective study of adherence and viral load in a large multi-center cohort of HIV-infected women. *AIDS* 2002;16:2175–2182. [PubMed: 12409739]
24. Gebo KA, Fleishman JA, Conviser R, et al. Racial and gender disparities in receipt of highly active antiretroviral therapy persist in a multistate sample of HIV patients in 2001. *J Acquir Immune Defic Syndr* 2005;38:96–103. [PubMed: 15608532]
25. Arnsten JH, Demas PA, Grant RW, et al. Impact of active drug use on antiretroviral therapy adherence and viral suppression in HIV-infected drug users. *J Gen Intern Med* 2002;17:377–381. [PubMed: 12047736]
26. Tucker JS, Burnam MA, Sherbourne CD, et 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;114:573–580. [PubMed: 12753881]
27. de Jong BC, Prentiss D, McFarland W, et al. Marijuana use and its association with adherence to antiretroviral therapy among HIV-infected persons with moderate to severe nausea. *J Acquir Immune Defic Syndr* 2005;38:43–46. [PubMed: 15608523]

28. Bagby GJ, Stoltz DA, Zhang P, et al. The effect of chronic binge ethanol consumption on the primary stage of SIV infection in rhesus macaques. *Alcohol Clin Exp Res* 2003;27:495–502. [PubMed: 12658116]
29. Kumar R, Perez-Casanova AE, Tirado G, et al. Increased viral replication in simian immunodeficiency virus/simian-HIV–infected macaques with self-administering model of chronic alcohol consumption. *J Acquir Immune Defic Syndr* 2005;39:386–390. [PubMed: 16010157]
30. Poonia B, Nelson S, Bagby GJ, et al. Chronic alcohol consumption results in higher simian immunodeficiency virus replication in mucosally inoculated rhesus macaques. *AIDS Res Hum Retroviruses* 2005;21:863–868. [PubMed: 16225413]
31. Spire B, Duran S, Souville M, et al. Adherence to highly active antiretroviral therapies (HAART) in HIV-infected patients: from a predictive to a dynamic approach. *Soc Sci Med* 2002;54:1481–1496. [PubMed: 12061483]
32. Li X, Margolick JB, Conover CS, et al. Interruption and discontinuation of highly active antiretroviral therapy in the multicenter AIDS cohort study. *J Acquir Immune Defic Syndr* 2005;38:320–328. [PubMed: 15735452]
33. Parienti JJ, Massari V, Descamps D, et al. Predictors of virologic failure and resistance in HIV-infected patients treated with nevirapine- or efavirenz-based antiretroviral therapy. *Clin Infect Dis* 2004;38:1311–1316. [PubMed: 15127346]
34. Bertholet N, Daepfen JB, Wietlisbach V, et al. Reduction of alcohol consumption by brief alcohol intervention in primary care: systematic review and meta-analysis. *Arch Intern Med* 2005;165:986–995. [PubMed: 15883236]

TABLE 1
 Characteristics of All Interview Participants at the First Interview

Characteristic	All Participants (N = 1957)
Age (y)	
≤35	40.8%
36–49	50.5%
≥50	8.7%
Sex (% male)	63.7%
Race	
Caucasian/other	19.1%
African American	80.9%
HIV risk factor	
MSM	23.6%
Illicit drug use	47.9%
Heterosexual infection	28.5%
CD4 nadir (median + IQR)*	153 (38–313)
Duration in clinic (y) (median + IQR)	2 (1–4)
Surveys completed (median + IQR)	2 (1–4)
Active drug use	32.6%
Alcohol use	
None	54.2%
Moderate	35.1%
Hazardous	10.7%
Active drug use and alcohol combined	
Neither	40.3%
Moderate alcohol only	22.2%
Hazardous alcohol only	4.8%
Active drug use only	13.9%
Active drug use + moderate alcohol	12.8%
Active drug use + hazardous alcohol	5.9%

* Interquartile range.

TABLE 2
 Bivariate and Multivariate Analyses of Effects of Alcohol and Drug Use on Antiretroviral Utilization, Adherence, and Viral Suppression (ORs and 95% CIs)

Characteristic	ART Utilization*		Antiretroviral Adherence		Viral Suppression	
	Bivariate	Multivariate [†]	Bivariate	Multivariate [‡]	Bivariate	Multivariate [‡]
Age (y)						
≤35	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)
36–49	1.39 (1.16–1.65)	1.38 (1.15–1.66)	1.29 (1.05–1.60)	1.30 (1.05–1.61)	1.44 (1.19–1.76)	1.50 (1.22–1.83)
≥50	1.95 (1.38–2.77)	1.89 (1.32–2.71)	1.61 (1.09–1.38)	1.55 (1.05–2.29)	2.33 (1.65–3.28)	2.14 (1.49–3.08)
Sex						
Female	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)
Male	1.40 (1.17–1.67)	1.33 (1.11–1.59)	1.30 (1.06–1.61)	1.25 (1.01–1.56)	1.18 (0.97–1.43)	1.09 (0.88–1.33)
Race/ethnicity						
Caucasian/other	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)
African American	0.47 (0.37–0.60)	0.53 (0.41–0.69)	0.56 (0.41–0.75)	0.54 (0.40–0.73)	0.62 (0.48–0.79)	0.66 (0.51–0.85)
Active drug use						
No	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)
Yes	0.58 (0.48–0.68)	0.58 (0.49–0.69)	0.49 (0.40–0.61)	0.55 (0.44–0.68)	0.61 (0.50–0.72)	0.62 (0.52–0.75)
Alcohol use						
None	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)
Moderate	1.11 (0.96–1.28)	1.18 (1.01–1.37)	0.76 (0.63–0.92)	0.78 (0.64–0.95)	0.99 (0.85–1.14)	1.02 (0.86–1.20)
Hazardous	0.58 (0.46–0.72)	0.65 (0.51–0.82)	0.43 (0.32–0.57)	0.46 (0.34–0.63)	0.71 (0.56–0.91)	0.76 (0.57–0.99)
Years on ART	—	—	1.03 (1.00–1.06)	1.02 (0.99–1.05)	1.04 (1.01–1.08)	1.04 (1.01–1.08)

* Sample includes individuals either on antiretroviral therapy or with a CD4 cell count ≤350.

[†] Analysis adjusted for age, sex, race, CD4 nadir, and time (days) enrolled in clinic.

[‡] Analysis adjusted for age, sex, race, CD4 nadir, and years on ART.

TABLE 3
 Multivariate Analysis* of the Effects of Alcohol and Drug Use on Viral Suppression Adjusting for Adherence (ORs and 95% CIs)

Characteristic	Viral Suppression
Age (y)	
≤35	1.0 (Reference)
36–49	1.49 (1.21–1.82)
≥50	2.19 (1.53–3.11)
Sex	
Female	1.0 (Reference)
Male	1.07 (0.87–1.31)
Race/ethnicity	
Caucasian/other	1.0 (Reference)
African American	0.71 (0.55–0.92)
Active drug use	
No	1.0 (Reference)
Yes	0.65 (0.54–0.78)
Alcohol use	
None	1.0 (Reference)
Moderate	1.06 (0.90–1.23)
Hazardous	0.83 (0.63–1.08)
Adherence	
No	1.0 (Reference)
Yes	2.17 (1.82–2.58)

* Analysis adjusted for age, sex, race, CD4 nadir, adherence, and years on ART.

TABLE 4

Individual and Combined Effects of Active Drug and Alcohol Use on HIV Outcomes (Adjusted ORs and 95% CIs)*

Category	ART [†]	Adherence [‡]	Virological Suppression [‡]
– Drug use – Alcohol	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)
– Drug use + Moderate alcohol	1.14 (0.95–1.37)	0.77 (0.62–0.98)	1.00 (0.84–1.20)
– Drug use + Hazardous alcohol	0.57 (0.42–0.77)	0.36 (0.25–0.53)	0.72 (0.52–0.99)
+ Drug use – Alcohol	0.54 (0.43–0.68)	0.50 (0.37–0.68)	0.60 (0.46–0.78)
+ Drug use + Moderate alcohol	0.68 (0.54–0.88)	0.40 (0.30–0.54)	0.64 (0.50–0.82)
+ Drug use + Hazardous alcohol	0.40 (0.29–0.57)	0.32 (0.20–0.51)	0.50 (0.32–0.76)

* Adjusted for age, sex, race, CD4 nadir, and time enrolled (days).

[†] Sample includes individuals either on antiretroviral therapy or with a CD4 cell count ≤ 350 .[‡] Adjusted for age, sex, race, CD4 nadir, and years on ART (days).