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ORIGINAL PAPER

Changes in Days of Unhealthy Alcohol Use and Antiretroviral Therapy Adherence, HIV RNA Levels, and Condomless Sex: A Secondary Analysis of Clinical Trial Data

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Abstract

In a sample of people with HIV (PWH) enrolled in an alcohol intervention trial and followed for 12 months, we examined the association of changes in days (i.e., decrease, increase, no change [reference]) of unhealthy drinking (consuming ≥ 4/≥ 5 drinks for women/men) with antiretroviral therapy adherence (≥ 95% adherent), viral suppression (HIV RNA < 75 copies/mL), condomless sex with HIV-negative/unknown status partners, and dual-risk outcome (HIV RNA ≥ 75 copies/mL plus condomless sex). The sample included 566 PWH (96.8% male; 63.1% White; 93.9% HIV RNA < 75 copies/mL) who completed baseline, 6-, and 12-month assessments. Decrease in days of unhealthy drinking was associated with increased likelihood of viral suppression (odds ratio [OR] 3.78; 95% confidence interval [CI] 1.06, 13.51, $P = .04$) versus no change. Increase in days of unhealthy drinking was associated with increased likelihood of condomless sex (OR 3.13; 95% CI 1.60, 6.12, $P < .001$). Neither increase nor decrease were associated with adherence or dual-risk outcome. On a continuous scale, for each increase by 1 day of unhealthy drinking in the prior month, the odds of being 95% adherent decreased by 6% (OR 0.94, 95% CI 0.88, 1.00, $P = 0.04$).

Keywords Alcohol · Antiretroviral therapy adherence · Viral control · HIV transmission risk · Primary care

Introduction

Unhealthy alcohol use is a spectrum ranging from drinking above nationally recommended limits to meeting diagnostic criteria for alcohol use disorders [1]. Prior studies have found that unhealthy alcohol use is common among people with HIV (PWH) [2–4], and that prevalence of alcohol use disorders is 2–4 times higher among PWH than among those

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without HIV [3, 5–7]. In samples of PWH receiving healthcare, 27–30% report unhealthy alcohol use and/or meet criteria for alcohol use disorder [8, 9]. Unhealthy alcohol use has serious consequences for the HIV care continuum [10, 11]. It has been associated with decreased care engagement [12], poor antiretroviral therapy (ART) adherence [13–17], and decreased likelihood of HIV viral suppression [14, 18–21]. Consequently, unhealthy alcohol use is implicated as an important driver of morbidity and mortality in PWH [13, 22] and is a key behavioral challenge to address in order to improve HIV care [4, 23] .

In addition to adversely impacting clinical HIV outcomes, unhealthy alcohol use also increases the risk of HIV transmission by reducing inhibition around risky sexual behaviors, including having sex without a condom or having multiple partners [24–29]. Alcohol is known to impair risk assessment and sexual negotiation [28, 30]. Studies examining the circumstances of specific sexual encounters have found that individuals who used alcohol prior to sex were significantly more likely to engage in condomless sex [31]. Unhealthy alcohol use and HIV infection also have additive adverse effects on executive functioning, which may mediate health-related behaviors [32].

When PWH do reduce alcohol or other substance use, there is evidence that HIV behavioral and clinical outcomes improve [33–35], although few studies have examined outcomes longitudinally. A small number of prior studies of alcohol use patterns among PWH have found a benefit of cutting down on alcohol use, e.g., in an alcohol intervention trial of women with HIV [34], as well as negative outcomes associated with large changes in alcohol consumption among PWH receiving care in the Veterans Health Administration [36, 37]. While prior studies have built a foundation for understanding potential influences of decreased alcohol use on HIV-related outcomes, they are limited in several ways. First, alcohol use reduction may be driven by declines in health [38, 39], and thus the potential benefits of cutting back are not always discernable in HIV cohort studies. Second, prior studies have only examined the association between either unhealthy alcohol use and HIV clinical outcomes or HIV transmission risk behaviors, but not the combination of behavioral and clinical outcomes. Finally, little is known about the influence of changes in alcohol use on HIV behavioral and clinical outcomes in samples of PWH who historically were at greatest risk for HIV transmission but are now relatively healthy, such as men who have sex with men (MSM) with suppressive HIV treatment, and those with private insurance and regular access to care. Longitudinal analysis of alcohol treatment samples that include measures of both ART adherence and viral suppression over time are needed to examine how both increases and decreases in unhealthy alcohol use may impact both HIV behavioral and clinical outcomes, as well as combined behavioral and clinical outcomes, especially in samples of patients for whom HIV is otherwise relatively controlled.

The current study builds on prior investigations by addressing these gaps in the literature. Specifically, we followed PWH longitudinally over 1 year to examine the association between changes in number of days per month of unhealthy alcohol use over time (both decreases and increases) and adverse HIV-related behavioral and clinical outcomes, and their combination, within a primary care sample of PWH recruited to an alcohol-reduction intervention study in a large healthcare plan in the western United States. We anticipated that decreases in frequency of unhealthy alcohol use would be associated with higher likelihood of ART adherence and HIV viral control and lower likelihood of condomless sex over time, but that increases in frequency of unhealthy drinking would have an adverse effect on these same outcomes.

Methods

Participants

This study was conducted in the Kaiser Permanente Northern California (KPNC) health care system. Participants included PWH in a KPNC San Francisco HIV primary care clinic who enrolled in a randomized trial assessing the effects of two behavioral interventions to reduce unhealthy alcohol use [40]. Study inclusion criteria were based on self-report of any unhealthy alcohol use in the prior year.

The two intervention arms were motivational interviewing (MI) and electronic feedback (EF), both of which used brief treatment models focused on alcohol use reduction; the control arm was usual care (UC). UC included primary care-based implementation of screening, brief intervention and referral to treatment for unhealthy alcohol use [41]. Of the 614 participants enrolled at baseline, 582 (94.8%) completed the 6-month telephone follow-up interview and 583 (95.0%) completed the 12-month telephone follow-up interview. Participants in all three arms showed reduction in alcohol consumption over time, with no overall differences by treatment arm [42]. In the current analyses we only included participants who completed assessments at baseline, 6- and 12-month time points (N = 566).

Measures

Details about measures and data collection procedures for this randomized control trial have been reported previously [40, 42]. Below, we describe measures specific to the secondary analyses presented here.

Primary Predictor: Changes in the Number of Days Reporting Unhealthy Alcohol Use

In the current analyses, self-reported data on frequency of recent unhealthy alcohol use was used to derive a measure of change in the number of unhealthy drinking days in the past month, denoted as Δ_{UD}. Specifically, unhealthy alcohol use was measured based on reported number of days of consuming ≥ 4 drinks (women) and ≥ 5 drinks (men) in a day in the month prior to each interview. This cutoff has been validated as having adequate sensitivity and specificity as an indicator of unhealthy alcohol use [43] and is recommended as an indicator of intervention need based on national clinical guidelines [44]. To estimate Δ_{UD} at each time point, we first subtracted the preceding time point's unhealthy drinking days' values from that at the subsequent time point. Depending on whether the difference was positive, negative or zero, we categorized Δ_{UD} into one of three groups representing an increase, decrease or no change in number of unhealthy drinking days, respectively. For example, to estimate Δ_{UD} at 6 months, we subtracted the unhealthy drinking days' value at baseline from that at 6 months, and if the difference was positive the Δ_{UD} at 6 months represented an increase in comparison with baseline. At baseline, Δ_{UD} was considered missing, since there was no prior time point available for comparison. Secondary analysis examined the effects of a continuous measure of changes in unhealthy drinking days (either increases or decreases).

Study Outcomes

Four dichotomous outcomes were assessed:

Antiretroviral Therapy Adherence

For each time point following baseline, a dichotomous measure of 95% adherence to antiretroviral therapy (ART) (yes/no) was obtained based on self-report. Participants were asked whether they were currently taking ART medication (yes/no); and "What is your best guess (in %) about how much of your prescribed HIV medications you have taken in the last month?" Responses were dichotomized at ≥ 95%, a widely used cutoff that has been shown to be associated with viral control [17, 45]. Self-report ART adherence has been validated against other methods such as medication refills [46]. Using a self-reported adherence question in our analysis allowed us to simultaneously examine alcohol use and adherence at the same point in time.

Viral Suppression

A dichotomous measure of viral suppression was also measured based on HIV RNA level obtained from the KPNC HIV registry [47]. The registry is populated through electronic monitoring of inpatient, outpatient and laboratory testing databases [48]. HIV RNA levels were measured using lab values closest to the dates of enrollment, 6-month and 12-month follow-up (either before or after these time points), and levels of < 75 copies/mL (lower limit of quantification for the KPNC laboratory) were considered virally suppressed. The viral load measures taken more than 2 years (730 days) before the alcohol assessment dates were set to missing in all analyses that utilized these measures.

Condomless Sex

A dichotomous measure of engagement in risky sexual behavior was derived based on self-report of any condomless sex in the prior 6 months with someone who may or may not have been the participant's main partner, and who was of negative or unknown HIV status. We chose this measure for the purpose of examining HIV transmission risk. Although condomless sex with individuals of HIV-negative or unknown status might be considered less concerning in light of the overall high rate of viral suppression in the study sample, condomless sex remains important to examine given the potential for variability in viral suppression across time, which implies that even PWH with strong viral suppression may wish to be cautious about condomless sex in order to minimize transmission risk; and for comparability with other studies of unhealthy drinking effects [26, 27].

Dual-Risk Outcome

Finally, higher HIV RNA level and risky sexual behavior can each have unfavorable health effects on PWH and their partners. These outcomes can work synergistically to increase harm because higher HIV RNA level indicates greater HIV infectivity and involvement in risky sexual behavior then increases the chance of transmitting the virus to partners [49]. Thus, we developed a dichotomous dual-risk outcome reflecting a combination of inadequate viral suppression and involvement in risky sexual behavior, in which participants had to have both HIV RNA level ≥ 75 copies/mL and reported condomless sex with a partner of HIV-negative or unknown status. We included this outcome due to its public health importance and because it has rarely been examined among PWH who use alcohol.

Covariates

Demographic characteristics were collected in the baseline survey and included sex (female, male [reference]), age (40–49, 50–59, ≥60, 20–39 [reference]), race/ethnicity (Hispanic, non-Hispanic Black, Other/Unknown, non-Hispanic White [reference]), income (unknown, <$50 K, ≥$50 K [reference]) and HIV exposure risk factor (injection drug use, heterosexual/other, unknown, men who have sex with men-MSM [reference]). Although neither intervention resulted in improvements to unhealthy alcohol use relative to usual care in the full study sample, intervention group assignment (MI, EF, UC [reference]) was also considered a covariate due to the potential for group assignment to have small effects on alcohol use and/or clinical outcomes of interest. Baseline number of unhealthy drinking days and baseline values for outcomes of interest (no, yes [reference]) were also considered covariates.

Statistical Analysis

First, we examined the study participants' baseline characteristics descriptively. We then estimated the odds ratio (OR) and 95% confidence interval (CI) of each outcome associated with time-varying change in the number of unhealthy drinking days Δ_{UD} (increase, decrease, no change [reference]). Odds first were estimated unadjusted and then adjusted for covariates using a generalized linear mixed model (PROC GLIMMIX) in SAS 9.4. Statistical significance was defined at $P < .05$.

Results

The trial study sample included 566 adult PWH. Baseline characteristics are described in Table 1; 96.8% of participants were male, the majority (63.3%) were between 40 and 60 years old with an average age of 49.1 years (SD = 10.9 years); 63.1% of participants were non-Hispanic white and 59.7% had annual income ≥ $50,000. The average number of unhealthy drinking days reported in the 30 days prior to baseline was 3.0 (SD = 5.9) days, and 23.9% met DSM-IV criteria at baseline for alcohol dependence. HIV infection was well-controlled with 93.9% having HIV RNA level < 75 copies/mL and 75.8% reporting ART medication adherence ≥ 95%; 40.1% participants reported condomless sex in the 6 months prior to baseline, and 2.3% of participants were categorized as dual-risk (having both HIV RNA level ≥ 75 copies/mL and reporting condomless sex) at baseline. The baseline demographics characteristics of those who were included in the analysis (N = 566) and those who were excluded due to missing data at one or more follow up interviews (N = 48) were comparable. The mean (SD) difference in days between the self-report alcohol measure and viral load assessments were 93.8 (109.2) days for baseline, 113.0 (112.5) days for the 6-month survey, and 120.5 (112.4) for the 12-month survey.

Table 1 Baseline characteristics of 566 people with HIV (PWH) included in longitudinal analyses of changes in unhealthy alcohol use over time

Characteristics	N (%)
Sex	
Male	548 (96.8)
Female	18 (3.2)
Age (years)	
20–39	103 (18.2)
40–49	177 (31.3)
50–59	181 (32.0)
≥60	105 (18.6)
Mean (SD)[a]	49.1 (10.9)
Race/ethnicity	
Non-Hispanic White	357 (63.1)
Non-Hispanic Black	54 (9.5)
Hispanic	78 (13.8)
Other/unknown	77 (13.6)
Annual income	
≥$50,000	338 (59.7)
<$50,000	208 (36.8)
Unknown	20 (3.5)
HIV exposure risk factor	
Men who have sex with men	412 (72.8)
Injection drug use	38 (6.7)
Heterosexual/other	25 (4.4)
Unknown	91 (16.1)
Unhealthy drinking frequency (days)	
Mean (SD)[a]	3.0 (5.9)
Alcohol use intervention group[b]	
MI	181 (32.0)
EF	191 (33.8)
UC	194 (34.3)
DSM-IV alcohol dependence[c]	
Yes	135 (23.9)
ART adherence ≥ 95%[d]	416 (75.8)
HIV RNA < 75 copies/mL[e]	524 (93.9)
Condomless sex in prior 6 months[f]	227 (40.1)
Dual-risk (HIV RNA ≥ 75 copies/mL and condomless sex)[e]	13 (2.3)

[a] *SD* standard deviation

[b] Alcohol use intervention groups: *MI* motivational interviewing, *EF* emailed feedback, *UC* usual care

[c] *DSM-IV* Diagnostic and Statistical Manual, 4th Edition

[d] Antiretroviral therapy (ART) adherence information was unavailable for 17 PWH

[e] Viral load and dual-risk information was unavailable for 8 PWH

[f] Condomless sex with a partner of negative or unknown HIV status

Table 2 Unadjusted and adjusted association between time-varying change in days of unhealthy alcohol use (categorized into increase, decrease, no change) and HIV clinical and behavioral outcomes with estimates for covariates

Variable	ART adherence ≥ 95%		HIV RNA < 75 copies/mL[e]		Condomless sex		Dual risk[f]	
	OR (95% CI)[a]	*P* value	OR (95% CI)[a]	*P* value	OR (95% CI)[a]	*P* value	OR (95% CI)[a]	*P* value
Unadjusted primary results								
Δ_{UD}^{b}								
Increase	0.43 (0.18, 1.04)	0.06	1.65 (0.29, 9.46)	0.57	**4.54 (2.25, 9.16)**	**< .0001**	1.33 (0.13, 14.05)	0.81
Decrease	0.72 (0.38, 1.37)	0.32	1.30 (0.42, 4.02)	0.65	**1.92 (1.13, 3.25)**	**0.02**	1.27 (0.23, 7.11)	0.78
No change	Reference		Reference		Reference		Reference	
Adjusted primary results								
Δ_{UD}^{b}								
Increase	0.57 (0.24, 1.37)	0.21	3.49 (0.69, 17.79)	0.13	**3.13 (1.60, 6.12)**	**< .001**	0.53 (0.06, 4.42)	0.56
Decrease	1.46 (0.70, 3.01)	0.31	**3.78 (1.06, 13.51)**	**0.04**	1.43 (0.82, 2.49)	0.21	0.43 (0.06, 2.99)	0.39
No change	Reference		Reference		Reference		Reference	
Associations between Covariates and Each Outcome from Adjusted Models								
Sex								
Female	0.30 (0.07, 1.33)	0.11	0.93 (0.08, 11.38)	0.96	0.41 (0.08, 2.04)	0.27	3.78 (0.14, 99.28)	0.42
Male	Reference		Reference		Reference		Reference	
Age (years)								
40–49	2.04 (0.78, 5.32)	0.14	0.59 (0.12, 2.95)	0.52	0.57 (0.28, 1.19)	0.14	0.84 (0.13, 5.30)	0.85
50–59	0.45 (0.18, 1.14)	0.09	1.24 (0.22, 6.92)	0.80	0.48 (0.22, 1.04)	0.06	0.11 (0.01, 1.63)	0.11
≥ 60	1.51 (0.48, 4.71)	0.48	1.01 (0.15, 6.76)	0.99	0.21 (0.08, 0.53)	< .01	0.13 (0.01, 2.26)	0.16
20–39	Reference		Reference		Reference		Reference	
Race/ethnicity								
Non-Hispanic Black	0.39 (0.13, 1.15)	0.09	3.18 (0.42, 23.86)	0.26	0.66 (0.26, 1.66)	0.37	–	–
Hispanic	0.74 (0.28, 1.92)	0.53	0.60 (0.13, 2.77)	0.51	0.43 (0.19, 0.96)	0.04	1.19 (0.17, 8.24)	0.86
Other/unknown	0.39 (0.15, 1.01)	0.05	2.93 (0.44, 19.45)	0.27	0.84 (0.39, 1.81)	0.65	0.41 (0.04, 4.68)	0.47
Non-Hispanic White	Reference		Reference		Reference		Reference	
Annual income								
Unknown	2.40 (0.24, 23.64)	0.45	–	–	0.30 (0.06, 1.64)	0.16	–	–
< $50k	0.50 (0.26, 0.99)	0.05	0.34 (0.10, 1.12)	0.08	0.77 (0.44, 1.35)	0.37	1.55 (0.31, 7.62)	0.59
≥ $50,000	Reference		Reference		Reference		Reference	
Baseline unhealthy drinking day frequency	0.99 (0.94, 1.04)	0.69	0.87 (0.79, 0.95)	< .01	0.99 (0.94, 1.03)	0.59	1.05 (0.94, 1.18)	0.37
Baseline outcome[c]								
No	0.03 (0.01, 0.07)	< .001	0.004 (0.00, 0.04)	< .001	0.04 (0.02, 0.08)	< .001	0.01 (0.00, 0.25)	0.01
Yes	Reference		Reference		Reference		Reference	
Time	1.40 (0.84, 2.35)	0.20	1.64 (0.68, 3.95)	0.27	0.84 (0.57, 1.23)	0.37	0.98 (0.23, 4.17)	0.98
Treatment groups[d]								
MI	1.12 (0.50, 2.49)	0.78	0.31 (0.07, 1.40)	0.13	1.06 (0.57, 1.98)	0.86	0.96 (0.16, 5.98)	0.97
EF	0.69 (0.32, 1.49)	0.35	0.22 (0.05, 0.96)	0.04	1.05 (0.57, 1.94)	0.88	0.91 (0.13, 6.22)	0.92
UC	Reference		Reference		Reference		Reference	

[a]*OR (95% CI)* odds ratio (95% Confidence Interval)

[b]Δ_{UD} is the time-varying change in unhealthy drinking, and we categorized Δ_{UD} into one of three groups representing an increase, decrease or no change in number of unhealthy drinking days

[c]Depending on the outcome of interest, we included the corresponding outcome at baseline as a predictor

[d]Treatment groups: *MI* motivational interviewing, *EF* emailed feedback, *UC* usual care

[e]In the adjusted model, we excluded participants with unknown income (20 PWH) to avoid issues related to sparse data

[f]Dual risk is the joint condition of having HIV RNA level ≥ 75 copies/mL and reporting condomless sex; when analyzing this outcome, in the adjusted model, we excluded the unknown income group and Non-Hispanic Black race (72 PWH) to avoid issues related to sparse data

At 6 months, in comparison with the baseline, more than half of the study participants (50.5%) had no change in their unhealthy drinking days; 41.3% had a decrease and 8.1% had an increase. The average number of unhealthy drinking days reported in the prior 30 days at 6 months was 1.2 (SD = 3.5) days. Compared to drinking at 6 months, at 12 months 69.6% of participants had no change in their unhealthy drinking days, 13.4% had a decrease, and 17.0% had an increase. The average number of unhealthy drinking days reported in the prior 30 days at 12 months was 1.4 (SD = 3.8) days.

ORs and 95% CIs from both unadjusted and adjusted models are provided in Table 2. In the unadjusted models, compared with those who had no change in unhealthy drinking, PWH with an increase in unhealthy drinking days trended toward lower odds of ART adherence ≥ 95% (OR 0.43, 95% CI 0.18, 1.04, P = 0.06) and had higher odds of reporting condomless sex (OR 4.54, 95% CI 2.25, 9.16, $P < .0001$). A decrease in unhealthy drinking days was associated with a decrease in condomless sex (OR 1.92, 95% CI 1.13, 3.25, $P = 0.02$). No significant association was observed between changes in unhealthy drinking days and HIV RNA level or the dual-risk outcome of having both higher RNA level and reporting condomless sex.

In the adjusted models, reduction in unhealthy drinking days was significantly associated with increased likelihood of viral suppression (OR 3.78, 95% CI 1.06, 13.51, $P = 0.04$) compared with those who had no change in unhealthy drinking. Compared with the reference group, those who had an increase in unhealthy drinking days had higher odds of reporting condomless sex with someone of negative or unknown HIV status (OR 3.13, 95% CI 1.60, 6.12, $P < .001$). We did not observe any significant association between changes in unhealthy drinking days and self-reported ART adherence or the dual-risk outcome in adjusted models.

To further understand our results, we conducted a secondary analysis to examine a continuous measure of change in unhealthy drinking days, calculated as the difference between the preceding time point's number of unhealthy drinking days and those at the subsequent time point. This continuous measure accommodates those with decreases or increases in drinking days over time. For every 1-day increase in unhealthy drinking days comparing time points, the odds of ART adherence decreased by 6% (OR 0.94, 95% CI 0.88, 1.00, $P = 0.04$, Supplementary Table 1). The continuous measure was not associated with other outcomes.

Discussion

In this large sample of PWH receiving regular primary care who were recruited for an alcohol behavioral intervention study, we found that, after adjustment for potential confounders, a reduction in unhealthy drinking days was associated with greater odds of viral suppression, and an increase in unhealthy drinking days was associated with a greater odds of reporting condomless sex with a partner of HIV-negative or unknown HIV status. These findings highlight how changes in unhealthy drinking over time can impact both HIV clinical outcomes and transmission risk.

These findings build on and support the work of prior investigations that have found associations between changes in alcohol use and adverse outcomes among PWH [35, 36, 50]. These studies have examined both effects of increases and decreases in alcohol use. In two recent analyses of Veterans Aging Cohort Study (VACS) data [36], changes in alcohol use over time in both directions, based on change in routine Alcohol Use Disorders Identification Test-Consumption (AUDIT-C) screening scores, were associated with greater HIV disease severity (measured using clinical measures—CD4 and viral suppression—and a comprehensive composite risk index—the VACS Index 2.0) [36, 37, 51]. In both studies, HIV disease severity generally improved over time, and while those with stable alcohol use had the greatest improvements, those with greater increases in alcohol use had smaller improvements in HIV disease severity. Another VACS study used group-based trajectory analysis to examine associations between alcohol use groups and HIV disease based on VACS Index scores [52]. The study identified the greatest likelihood of high HIV severity risk among those with a high likelihood of consistent heavy alcohol use. In an alcohol intervention sample study conducted among women living with HIV, increases in drinking were associated with both improvement in adherence and viral suppression [35]. One survey-based study of medication adherence among Veterans with a history of unhealthy drinking found a temporal and dose–response relationship between drinking days and missed days of ART medication [50].

Although our findings are consistent with prior studies, we found that unhealthy drinking changes did not consistently predict study outcomes as expected. Specifically, only condomless sex was associated with increased drinking and only viral suppression was associated with decreased drinking after adjustment for covariates. And in the main models, neither adherence nor dual risk were associated with changes in drinking over time, though an increase in the number of unhealthy drinking days was associated with decreased likelihood of adherence. It is unclear why we found this pattern, given that the effects of alcohol on patients' ability to optimally adhere to ART are well-documented [13, 53]. Because viral control and ART adherence are tightly linked (i.e., it is unlikely that the former will be achieved without the latter), the non-significant results with regard to adherence could relate to measurement error. Specifically, our measure of adherence may have resulted in mis-categorization as a result of inaccurate self-report due to social desirability and/or misremembering.

It is also surprising that no association between increased alcohol use and viral suppression was observed, and that the point estimate suggested the possibility that increased alcohol use could improve likelihood of viral suppression. Further research is needed to investigate this issue especially given that most participants were virally suppressed at baseline and relatively few increased their drinking over time, and thus our ability to examine effects of drinking increase is limited. Finally, our findings indicated increased risk of condomless sex associated with increased unhealthy drinking but no association between condomless sex and decreased unhealthy drinking. This divergent finding potentially suggests that the effect of changes in drinking behavior on condomless sex may be mediated by different mechanisms. It is possible that while alcohol use is directly associated with condomless sex, reductions in alcohol use may not, by themselves, be sufficient to increase condom use behaviors.

Despite the somewhat inconsistent results, our findings highlight the adverse effects of increasing days of unhealthy drinking over time on subsequent transmission risk behaviors, even among PWH engaged in care with well-controlled HIV, and suggest several areas for further exploration. In contrast to most prior studies, we examined the effects of changes in number of days of unhealthy drinking on clinical outcomes, and found effects associated with this measure. Some participants identified as decreasing alcohol use over time therefore could still meet unhealthy drinking criteria (based on a categorical definition) at all time points. Potential factors also contributing to the effects we found could include unmeasured changes in health behavior [54, 55] and changes in frequency of intoxication (potentially associated with condomless sex) [24, 56]. Effects of changes in days of unhealthy drinking versus categorical measures, as well as potential factors contributing to the outcomes, are important areas for future study.

Reducing HIV transmission risk behavior among non-virally suppressed PWH is a key focus in effectively ending the HIV epidemic. In this analysis, we did not see any significant associations between change in unhealthy drinking days and the dual-risk measure we created to examine this outcome (i.e., HIV RNA level ≥ 75 copies/mL and engaging in condomless sex), although a lack of statistical power likely limited our ability to examine the longitudinal relationship of changes in unhealthy drinking days with this somewhat rare combined outcome. However, the question of whether changes in unhealthy alcohol use influence both outcomes in tandem warrants further investigation given its potential public health impact.

Study Strengths and Limitations

To our knowledge this study was the first longitudinal analysis of the relationship of changes in days of unhealthy drinking over time to HIV clinical outcomes as well as HIV transmission risk behaviors among PWH. The study was conducted in a large primary care-based sample of PWH who reported unhealthy drinking. The study had very high ($>95\%$) follow-up interview rates and our methods integrated self-report measures and electronic health record data sources to examine study outcomes. In contrast to most prior studies, we examined the potential effects of changes in days of unhealthy drinking using a continuous measure; an approach that can inform potential results of both increases and decreases in alcohol use frequency. However, limitations should also be noted. The study was based in a private health care system in a single geographic region and the sample was primarily MSM, relatively high income, and largely white; and findings may not be generalizable to public samples, those with higher alcohol problem severity, or to women. The study also had greater power for detecting effects of decrease rather than increase in unhealthy drinking over time, because relatively few participants in the sample increased their drinking. Some participants had missing viral load measures, which may have impacted our results in this analysis. Alcohol use and ART adherence measures were based on self-report. Objective measures would be helpful in supporting patient self-report data on condomless sex, e.g., sexually transmitted infection diagnoses. However, such infections could be diagnosed and treated outside the health plan, could be acquired from another PWH, and would not specifically indicate condomless sex from partners of unknown or HIV-negative status; therefore, we believe benefits outweigh the limitations of our self-report measure.

Conclusions

This study examined change in days of unhealthy alcohol use and its association with ART adherence, HIV viral suppression, and condomless sex over time among PWH engaged in care. Results suggest that reduction in the number of unhealthy drinking days could potentially improve viral suppression, but that increases in unhealthy drinking days could increase the likelihood of condomless sex. Increases in unhealthy drinking frequency may also adversely impact ART adherence. Findings highlight the clinical importance of reducing the frequency of unhealthy alcohol use in PWH.

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