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Alcohol use and antiretroviral adherence: Review and meta-analysis

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Abstract

Background—Alcohol use is frequently implicated as a factor in nonadherence to highly active antiretroviral therapy (HAART). There have not been efforts to systematically evaluate findings across studies. This meta-analysis provides a quantitative evaluation of the alcohol-adherence association by aggregating findings across studies and examining potential moderators.

Methods—Literature searches identified 40 qualifying studies totaling over 25,000 participants. Studies were coded on several methodological variables.

Results—In the combined analysis, alcohol drinkers were approximately 50–60% as likely to be classified as adherent [OR = 0.548, 95% CI: 0.490–0.612] compared to abstainers (or those who drank relatively less). Effect sizes for problem drinking, defined as meeting the National Institute on Alcohol Abuse and Alcoholism (NIAAA) criteria for at-risk drinking or criteria for an alcohol use disorder, were greater [OR = 0.474, 95% CI = 0.408–0.550] than those reflecting any or global drinking [OR = 0.604, 95% CI = 0.531–0.687]. Several variables moderated the alcohol-adherence association.

Conclusions—Results support a significant and reliable association of alcohol use and medication nonadherence. Methodological variables appear to moderate this association and could contribute to inconsistencies across studies. Future research would benefit from efforts to characterize theoretical mechanisms as well as mediators and moderators of the alcohol-adherence association.

Keywords

alcohol; antiretroviral therapy; HIV/AIDS; medication adherence; meta-analysis; review

Introduction

Since its widespread introduction in 1996, highly active antiretroviral therapy (HAART) has led to marked improvements in immunologic and virologic outcomes, quality of life and longevity among individuals living with HIV.[1,2] However, the optimal benefits of HAART are closely tied to adherence.3 The implications of nonadherence for disease progression are well documented and include adverse consequences for the individual as well as public health.

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4–6 Improving the ability to identify and remediate barriers to HAART adherence is therefore a clear priority of behavioral HIV/AIDS research. [7]

Among the most frequently studied correlates of HAART nonadherence is substance use.[8] Historically, most attention has focused on injection drug use (IDU),[9–11] but studies focusing on alcohol have been emerging with increasing frequency. A focus on drinking behavior in the context of HAART is warranted for several reasons. Alcohol use is prevalent among HIV-positive individuals; [10, 12–14] is cited by patients as a reason for nonadherence; [15–18] and is associated with nonadherence in numerous studies. Evidence also suggests a deleterious influence of alcohol use on markers of immunological functioning and viral suppression, [9, 19–22] effects that could be partly mediated by nonadherence.[9] Given these findings and the fact that alcohol use is a modifiable behavior, interventions targeting alcohol use among those living with HIV/AIDS have the potential to improve disease management and perhaps to delay disease progression. [16,18,22,23]

Although alcohol use has been associated with HAART nonadherence in numerous studies, the nature, strength and consistency of this association remain unclear. A number of null findings have been reported, leading to a somewhat equivocal literature.[8,24] Additionally, the question of whether adherence is progressively compromised as drinking levels increase (i.e., a “dose-response” effect) has not been systematically evaluated, in part due to the use of dichotomous drinking variables in most studies. Of the few studies to examine multiple levels of alcohol use, some have found a positive and linear relationship between drinking and medication nonadherence [9,25,26] whereas others have found similar adherence rates across moderate and high drinking levels.[14, 22, 27] Finally, some evidence suggests that the relation of alcohol use and nonadherence could be moderated by demographic or methodological variables, including gender [28,29] and how adherence is defined.[16,30–32] There have not been systematic efforts to evaluate hypothesized moderators of the alcohol-adherence association.

There are several potential explanations for heterogeneous findings across studies, including insufficient power in smaller studies and variable methodological and measurement approaches across investigations. [24] Discrepant findings could also reflect the influence of moderating variables that have yet to be systematically evaluated. It is also noteworthy that existing studies are largely based on retrospective survey data [33] and have often used alcohol and adherence measures that were not temporally concurrent. These methodological features are significant barriers to inferring causal associations [34] and leave open the possibility that some reported findings reflect the influence of third variables.[16] In sum, a detrimental influence of alcohol use on HAART adherence, though plausible and supported by some empirical data, has yet to be clearly, convincingly or reliably characterized. A causal effect of alcohol consumption on HAART adherence could be better substantiated if this relationship proved consistent and robust across studies, especially given the varied methods reported in the literature.

The current study provides a meta-analytic review of published studies examining the association of alcohol use and antiretroviral adherence. Meta-analytic techniques are well suited for maximizing statistical power by aggregating effect sizes across studies and allowing examination of effect moderators at the aggregate level. This study had the following specific aims: (1) to provide a descriptive account of studies examining alcohol-adherence associations; (2) to provide quantitative estimates of the magnitude and stability of alcohol-adherence associations across studies; (3) to provide an aggregate evaluation of “dose-response” effects by examining effect sizes across objectively defined categories of consumption; and (4) to evaluate methodological and demographic variables as moderators of the alcohol-adherence association.

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Method

Study selection

We aimed to identify published, peer-reviewed studies that reported on the association of alcohol consumption and HAART nonadherence. Both electronic and manual literature searches were conducted to identify candidate studies published from 1996 through the end of 2007. Searches of electronic databases (*MEDLINE, PubMed, PsycInfo*) were conducted by crossing terms related to HIV (*HIV; human immunodeficiency virus; AIDS; acquired immunodeficiency syndrome*), antiretroviral therapy (*HAART; highly active antiretroviral therapy; antiretroviral therapy; ARV; ART; combination therapy; HIV treatment*), medication adherence (i.e., *adherence, nonadherence, compliance, noncompliance*), and alcohol (i.e., *alcohol, drinking, substance use, drug use, AOD*). All resulting abstracts were screened. Candidate studies were defined as those that reported results from a data-based study and indicated that adherence and alcohol or substance use were assessed.

Results of the study selection process are depicted in Figure 1. All candidate studies were retrieved for full review and studies were retained for inclusion in the meta-analysis if they met the following criteria: (a) a measure of antiretroviral adherence was included in the study; (b) a measure of participants' alcohol use was included; (c) reported a quantitative test of the association of alcohol use and adherence; (d) provided sufficient statistical information for deriving an effect size; and (e) reported on a sample that did not overlap with that of another qualifying study. Studies that combined measures of alcohol with other substance use, or that combined measures of antiretroviral adherence with other medication adherence, were not considered for inclusion. In cases where two or more studies had overlapping samples only one study was retained; we used sample size and specificity of drinking measures as the primary criteria for choosing among them. After arriving at an initial list of qualifying studies we implemented two manual search strategies, which consisted of reviewing references cited in each of the qualifying studies (as defined above) and consulting review papers on correlates of antireteroviral adherence to identify additional candidate studies. Forty published studies were retained for the meta-analysis (denoted with asterisks in the references section).

Data abstraction and coding

All studies were coded on attributes within three categories: descriptive characteristics, characteristics of adherence measurement, and characteristics of alcohol use measurement. Descriptive characteristics included study location and year; gender composition; study aim (defined as whether alcohol/substance use was assessed as a primary or ancillary aim of the study); and sample size for the alcohol-adherence analysis. In cases where the number of participants for the alcohol-adherence analysis was smaller than that of the overall sample, sample size was coded based on the former. Studies from the U.S. were coded on racial composition of the sample using the two most commonly reported demographic groups (i.e., % African American and % White). Non-U.S. studies typically lacked data on race/ethnicity. Given the association of IDU with HAART adherence we also estimated the proportion of each sample that reported IDU using available indicators; these varied across studies (e.g., past-month IDU; lifetime IDU; IDU as the mode of HIV transmission).

For adherence measurement, studies were coded based on the assessment method (self-report, MEMS, etc.) and the length of time over which adherence was recalled or otherwise measured (e.g., 3 days, 7 days, etc.). Studies also were coded based on whether adherence was analyzed as a continuous (e.g., % adherence) or dichotomous (e.g., adherent vs. non-adherent) outcome. For dichotomous outcomes, criterion cutoffs for adherence (e.g., 95%) were recorded. With regard to alcohol use, studies were coded on the length of the alcohol use assessment period and whether the authors reported use of a previously validated measure to assess alcohol use

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or alcohol use disorders. The most frequently reported instruments/methods used to infer alcohol use disorders were the CAGE35 (4 studies), the Alcohol Use Disorders Identification Test (AUDIT)36 (4 studies), and DSM-IV criteria (2 studies). Each effect size was coded based on the type of drinking examined in relation to adherence. Specifically, effect sizes were categorized as assessing (a) *drinking frequency* (e.g., days per week); (b) *drinking quantity* (e.g., drinks per drinking day); (c) *drinking frequency and quantity* (e.g., 3+ drinks at least twice a week).

Our aim to examine a possible "dose response" effect of alcohol on adherence was complicated by the fact that the majority of studies used dichotomous drinking categories with highly variable cutoffs and/or definitions. Therefore, we created an objective index of drinking severity that was standardized across studies. Each effect size was coded on a variable reflecting *drinking intensity*, which included three levels— *problem drinking, moderate drinking,* and *any or global drinking*. A three-level variable was a chosen to allow evaluation of possible "dose-response" effects while retaining enough effect sizes per category for meaningful comparisons.

An effect size was coded as assessing *problem drinking* if it was derived from a dichotomous measure of alcohol use with a threshold that (a) met or exceeded the National Institute on Alcohol Abuse and Alcoholism (NIAAA) definition of at-risk drinking, using the threshold for men (> 14 drinks per week or > 4 drinks in a day)[37], or (b) met criteria for a probable alcohol use disorder based on diagnostic or screening criteria. For instance, a study that categorized participants based on whether they drank at least five drinks per drinking occasion, consumed at least 20 drinks per week, had a CAGE score of 2+ or an AUDIT score of 8+ would contribute an effect size to the *problem drinking* category. Effect sizes were coded as assessing *moderate drinking* when based on a dichotomous outcome with a clearly defined threshold that reflected moderate drinking levels that did not exceed NIAAA criteria for at-risk drinking. For example, studies that categorized participants on whether they drank at least 2 times per week or at least 10 drinks per month were assigned to this category because these levels fall below NIAAA-defined at-risk drinking. Effect sizes were coded as *any or global drinking* if they (a) used categories that were exceedingly broad (e.g., any alcohol use in the past month vs. none), (b) used a single, continuous drinking measure of drinking (e.g., drinking days in the past two months), or (c) used indicators that were so vague as to preclude clear assignment to another category. A separate category for heavy episodic ("binge") drinking (e.g., 5+ drinks on one occasion) was not included because few studies reported this outcome and because our *problem drinking* category encompassed this definition.

Some studies had more than one effect size because they compared more than two drinking patterns/categories. In these instances, we selected the effect size that represented the most extreme comparison between drinking levels for the primary analysis in order to avoid violating the independence of effect sizes. However, we also conducted separate analyses that included (a) the least extreme comparison per study and (b) an average effect size for those studies with multiple effect sizes (described below).

Studies were also coded based on whether the reported alcohol-adherence association was determined using unadjusted or adjusted odds ratios because these relations could differ after controlling for other variables. Finally, studies were coded based on the degree of temporal overlap among the alcohol use and adherence measurements (i.e., the degree to which these variables were assessed over the same time interval). This variable was included because temporal contiguity between the predictor and outcome variable has important implications for inferring causal relationships and could influence the pattern of effect sizes across studies. Temporal overlap was coded from 0–3. A score of 0 indicated that the alcohol and adherence measures had no overlap (or it was impossible to determine overlap based on the study

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description). A code of 1 indicated some but minimal overlap among assessment intervals. A code of 2 was used if there was evidence that the measures overlapped at least partially, and a code of 3 indicated that the assessment intervals were identical or almost identical.

Descriptive information

The 40 studies included in the meta-analysis spanned a 10-year period (1998–2007) and totaled over 25,000 participants. Most studies (33) were conducted in the U.S.; other locations were France (3), Canada (1), Brazil (1), India (1) and Italy (1). Examining alcohol/substance use was identified as a primary study aim in 9 studies. Typically, alcohol use was one of several demographic or behavioral variables that were assessed and was not a major focus of the report. Twenty-one studies were derived from prospective cohort investigations, 16 from cross-sectional studies and 3 from clinical trials. Of 24 studies derived from prospective designs (prospective cohort or clinical trial), 9 used prospective data to test the alcohol-adherence association. Table 1 presents descriptive information and results of the alcohol-adherence analysis for each study.

Effect size abstraction

Effect size data were entered and standardized prior to analysis. Odds ratios (ORs) were chosen for the effect size metric because the majority of studies compared two categories of alcohol use (e.g., drinkers vs. nondrinkers; 72.5% of studies,) on a dichotomous adherence indicator variable (e.g., adherent vs. nonadherent, 77.5% of studies). Nine studies (20.5%) included multiple comparisons involving an alcohol-related indicator (e.g., any use vs. none in addition to problematic vs. nonproblematic use or none). In order not to violate the assumption of independence of effect sizes, we did not include more than one comparison per study per analysis. Two alternative ways to extract effect sizes from these studies were explored: selecting the least extreme comparison (Alternative 1; e.g., any vs. no alcohol) and computing the average effect size (Alternative 2). When studies included multiple adherence outcomes (e.g., proportion of doses and timing of doses), one measure reflecting proportion of doses taken was selected because this was the primary outcome for most studies. If more than one adherence cutoff (e.g., 90% and 100%) was evaluated in relation to drinking the more stringent cutoff was used.

For each effect size estimate we computed a 95% confidence interval (CI), *Z*-statistic and *p*-value. Figure 2 presents the effect size data and the forest plot. For each study, the forest plot indicates the point estimate for the study's effect size (OR) and its 95% confidence interval. The size of the point represents the weight of the study in the context of the present meta-analysis. An OR of one indicates no effect of alcohol on adherence, ORs greater than one would indicate a benefit of alcohol on adherence, and ORs less than one indicate a detriment of alcohol on adherence. An initial test of homogeneity of variance indicated heterogeneity across samples, $Q(39) = 82.235$, $p < .001$; therefore, random effects models were used. The core analysis yielded an estimate of the overall effect. A sensitivity analysis was conducted whereby the overall effect was computed with each study removed in turn. A stratification analysis was conducted to examine the 3-level variable reflecting drinking intensity (any/global use, moderate use, problem drinking). Moderator variables were tested using linear meta-regression. Finally, for the overall effect, publication bias was evaluated via inspection of a funnel plot and Duvall and Tweedie's "Trim and Fill" method[38].

Results

Core and Sensitivity Analyses

Under the random effects model, the point estimate and 95% confidence interval for the combined studies was 0.548 (0.490, 0.612), $Z = -10.633$, $p < .001$, indicating that those who

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used alcohol, or who drank relatively more, were 0.548 times as likely to be classified as adherent as compared to nonusers, or those who drank relatively less. Sensitivity analysis found no individual effect size to unduly influence the estimate of the overall effect; therefore, all were retained. The primary analysis used the most extreme comparison for those that included comparison of multiple drinking levels. As might be expected, alternative methods of effect size extraction altered the estimate of the overall effect. Using Alternative 1, the overall OR was estimated to be 0.628 (0.568, 0.695), $Z = -9.042$, $p < .001$, indicating that when using the least extreme comparison per study, drinkers were 0.628 times as likely to be classified as adherent compared to nonusers. Using Alternative 2, the overall OR was estimated to be 0.586 (0.531, 0.647), $Z = -10.647$, $p < .001$, indicating that, when collapsing across multiple comparisons per study, alcohol users were 0.586 times as likely to be classified as adherent as nonusers.

Stratification Analysis of the Effect of Drinking Intensity

Participants classified as problem drinkers, defined in accordance with NIAAA guidelines for at-risk drinking or based on meeting diagnostic criteria for a probable alcohol use disorder, were 0.474 (0.408, 0.550) times as likely as non-problem drinkers or abstainers to be classified as adherent (14 effect sizes, $Q(13) = 13.034$, $Z = -9.803$, $p < .001$). Among studies examining drinking thresholds classified as moderate (i.e., falling short of problem drinking criteria), drinkers were 0.480 (0.360, 0.639) times as likely as abstainers, or those who consumed less, be adherent (6 effect sizes, $Q(5) = 2.180$, $Z = -5.021$, $p < .001$). Among studies examining any or global alcohol use (e.g., any use in the past year vs. none), the combined OR was 0.604 (0.531, 0.687) (20 effect sizes, $Q(19) = 17.312$, $Z = -7.704$, $p < .001$). Overlap in the confidence intervals for the effect sizes by level of drinking intensity indicates that, although the effect sizes are significantly different from zero, they are not significantly different from each other.

Moderator Analyses

Results of univariate moderator analyses are shown in Table 2. Findings indicate that the effect of alcohol on adherence was significantly moderated by a number of variables. Greater alcohol-related decrements in adherence were associated with higher proportions of men in study samples, lower proportions of participants reporting IDU, higher adherence criteria, nonuse of a self-report measure of adherence, nonuse of a dichotomous measure of adherence, assessing alcohol/substance use as a primary study aim, dichotomization of the alcohol variable, using an alcohol variable that took into account both quantity and frequency, use of a standardized alcohol measure, and use of the AUDIT in particular.

Publication Bias

Inspection of a funnel plot revealed slight asymmetry, which is an indicator of publication bias. The Trim and Fill Method[38] indicated missing studies to the right of the mean. Eight studies were identified for trimming; the imputed point estimate was 0.638 (0.600, 0.679). Since the imputed estimate is very close to observed estimate, 0.624 (0.585, 0.664), and their confidence intervals overlap considerably, publication bias appears to have been minimal.

Discussion

This study provides the first meta-analytic evaluation of the association of alcohol use and antiretroviral adherence. Effect sizes for the combined studies suggested that those who used alcohol were 50–60% as likely (OR = 0.548, 95% CI: 0.490–0.612) to be classified as adherent compared to those who abstained (or drank relatively less). Alcohol use that met or exceeded an objective threshold for problem drinking (defined as meeting NIAAA criteria for at-risk drinking or diagnostic criteria for an alcohol use disorder) was associated with the largest effect (OR = 0.474, 95% CI = 0.408, 0.550), whereas the overall effect was smaller among studies

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examining any or global alcohol use (OR = 0.604, 95% CI = 0.531, 0.687). Although these effect sizes were not significantly different from each other, they were significantly different from zero and the point estimates can be viewed as broadly consistent with "dose-response" effects reported in previous studies.[9,14,25,27]

Several variables moderated the alcohol-adherence association. This association was stronger in samples that included a higher proportion of men, a finding that is inconsistent with previous reports suggesting that alcohol's effects on adherence are more prominent among women.[28,29] The alcohol-adherence association was also stronger in samples with a lower reported prevalence of IDU. Given the established association of IDU with lower adherence, it is possible that any effects of alcohol on adherence are obscured in the context of IDU. The observation that effects were stronger in studies with larger samples presumably reflects greater statistical power. Aspects of alcohol use measurement also moderated the effects. Studies assessing both drinking quantity and frequency, as well as those using the AUDIT (which assesses quantity and frequency) showed stronger effect sizes. A recent study found that when disaggregating the NIAAA at-risk drinking criteria into its two components (> 4 drinks per day or > 14 drinks per week), only the former predicted reduced adherence. 26 Taken together, the available evidence suggests that drinking quantity is a more robust and important predictor of adherence than drinking frequency, a finding that appears consistent with dose-related alcohol effects on adherence.[14,27] Dichotomous (compared to continuous) drinking outcomes were also associated with stronger effects, perhaps because studies using continuous measures tended to rely on global variables (e.g., drinks per week) that did not index drinking quantity.

With respect to adherence assessment, moderator analyses indicated greater alcohol-related decrements in adherence in studies where adherence was defined using a higher criterion (e.g., 100% versus 90%). This result is consistent with event-level findings suggesting that alcohol's effects are more evident under more difficult adherence requirements[39] and suggests that alcohol use might be particularly detrimental to achieving perfect or near-perfect adherence. The alcohol-adherence association was also stronger when using continuous adherence measures. Continuous measures presumably afford greater statistical power and have been shown to explain the most variance in viral load.40 Incorporating continuous measures might allow more sensitive evaluation of alcohol-adherence associations in future studies. Finally, alcohol's effects on adherence were stronger when using assessment approaches other than self-report. Similarly, research on illicit drug use and adherence suggests that this association might be more reliable when using MEMS compared to self-report.41 Use of MEMS specifically was not a significant moderator in this study, perhaps due to low power given that only four studies used MEMS. Objective measures might be more likely to detect significant associations due to fewer sources of measurement error, including social desirability influences.40 Readers are referred elsewhere for comprehensive reviews of adherence assessment approaches.[40, 42, 43]

In addition to establishing provisional effect size estimates, this study offers a basis for discussing methodologic and conceptual issues in research on alcohol and HAART adherence. A primary concern is the substantial heterogeneity in the measurement and definition of alcohol use across studies, which makes it difficult to compare and aggregate findings. Researchers are encouraged to use standardized assessment approaches that include validated and multidimensional measures of alcohol use. The AUDIT36 is a particularly useful measure given its brevity (10 items), established validity44 and inclusion of items assessing drinking frequency, quantity, heavy episodes, and symptoms of alcohol dependence. Moreover, this measure is the recommended standard in primary care settings.37 Timeline Followback (TLFB) approaches, while relatively more time consuming, are extremely useful for providing nuanced assessments of the daily covariation among drinking and adherence.[25,26] Other event-level methods that permit fine-grained analyses45 warrant consideration in future

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studies. Relying solely on diagnostic criteria is probably less useful because traditional diagnostic schemes (as well as some brief screening methods) omit measures of drinking quantity, which is a significant limitation.46 Consistent with this reasoning, a recent study showed that drinking quantity/frequency, but not alcohol-related problems, predicted reduced adherence.47

Although the association of alcohol use and nonadherence is replicable and reliable, it remains difficult to speak to the causal nature of this association. The majority of studies included in this review were cross-sectional reports that evaluated global associations using retrospective measures of drinking and adherence. In a substantial proportion of studies there was little or no overlap among the alcohol use and adherence assessment intervals. These limitations restrict the ability to infer causal effects and leave open the possibility that these associations could be attributable to other variables. If alcohol use is embedded in a broader context of problematic behaviors that also influence adherence, including IDU or other substance use, spurious associations could emerge (the association of tobacco use with nonadherence[24] likely reflects this phenomenon). The possibility that alcohol use is simply a marker for broader substance use involvement cannot be ruled out based on the current analyses; however, our finding that the alcohol-adherence association was significantly stronger in the context of lower IDU argues against this possibility and suggests a unique association of alcohol with adherence. Moreover, recent studies using sophisticated measurement approaches[25, 26, 39] provide compelling evidence that that alcohol use is closely associated with decreased adherence. Continued use of these approaches would increase the ability to speak to causal associations. Researchers have also begun to examine specific intrapersonal and situational moderators of alcohol's effects on adherence.[26,39] We suggest that future research should continue to evaluate potential moderators in order to clarify the conditions under which alcohol use is likely to influence adherence. Because the association of alcohol and nonadherence appears significant and reliable across studies, further efforts to evaluate global associations may do little to extend knowledge in this area. That noted, there is a dearth of research on this issue in developing countries and establishing basic associations of alcohol and adherence in these settings would be useful.

A notable aspect of this literature is the omission of theoretical frameworks for understanding alcohol's association with adherence. Of the studies included in this review, the vast majority did not discuss possible mechanisms for these effects. One intuitive mechanism is cognitive impairment, such that acute intoxication might interfere with one's capacity to plan for or remember dosing requirements.[26] However, additional explanations are possible. Alcohol users might have decreased access to HAART,[48] or may use alcohol to reduce or avoid HIV-related negative affect,[49,50] a motive that could also lead one to neglect adherence requirements. It is also important to note that some patients intentionally skip medication doses when drinking due to misperceptions about possible toxic interactions.[15,18, 51] These various explanations each have unique theoretical and clinical implications for research and intervention at the intersection of alcohol and adherence. An important direction for future research is to specify mechanisms that explain the link between drinking and nonadherence, which should aid in identifying intervention targets. Such mechanisms are likely to involve cognitive factors such as alcohol-related beliefs, expectancies, and motives, in addition to environmental and event-level factors.

The present study has several limitations. Given that the measurement and definitions of drinking and adherence varied considerably across studies, effect sizes should be considered provisional and interpreted as relative (rather than absolute) estimates of the likelihood of nonadherence in the context of alcohol use. While we imposed a relatively objective measure of drinking intensity in the stratification analyses, there was still heterogeneity within categories due to measurement differences across studies and these analyses relied on a modest

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number of effect sizes. Results concerning significant moderators should also be interpreted with caution. Another limitation is the omission unpublished studies, although there was minimal evidence of publication bias.

The current findings support the need for interventions that address alcohol use in the context of HAART. [14,23] Given reported associations of alcohol use and immunologic function among those living with HIV/AIDS,[9,19,20,22] successful alcohol interventions could potentially show salutary effects on disease progression and, theoretically, life expectancy.[52] Few such interventions have been tested and more are needed.[12] In one recent study, [23] an alcohol/adherence intervention did not influence drinking but nonetheless led to improved adherence, decreased viral load and increased CD4 cell counts, suggesting that adherence and biological outcomes can be improved even in the context of continued alcohol use. Similarly, meta-analytic research suggests that drug users often maintain adequate adherence, especially in the context of medical and psychosocial support.[11] Interventions might therefore aim not only to reduce alcohol use, but also to promote strategies for maximizing adherence among those who are unlikely or unwilling to cease drinking. These efforts will benefit from an improved characterization of alcohol's relation to adherence and identification of factors that mediate or moderate this association.

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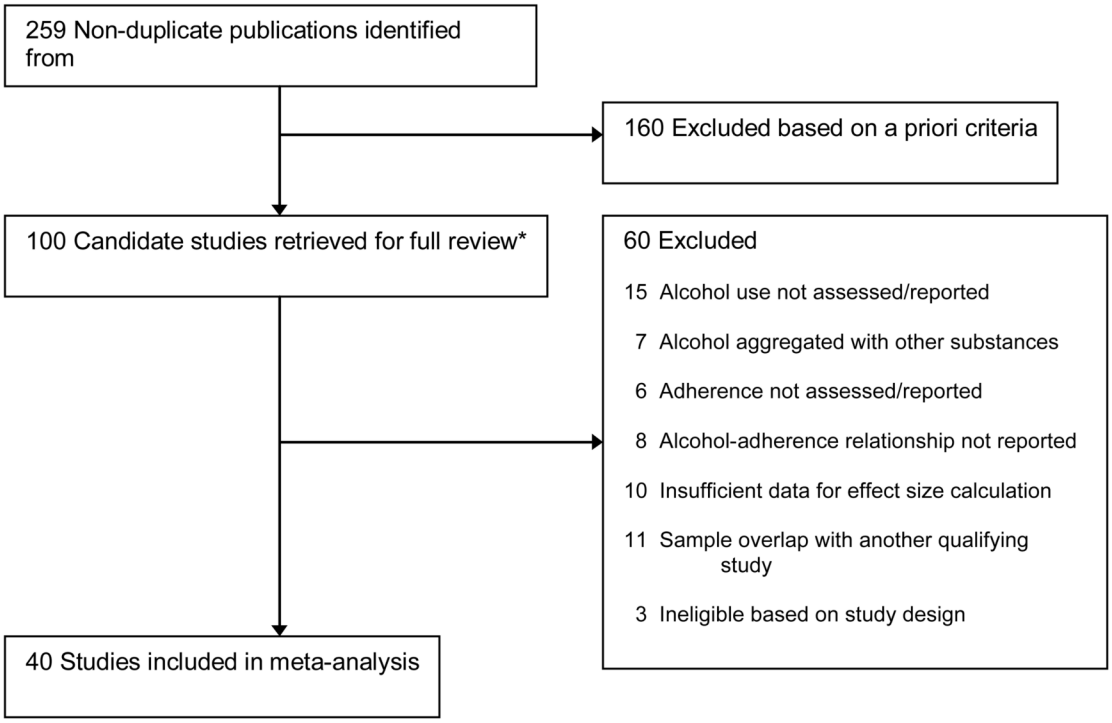

*Note. One paper contributed two studies (Lazo et al., 2007).

Figure 1.
Results of study selection process.

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Study	Drinking Intensity	OR	95% CI Lower	95% CI Upper	Z	p
Berg, 2004	1	0.300	0.130	0.691	-2.828	0.005
Bonolo, 2005	0	0.546	0.334	0.894	-2.407	0.016
Catz, 2001	0	0.388	0.193	0.782	-2.647	0.008
Chander, 2006	2	0.430	0.322	0.574	-5.730	0.000
Cook, 2001	2	0.666	0.261	1.698	-0.852	0.394
deJong, 2004	0	0.510	0.268	0.972	-2.047	0.041
Eldred, 1998	1	0.580	0.229	1.466	-1.151	0.250
Gollin, 2002	0	0.391	0.196	0.781	-2.658	0.008
Heckman, 2004	0	0.640	0.394	1.040	-1.801	0.072
Hicks, 2007	2	0.450	0.263	0.769	-2.918	0.004
Hinkin, 2004	2	0.772	0.423	1.407	-0.845	0.398
Holmes, 2007	0	0.382	0.178	0.818	-2.475	0.013
Holstad, 2007	0	0.662	0.342	1.278	-1.229	0.219
Howard, 2002	0	0.406	0.190	0.866	-2.333	0.020
Johnson, 2003	1	0.454	0.304	0.680	-3.840	0.000
Kalichman, 2003	0	0.631	0.384	1.039	-1.809	0.071
Kleeberger, 2001	2	0.640	0.272	1.505	-1.023	0.306
Lazo, 2007a	2	0.880	0.454	1.705	-0.379	0.705
Lazo, 2007b	2	0.570	0.381	0.852	-2.737	0.006
Liu, 2006	2	0.437	0.070	2.723	-0.887	0.375
Martini, 2004	1	0.587	0.214	1.609	-1.035	0.300
Moatti, 2000	0	0.830	0.719	0.958	-2.539	0.011
Mohammed, 2004	2	0.386	0.168	0.885	-2.248	0.025
Moss, 2004	2	0.744	0.239	2.315	-0.511	0.609
Mugavero, 2007	0	0.590	0.410	0.850	-2.837	0.005
Murphy, 2002	0	0.345	0.092	1.297	-1.575	0.115
Murphy, 2004	0	0.510	0.330	0.789	-3.024	0.002
Murphy, 2005	0	0.790	0.647	0.965	-2.308	0.021
Parsons, 2007	0	0.553	0.395	0.774	-3.452	0.001
Peretti-Watel, 2006	2	0.399	0.303	0.525	-6.546	0.000
Rothlind, 2005	2	0.357	0.164	0.775	-2.603	0.009
Samet, 2004	2	0.230	0.103	0.515	-3.573	0.000
Shannon, 2005	1	0.644	0.202	2.054	-0.744	0.457
Sharma, 2007	0	0.258	0.101	0.655	-2.848	0.004
Spire, 2002	0	0.667	0.399	1.114	-1.548	0.122
Sullivan, 2007	0	0.770	0.656	0.904	-3.190	0.001
Tesoriero, 2003	1	0.600	0.278	1.293	-1.304	0.192
Tucker, 2003	2	0.461	0.293	0.726	-3.338	0.001
Wagner, 2001	0	0.417	0.295	0.589	-4.951	0.000
Wilson, 2002	0	0.728	0.538	0.986	-2.051	0.040
Overall		0.548	0.490	0.612	-10.633	0.000

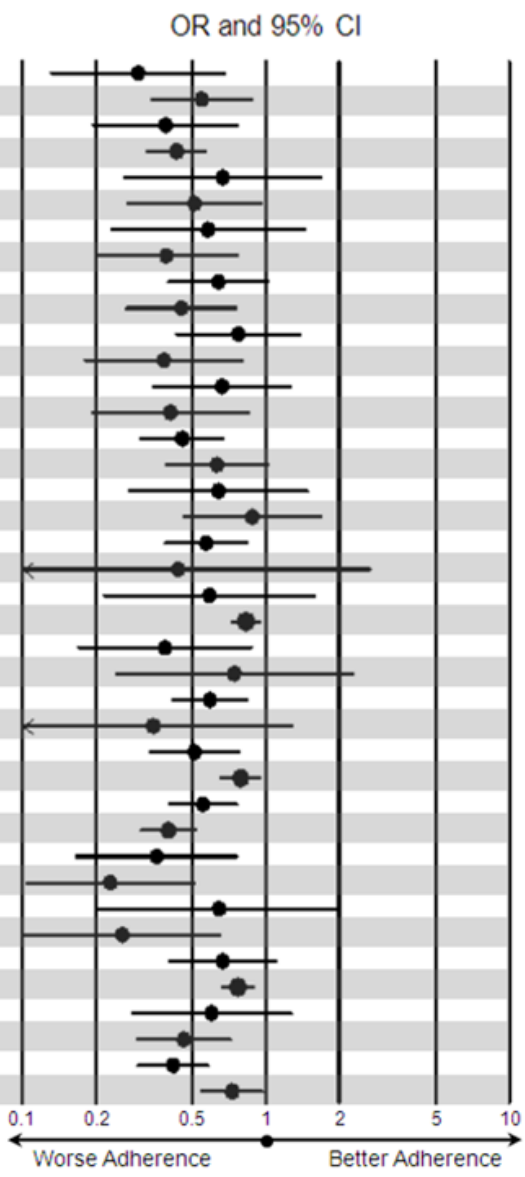

Figure 2.

Forest plot indicating the effect size contributed by each study, using the most extreme comparison per study. Drinking intensity: 0 = global (e.g., any use vs. none), 1 = moderate drinking (that did not exceed the NIAAA definition of at-risk drinking or constitute an alcohol use disorder) vs. nonuse, 2 = problem drinking (that met the NIAAA definition for at-risk drinking or criteria for an alcohol use disorder) vs. nonproblem use/nonuse.

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Table 1

Study characteristics and findings

Source Author Date	**Sample Location Setting Sample size % Male % MSM % AA % LAT % WH**	**Study Design Inclusion Criteria**	**Medication Adherence Definition Measure/Timeframe Used in Analyses Adherence Rate for Sample**	**Alcohol Use Definition Measure/Timeframe Used in Analyses Prevalence in Sample**	**Adherence × Alcohol Rates Primary Findings**
Berg et al. 2004	Bronx, NY, USA Methadone maintenance program *N*= 113 57% Male 22% AA 66% LAT 12% WH	Prospective cohort Previous participation in HIV Epidemiologic Research on Outcomes (HERO) study, currently prescribed HAART, willing to use EDM	Measured as continuous variable EDM measured at 6 research visits at 4-week intervals (#openings/ prescribed doses) Median adherence rate 62%	Alcohol use while in the study Number of drinks and frequency of drinking 6 month timeframe of the study “Problem alcohol use” defined as 1+ of the following: (a) more than 5 drinks on one occasion, or (b) drinking “everyday” or “several days per week” at any time during the study 30% problem alcohol use	Bivariate: participants reporting problem alcohol use had a median adherence 29% lower than those without problem alcohol use; non-significant trend (40 vs 69%, p<.07). Problem alcohol use was not associated with adherence for men. Women endorsing problem alcohol use reported significantly lower median adherence (25 vs. 57%, p=.003)
Bonolo et al. 2005	Belo Horizonte, Brazil Public AIDS referral centers *N = 306* 65% Male 22% endorsed male-male sex as transmission route 74% African descent 26% WH	Prospective cohort Patients initiating ART: ART naive, 18+ years, signed written informed consent, had their antiretroviral drugs dispensed in one of the centers	>95% of prescribed doses taken Number of prescribed doses for the 3 days prior to each follow-up visit Self-report via interview. Follow-up visits at 1st, 4th, and 7th month after initiating HAART 63% adherent	Any alcohol use in the month prior to the baseline interview Self-report of use lifetime and past month 38% past month 89% lifetime	Bivariate: significant effect of alcohol on adherence for the full sample (p=.018). Multivariate: alcohol use in the month preceding baseline was associated with non-adherence (hazard ratio 2.27, CI 1.58–3.25, p<.001).
Catz et al. 2001	Baltimore MD, & Milwaukee, WI, USA AIDS Service Organizations *N = 113 (total) N=84 (on HAART)* 75% Male 51% gay, 13% bi 36% AA 7% LAT 48% WH	Cross-sectional Late middle-aged & older adults: 45+ years old, HIV+	No skipped or late doses Self-report via questionnaire (likert-scale) past 7 days 69% adherent	Number of days alcohol was used Self-report via questionnaire in past two months (60 days) N/R alcohol rate	Bivariate: Older adults who adhered more consistently to HIV treatment regimens used alcohol less frequently (r= −. 27, p< .01) Multivariate: significant for full sample, fewer drinking days in past 60 days predicted more consistent treatment adherence (OR=.88, CI .79–. 98, p=.03).
Chander et al. 2006	Baltimore, MD, USA University-based HIV Clinic *N= 1957 (subsample on HAART)* 64% Male 24% MSM 81% AA 19% WH/Other	Prospective cohort On HAART, attending clinic	< 2 Missed Doses (dichotomous) Self-report via survey Past two weeks N/R adherent	NIAAA-defined hazardous drinking, based on mean quantity and frequency per week in previous 6-months Self-report via interview Assessed in approx 6- month intervals 46% use alcohol 35% moderate (any use below NIAAA definiton)	Bivariate: both moderate (OR . 78, CI .63–.92) and hazardous (OR .43, CI .32–.57) drinkers were less likely to be adherent than nondrinkers Multivariate: hazardous drinkers (adj OR .46, CI .57–. 99) and moderate drinkers (adj

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Source Author Date	**Sample Location Setting Sample size % Male % MSM % AA % LAT % WH**	**Study Design Inclusion Criteria**	**Medication Adherence Definition Measure/Timeframe Used in Analyses Adherence Rate for Sample**	**Alcohol Use Definition Measure/Timeframe Used in Analyses Prevalence in Sample**	**Adherence × Alcohol Rates Primary Findings**
				11% hazardous (meeting NIAAA definition)	OR .78, CI .64–.95) were less likely to be adherent than nondrinkers
Cook et al. 2001	Pennsylvania, USA 1 University-based HIV clinic 1 Community-based HIV clinic *N=219* 72% Men 48% gay/bisexual 24% AA 15% LAT 58% WH	Cross-sectional HIV+ pts who attended clinic during study enrollment period	No doses missed in previous 24 hours and no doses taken off schedule in past 7 days Self-report via questionnaire (likert-scale) 86% adherent (24 hours) 70% adherent (7 day)	Drinking patterns examined: Binge [5+ (women) or 6+ (men) drinks in one sitting at least monthly]; Heavy (12+ (women) or 16+ (men) drinks/week in past month; Hazardous: AUDIT of 8+ AUDIT (past year) and 2 Q/F questions (past month) 52% alcohol use in past year 19% problem drinking (hazardous, heavy, or binge) 33% mild-moderate drinking (do not meet criteria for problem use)	Bivariate: No significant associations found between any category of problem drinking and missed doses. Multivariate: Problem drinkers (hazardous, heavy or binge drinking) were more likely to have taken a dose off schedule in the past 7 days (adj OR 2.64, CI 1.07–6.53, & adj OR 4.70, CI 1.49–14.84, respectively). No association of alcohol with missed dose in past 24 hours.
De Jong et al. 2005	California, USA Public Health Clinics *N=168* 75% Men 30% AA 29% LAT 35% WH	Cross-Sectional N/R explicitly; pts on HAART attending clinics	No missed doses in past 7 days Self-report via questionnaire 66% adherent	Use in past month (yes/no) Self-report via questionnaire, past month 47% use in past month 14% heavy drinkers (not defined)	Statistically significant for the sample. 58% of adherent and 42% of non-adherent pts used alcohol in past month (crude OR .51, CI .27–.98, p=.045).
Eldred et al. 1998	Baltimore, MD, USA HIV Outpatient Clinic *N=244* 63.1% Men 19.7% MSM 85.2% AA 14.8% WH	Cross-sectional 18+ years, enrolled in state medical assistance, at least one clinic visit in past 6 months, prescription of ART for at least 6 months	Percent of prescribed pills taken in past week and percent of days in which at least one dose was taken in past two weeks (>80% doses taken = adherent) Self-report via structured interview and medical record review of # pills prescribed *Self-Report* 60% adherent (dose) 74% medication days	Frequency and quantity of alcohol consumption Self-report via interview (timeframe N/R) N/R alcohol rate	Adherence and alcohol were not associated in bivariate analyses. The sample was queried about reasons for missing doses, and 16% of the sample endorsed “alcohol or drug use” as the primary reason.
Golin et al. 2002	USA Public hospital HIV clinic *N=117* 80% Men N/R MSM 27% AA 47% LAT 16% WH	Prospective Cohort Speak English or Spanish, initiating ART medication (PI or NNRTI)	Percent of prescribed doses taken in past four weeks (continuous measure) Composite score: EDM data, pill counts, & self-report (every 4 weeks) Summed over 48 weeks 71% adherent 4% classified as >95% adherent	Any use in past 30 days (yes/no) 37% alcohol use	Bivariate: alcohol use and adherence significantly associated for full sample (p=.008). Multivariate: alcohol use is a significant predictor of non-adherence; non-drinkers report 75% of doses taken compared to 66% for drinkers (p<.01).

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Source Author Date	**Sample Location Setting Sample size % Male % MSM % AA % LAT % WH**	**Study Design Inclusion Criteria**	**Medication Adherence Definition Measure/Timeframe Used in Analyses Adherence Rate for Sample**	**Alcohol Use Definition Measure/Timeframe Used in Analyses Prevalence in Sample**	**Adherence × Alcohol Rates Primary Findings**
Heckman et al. 2004	Multiple rural sites in 12 states, USA *N=329* *N=272 (on HAART)* 72% Men 74% gay/bisexual 18% AA 3% LAT 74% WH	Baseline data from RCT of phone delivered intervention HIV+, 18+ years, living in rural location, accessing health or social services from participating agencies	No missed doses in past week Self-report via questionnaire (1 item, Likert-type scale) 50% adherent	Number of drinking days in past 2 months Self-report via questionnaire Mean 7.7 drinking days in past two months	Bivariate: non-significant trend. Adherent pts reported avg of 6.2 drinking days in past 2 months; non-adherent reported 9.1 (OR .64, CI .39–1.03, p=.07).
Hicks et al. 2007	Multiple Sites, USA HIVRN Cohort *N=659* 70% Men 36% MSM 3% MSM/IDU 51% AA 14% LAT 31% WH	Cross-sectional N/R explicitly; HIV+, in care	>95% adherence to all medications in past 2 weeks ACTG; number of missed doses in past 2 weeks for each drug prescribed 67% adherent	Used NIAAA criteria; quantity and freq of drinking Self-report via questionnaire Past 4 weeks 58% - no drinking 31% - social drinking (any consumption other than hazardous/binge) 11% - hazardous (7+ drinks/wk for women; 14 drinks/wk for men) or binge (5+ drinks per occasion)	Bivariate: no association between social drinking and adherence. Significant effect of hazardous/binge drinking on adherence (OR .45, CI .26–.76).
Hinkin et al. 2004	Los Angeles, CA, USA Community agencies/ Medical Centers *N=148* 83% Men 70% AA 9% LAT 17% WH	Cross-sectional HIV+ adults	>95% of prescribed doses EDM data Past four weeks 81% adherent	DSM-IV alcohol abuse/dependence criteria SCID-Substance Use Module N/R alcohol rate	Bivariate: 77% of pts with DSM-IV AUD were non-adherers; approximately 65% without AUD were non-adherers (ns).
Holmes et al. 2007	Pennsylvania, USA University-affiliated HIV Clinics *N=116* 81% Men 43% MSM 66% AA N/R LAT N/R WH	Prospective Cohort 18+, VL less than 75, on 2 or 3 ARVs	>95% of doses taken EDM data (modified with diaries kept to record erroneous openings, etc.) 3 months prior to participant completion 52% adherent	Any use in past year Measure N/R 58% alcohol use in past year	Bivariate: association between alcohol use and adherence was statistically significant for full sample. More high- than low-adherence pts reported no current alcohol use (53 vs. 30%; p<0.01).
Holstad et al. 2006	Georgia, USA 2 urban HIV clinics *N=120* 65% Men 46% gay, 12% bi 66% AA 3% LAT 27% WH	Cross-sectional Speak English, on HAART for at least one month	% of doses taken (continuous) Self-report via AGAS scale (5 items, Likert- scale) Past month Mean 83% adherent 43% perfect adherence	No use, past use, weekly use, occasional use Measure N/R Dichotomized into current vs. no current use 44% no use 7% past use 44% occasional use 5% weekly use	Multivariate: Current alcohol users had slightly lower mean adherence scores (81%) than non- current drinkers (85%) but this difference was a non-significant trend (stdzd B = −.177, p=.065).
Howard et al. 2002	Multiple Sites, USA Multi-center cohort study *N=161* 0& Men	Prospective cohort Already participating in AGR/HER study,	% of doses taken EDM data (# openings/# doses prescribed) modified by interview	One day or more per week versus no use during study period	Bivariate: significant effect of alcohol use on adherence for women only. Women who

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	69% AA 14% LAT 16% WH	taking 2+ HAART meds	data about errors Monthly rates over 6 months 64% adherent, month 1 45% adherent, month 6	Self-report measure, 6 months prior to enrollment 17% 1+ drinking day/week (baseline) 25% 1+ drinking day/week (6 months)	reported 1+ drinking days per week had a lower mean adherence rate (43%) compared to women who drank less frequently (56%; p=.02). Multivariate: 1+ drinking days/week was a significant predictor of lower adherence (p=.04)
Johnson et al. 2003	Multiple Sites, USA Multi-center study (Healthy Living Project) *N=2765* 74% Men 43% gay, 12% bi 49% AA 18% LAT 26% WH	Cross-sectional 18+, provided informed consent, documented HIV+, no severe neuropsych impairments, not involved in another behavioral HIV intervention	>90% prescribed doses Self-report via computer assisted interview (#doses skipped) Past 3 days 68% adherent	Use in past three months (none, less than daily, daily) Measure N/R N/R alcohol rate	Bivariate: significant alcohol effects on adherence (X^2 = 17.49, p<.001) by frequency of use category; no use, 71% adherent; less than daily, 69% adherent; daily, 43% adherent. Multivariate: not significant. Significant factors in the multivariate model examining contextual factors include black/African American ethnicity, being in a primary relationship, history of homelessness or living in a housing shelter, history of IV drug use, and current crack cocaine use.
Kalichman & Rompa 2003	Georgia, USA HIV treatment/ social services *N=255* (analytic sample) 70% Men 53% gay, 11% bi 71% AA N/R LAT 24% WH	Cross-sectional HIV+, on HAART	No missed doses Self-report of missed doses Past 7 days 56% adherent	Use in past three months (yes/no) Measure N/R 46% used alcohol in the past 3 months	Bivariate: results not significant. Alcohol use in past 3 months did not differ for adherers (43%) vs. non-adherers (54%).
Kleeberger et al. 2001	Multiple Sites, USA MACS, multi-center AIDS cohort study N=539 100% Men 100% MSM 84%WH	Prospective cohort MACS pts with adherence data from visit 30	100% of doses taken Self-report measure adapted from ACTG survey (# missed doses/# prescribed) Past four days 78% adherent	>14 vs. ≤ 14 drinks per week Measure N/R N/R alcohol rate	Bivariate: no significant effect of alcohol on adherence for more vs. less drinking groups (70 vs. 79% adherence rates).
Lazo et al. 2007	Multiple sites, USA MACS (Men) *N= 640* WIHS (Women) *N=1304*	Prospective cohort	100% of doses taken Self-report/ACTG 4 days (men); 3 days (women). Reported outcome as	Quantity and frequency of alcohol use, grouped into: *Low*: 0–2/day (men); 0–1/day (women)	Bivariate: any drinking was positively and significantly related to decreasing

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	MACS/Men 100% MSM 19% AA 7% LAT 73% WH WIHS/Women 52% AA 30% LAT 15% WH	On HAART for whom adherence data were available	change in adherence over time (increasing vs. decreasing). N/R adherent (men) 77% adherent (women)	*Moderate/Heavy:* 3–4 at least 3 times a month; or >5 less than once a month (men & women) *Binge:* >5 at least once per month (men); >4 at least once per month (women) Past 6 months Measure N/R Men: 55% low, 15% heavy, 7% binge Women: 28% low, 8% heavy, 4% binge	adherence over time for women only: Binge – OR 1.75, CI 1,17–2.64 Mod/Heavy – OR 1.47, CI 1.08–1.99 Low – OR 1.28, CI 1.05–1.54 Drinking was negatively related to increasing adherence over time for women only: Binge – OR .38, CI .21–.72 Low – OR .74, CI .57–.97 Multivariate: drinking was a significant predictor of decreasing adherence over time for women only: Binge – OR 1.81, CI 1.20–2.72 Mod/Heavy – OR 1.52, CI 1.11–2.07 Low – OR 1.29, CI 1.06–1.57 As well as to increasing adherence over time for women only: Binge – OR .41, CI .21–.78 Low – OR .73, CI .57–.95 For women, a dose-response associated was found. Low-to-moderate, moderate-to-heavy, and binge drinking associated with 29%, 52%, and 81% higher odds of decreasing adherence over time, respectively. Alcohol was not associated with adherence among men.
Liu et al. 2006	Los Angeles, CA, USA Community-based clinics, county hospitals, ethnic- and AIDS-specific organizations *N=148* 0% Men 54% AA 40% LAT 6% WH	Cross-sectional (baseline data from an intervention study) HIV+, history of CSA	>90% of doses taken / 100% doses taken Self report via questionnaire Past 1, 2, 3, and 14 days from baseline 91% adherent, past day 91% adherent, past 2 days 93% adherent, past 3 days 88% adherent, past 14 days	Problem drinking = AUDIT score ≥ 8 Self report via AUDIT (past year); current drinking (past 4 weeks) 7% met criteria for problem drinking AUDIT mean 2.3 (SD 5.5)	Current drug use, problem drinking, and current alcohol use were not significantly associated with adherence.
Martini et al. 2004	Italy Multi-center study *N=214*	Cross-sectional case control 18+, on HAART	No errors in adherence behavior: errors include missed doses, off-	Greater than 6 units (~4 standard drinks) per day Measure N/R	No significant effects of alcohol use on adherence.

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			schedule dose, not following special instructions, etc. <2 errors (high adh) 3–4 errors (med adh) ≥ 5 errors (low adh) N/R adherent	9% report alcohol use of 6+U/day	
Moatti et al. 2000	France MANIF study Hospital Clinics *N=164* 68% Male	Prospective cohort Pts enrolled in MANIF cohort: 18+, CDC 300 +, no opportunistic infections, HIV-infected through IV drug use	>80% of total prescribed HAART doses Self-report via nurse interview (# pills taken/# prescribed) Past 7 days 65% adherent	Mean number of glasses per month. Reported that one glass was equivalent to 2 units (~1–2 standard drinks) Measure N/R Past 6 months N/R alcohol rate	Multivariate: alcohol use was a significant predictor of nonadherence. The non-adherent group reported drinking more drinks/month on average (56) compared to the adherent group (33), adj OR 1.20, CI 1.04–1.41.
Mohammed et al. 2004	Louisiana, USA Rural HIV clinics *N=273* 71% Male 60% AA	Cross-sectional 18+, rural residence	No missed doses Self-report via interview Past 7 days 66% adherent	Problem drinking, past month: 2+/4 items on CAGE or binge drinking (5+ drinks per sitting) Self-report via interview Past month 13% problem drinking 13% binge drinking	Bivariate: significant effect of problem drinking on adherence (OR 2.60, CI 1.13–2.60, p=.02). Adherent pts reported significantly lower rates of problem drinking (9% binge, 6% CAGE+) vs. non-adherent pts (19% binge, 23% CAGE+). In problem drinkers, mean adherence was 37% vs. 70% in non-problem drinkers.
Moss et al. 2004	San Francisco, CA, USA Homeless services *N=102* (analytic sample who remained on HAART during the study) 86% Male 55% MSM 38% AA 5% LAT 44% WH *(demographics of N=56 pts who remained on HAART)*	Prospective cohort Homeless or marginally housed, HIV+	Percentage of pills taken out of total pills prescribed (continuous) 3 methods: unannounced pill count at home visits, self-report, EDM Mean adherence rates (pill count) across visits: Full sample: 67% Continued HAART: 74% Discontinued HAART: 51%	Consuming 5+ drinks a day (yes/no) Self-report Timeframe N/R 13% full sample 11% of those continuing HAART	Bivariate: alcohol use did not predict discontinuation of HAART, nor was there a significant association between alcohol use and adherence rates (drinkers vs. nondrinkers, 71 vs. 74% adherent).
Mugavero et al. 2007	Multiple sites, USA CHASE cohort *N=474* 71% Male 35% MSM 33% WH	Prospective cohort Participation in larger study, on HAART	No missed doses Self-report based on ACTG Past 7 days 76% adherent	ASI composite alcohol score Self-report via interview Past 30 days N/R alcohol rate	Bivariate: 10-point increase in ASI alcohol score was significantly associated with non-adherence (OR 1.71, CI 1.18–2.45, p<.01). Multivariate: 10-point increase in ASI alcohol score was an predictor of non-

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					adherence (OR 1.57, CI 1.06–2.32, p=.02).
Murphy et al. 2002	California, USA PACT study cohort *N=46* 0% Male 0% MSM 59% AA 24% LAT 7% WH	Prospective cohort Female PACT participants on HAART	>95% of doses taken on schedule 4 outcomes: 3 self-report via questionnaire (3- and 7-day dose adherence, 3- day schedule adherence) and a 4-week pill count Past 3 & 7 days, past 4 weeks Dose: 56% 3-day, 50% 7- day Schedule: 50% 3-day \ Pill count: 43%	Any alcohol use Self report via the NIDA Risk Behavior Assessment (quantity/freq, past 3 months) 50% alcohol use in past month	Bivariate: significant effect of alcohol use on schedule (but not dose) adherence (OR .20, CI N/R, p<.05).
Murphy et al. 2004	Los Angeles, CA, USA HIV clinic *N=115* 85% Male 52% MSM 50% AA 20% LAT 24% WH	Cross-sectional 18+, on HAART, non-adherent to regimen, CD4 >100, no opportunistic infections/past month, no active psychiatric condition, no participation in another clinical or adherence study	No missed doses Self-report via modified ACTG questionnaires (on CASI) 3 day, 7 day, past month 3-day, 58% adherent 7 day, 35% adherent Past month, 26% adherent	Frequency of recent drinking (ordinal) Self-report via CASI Past three months Measure N/R 37% no use 19% weekly use 4% daily use	Multivariate: more frequent alcohol use associated with non-adherence in the past month (OR .51, CI .33–.79).
Murphy et al. 2005	Multiple Sites, USA REACH study pts *N=231* 27% Men 75% AA 11% LAT 14% WH	Prospective cohort Adolescents on HAART	Reported taking meds “most of the time” or “all of the time” Self-report via interview Past month, preceding weekday, preceding Saturday 70% adherent, past month 69% adherent, preceding weekend 63% adherent, preceding Saturday	Intensity of alcohol use (past 3 months) Problem alcohol use (ever) CAGE (2+ items = problem drinking) Self-report via questionnaire 5-point Likert scale assessing frequency in past 3 months N/R alcohol rate	Bivariate: higher intensity of alcohol use was significantly associated with lower adherence rates for adherence on the preceding Saturday (adj OR .67, CI .55–.82, p<.05) and in the past month (adj OR .80, CI .66–.98, p<.05). Both associations remained significant in multivariate analyses. Other alcohol variables were not associated with adherence outcomes.
Parsons et al. 2007b	New York, USA HIV clinics N = 272 (N=154 with adherence data) 78% Men 48% gay, 12% bi 58.% AA 25% LAT 11% WH	Randomized controlled intervention trial HIV+ problem drinkers: 18+, score of 8+ on AUDIT, currently on HAART	>95% doses taken % Adherence among those without perfect adherence (continuous) Self-report via TLFB 14 days 43% adherent	Composite alcohol factor comprising three measures of alcohol use/problems: AUDIT (30-day timeframe) DrinC (90 days) TLFB (30 days) N/R alcohol rate	Multivariate: the alcohol factor significantly predicted dichotomous non-adherence (*B* = −.593, p<.001) as well as continuous non-adherence (with pts reporting 100% adherence removed; *B* = −.214, p<.021). Also, number of drinks in the past 30 days was

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					a significant negative predictor of perfect adherence (B=.834, p=.002).
Peretti-Watel et al. 2006	France Hospital HIV depts N=2484 74% Men 41% Gay/bi	Cross-sectional On HAART	Perfect adherence Self-report via 4 dichotomous interview questions 7 days 60% adherent	Regular use (2x/week or more) Regular binge drinking (drinking 5+ drinks in a row 2x/month or more), Potential alcohol abuse (2+ items on CAGE) Self-report via computer-assisted interview; quantity/frequency and CAGE 12 months 31% regular drinking 9% binge drinking 12% potential abuse	Bivariate: significant effects of alcohol use on adherence for all alcohol use groups, including: Regular drinkers, 36% low adh vs. 28% high adh (p<.001) Binge drinkers, 14% low adh vs. 6% high adh (p<.001) Potential alcohol abusers, 19% low adh vs. 8% high adh (p=.003) Multivariate: alcohol abuse was a significant predictor of nonadherence (OR 2.55, 2.00–3.26).
Rothlind et al. 2005	San Francisco, CA, USA VA Medical Center N = 268 (N=126 HIV+ subset) 95% Men 78% gay/bi 20% AA 7% LAT	Prospective cohort HIV+, English speaking, no psychiatric disorders, non-alcohol substance use disorders, or head injuries	Composite measure: sum of formula on a scale of 0 (no doses taken) to 1 (100% doses taken) Self-report, based on Chesney (2000), assessed 12 reasons for missing doses & ordinal freq measures for each reason (timeframe N/R) N/R adherent	Mean # of drinks per month Categorized into *light drinkers*: 45 (men)/35 (women) drinks or less per month and no past or current dependence or significant periods of drinking more than 45 drinks per month; and *heavy drinkers:* at least 100 (men)/ 80 (women) drinks per month for the prior 3 years and current active drinking SCID, lifetime LDH, past week 56% light drinkers 44% heavy drinkers	Bivariate: significant effect of heavy alcohol use on adherence. Mean adherence (0–1) for heavy drinkers was . 68 and .78 for light drinkers (inferential test N/R).
Samet et al. 2004	Boston, MA, USA Community/ Medical Centers *N= 267 (on HAART)* 81% Male 42% AA 23%Other 35% WH	Prospective cohort HIV+, history of alcohol related problems, English or Spanish speaking, MMSE score >20, no plans to move from Boston in next 2 years	No missed doses Self-report via ACTG survey Past 3 days 66% adherent	Used NIAAA criteria for at-risk drinking (men: >14 drinks/wk or >4 drink/day; women: >7 drinks/wk or >3 drinks/day) Self-report via ASI Past 6 months At baseline (N=205): 60% abstinent 24% moderate (any drinking below at-risk) 16% at-risk	Bivariate: significant effects of drinking level on 100% 3-day adherence; 76% of abstinent, 57% moderate drinkers, 42% of at-risk drinkers (p=.0004). Multivariate: abstinent group was more likely to report 100% adherence compared to at-risk group (adj OR 3.6, CI 2.1–6.2) and compared to moderate group (adj OR 3.0, CI 2.0-4.5)

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					No significant difference in adherence between moderate and at-risk groups
Shannon et al. 2005	Vancouver, Canada High-risk community sample *N=184* 66% Male 39% Aboriginal	Prospective cohort In CHASE cohort (engaged in drug treatment), had data available	Percent of months during follow-up in which refills were picked up (>95% = adherent) Monthly pharmacy refill compliance (from medical records 35 months 30% adherent	Frequent of alcohol use (defined as daily or most days) Self-report via questionnaire (timeframe unclear) N/R prevalence	Bivariate: no significant association of alcohol use with adherence (non-adherent, 11% frequent drinkers; adherent, 7% frequent drinkers).
Sharma et al. 2007	India Hospital/Clinic *N=226* 97.8% Male	Cross-sectional On ART, current or previous IV drug use	No missed doses/never discontinued medication Measure N/R N/R adherence rate	Any use (yes/no) Self-report Past month/year 10% past month 31% past year	Bivariate: significant effect of alcohol use on adherence. Of pts reporting missing a dose, 18% were current drinkers. Of those who never missed a dose, 5% were current drinkers (p=.003). The proportion of current drinkers was significantly higher among those who did (16%) vs. those who did not (7%) discontinue medication use (p=.031).
Spire et al. 2002	France Hospitals *N=445* 78% Male 45% male-male HIV transmission	Prospective cohort APROCO patients who had necessary data	100% of doses taken and “totally followed” regimen Self-report # of doses taken; ordinal freq of how often regimen followed Past 4 days 73% adherent	>1 unit (~.5 – 1 standard drinks) per day Measure N/R Past month 26% reported 1+ unit/day	Bivariate: greater alcohol use marginally associated with being non-adherent (p=.09). Increased use of alcohol (increasing >1 unit/day) from baseline to 4 month follow-up associated with increased likelihood of non-adherence (adj OR 2.24, CI 1.35–3.71).
Sullivan et al. 2007	Multiple Sites, USA Health centers *N=5,887* 74% Male 40% MSM 51% AA 21% LAT 24% WH	Cross-sectional 18+, in SHAS study, on HAART	>95% of prescribed doses taken Self-report via interview (measure N/R) 48 Hours 84% adherent	Any alcohol use in past year CAGE 12 months N/R alcohol prevalence	Bivariate: significant effect of alcohol on adherence. Pts who reported alcohol use in the past year were more likely to be <95% adherent (OR 1.3, CI 1.1–1.5).
Tesoriero et al. 2003	Multiple sites, USA Hospitals/ clinics *N=435* 61% Male 48% AA 32% LAT 13% WH	Prospective cohort Enrolled in TADP, on HAART at baseline	100% doses taken Self-report ACTG (# of doses missed) Past 3 days 65% adherent at baseline 46% adherent across all time points	3+ drinks/day (yes/no) Self-report Past 3 months 22% drank 3+ drinks/day	Bivariate: significant effect of alcohol on adherence only for pts who transitioned from non-frequent to frequent drinking over time (adj OR 2.92, CI 1.18–7.25, p<.05).

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Tucker et al. 2003	Multiple sites, USA HIV service organizations *N=1,910 (on HAART)* 78% Male 32% AA 15% LAT	Prospective cohort HCSUS pts: data from all three interviews & on HAART at second follow-up	No missed doses, taken as directed “all the time” Self-report via interview Past week 46% adherent	Quantity/freq of alcohol use: no drinking; non-heavy drinking (always <5 drinks per day), heavy drinking (5+ drinks on 1–4 occasions); frequent heavy drinking (5+ drinks on 5+ occasions). Self-report via interview (measure N/R) Past 4 weeks 5% frequent/heavy 9% heavy 38% non-heavy	Bivariate: significant effect of alcohol on adherence. Among pts reporting no alcohol use, 52% were adherent; non-heavy, 43% adherent; heavy, 39% adherent; frequent heavy, 31% adherent (p<.001). Multivariate: significant effect of drinking category on nonadherence. Non-heavy, adj OR 1.6, CI 1.3–2.0, p<.001 Heavy, adj OR 1.7, CI 1.3–2.3, p<.001 Freq heavy, adj OR 2.7, CI 1.7–4.5, p<.001
Wagner et al. 2002	Multiple sites, USA VA Infectious Disease Clinics (Veterans Aging Cohort Study; VACS3) *N=793 (on HAART)* Demographics N/R	Observational cohort VACS3 pts on HAART	Perfect (100%) adherence ACTG survey & provider report Past 4 days 27% perfect adh 46% intermediate adh 25% poor adh	Problem drinking (8+ on AUDIT) AUDIT & provider-reported current alcohol use N/R alcohol rate	Bivariate: among pts reporting current drinking, 26% of perfect adherers drank, 39% of intermediate adherers drank, and 58% of poor adherers drank (p<.001). Multivariate: current drinkers vs. non-drinkers were more likely to report missed doses (OR 1.88, CI 1.4–2.5, p<.001).
Wilson et al. 2002	Multiple sites, USA WIHS study cohort *N=766* 0% Male 0% MSM 53% AA 26% LAT 19% WH	Prospective cohort On HAART for >1 month, not enrolled in ACTG study, not pregnant	>95% doses taken Self-report via interview 6 Months 76% adherent	# of drinks per week Mean # of drinks per week in the previous 6 months N/R alcohol rate	Bivariate: no significant effect of alcohol use on likelihood of reporting >95% adherence. Adherent group reported mean 2.2 drinks/week, non-adherent group reported 3.8 drinks/ week.

Note. N/R = Not reported. Pts = Participants. MSM = Men who have sex with men. Bi = bisexual. Adh = adherence. AA = African American. LAT = Latino. WH = White/Caucasian. EDM = Electronic drug monitoring. ASI = Addiction Severity Index measure. Freq = frequency. Avg = average. HAART = highly active antiretroviral therapy. CSA = childhood sexual abuse. TLFB = timeline follow-back interview method. SCID = Structured Clinical Interview for the DSM-IV. LDH = Lifetime Drinking History questionnaire. ACTG = AIDS Clinical Trials Group. AGAS = Antiretroviral General Adherence Scale.

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Table 2

Results of univariate analyses of potential moderators of the association of alcohol and adherence.

	k	B	SE	Z	Q	p
Proportion of sample male (%)	40	−0.003	0.001	−2.301	5.293	0.021
Proportion of sample White (%)	27	−0.001	0.003	−0.267	0.071	0.789
Proportion of sample African American (%)	31	0.002	0.002	0.971	0.943	0.332
Proportion of sample reporting IDU (%)	23	0.008	0.003	2.772	7.682	0.006
Effect size based on adjusted odds ratio*	40	−0.113	0.119	−0.947	0.897	0.344
Temporal overlap for alcohol and adherence†	38	−0.049	0.038	−1.293	1.672	0.196
Design of alcohol-adherence analysis‡	40	−0.083	0.118	−0.707	0.500	0.480
Adherence criterion (% doses)	30	−0.022	0.005	−4.751	22.573	0.000
Length of adherence recall period (days)	35	−0.001	0.001	−1.111	1.234	0.267
Used self-report measure of adherence*	40	0.340	0.150	2.264	5.126	0.024
Used MEMS to assess adherence*	40	−0.235	0.179	−1.314	1.727	0.189
Used a dichotomous measure of adherence*	40	0.384	0.121	3.179	10.104	0.001
Assessing alcohol was a primary study aim*	40	−0.415	0.083	−4.996	24.964	0.000
Length of alcohol recall period (days)	31	0.000	0.000	1.389	1.930	0.165
Alcohol assessed as a continuous variable*	40	0.214	0.068	3.160	9.987	0.002
Alcohol variable reflected frequency and quantity*	40	−0.340	0.095	−3.596	12.930	0.000
Reported use of a standardized alcohol measure*	40	−0.411	0.075	−5.514	30.403	0.000
Used the AUDIT*	40	−0.372	0.126	−2.954	8.726	0.003

Note. Negative *B*s indicate the higher the moderator, the lower the odds ratio, i.e., the stronger the deleterious effect of alcohol on adherence. Variables were continuous unless otherwise noted. *k* = number of effect sizes.

*Coded 0=no, 1=yes.

†Coded 0= no/unclear, 1=some/very broad, 2=fair/moderate, 3=good/extensive overlap in assessment periods for alcohol use and adherence.

‡Coded 1=cross-sectional, 2=prospective.