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The role of alcohol use in antiretroviral adherence among individuals living with HIV in South Africa: Event-level findings from a daily diary study

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Abstract

Objective—Using daily diary methods, we aimed to test the hypothesis that at the event-level consuming alcohol increases the likelihood that antiretrovirals (ARV) will be missed on a particular day.

Methods—This prospective cohort study of 74 (52 female, 22 male) PLHIV in South Africa collected event-level data on ARV adherence and alcohol consumption using structured daily phone interviews over a period of 42 days generating 2,718 data points. We used generalized estimating equations (GEE) analyses to assess univariate and multivariate associations between alcohol and adherence, controlling for sociodemographics and testing for effect modification.

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Katelyn M. Sileo contributed to conceptualizing the research questions for this manuscript, carried out data analysis, and took the lead role in writing this manuscript.

Amber Abrams played a major role in data collection and provided substantive and editorial feedback on this manuscript.

Allanise Cloete played a major role in data collection and provided substantive and editorial feedback on this manuscript.

Leickness C. Simbayi contributed to conceptualizing the original study and helped oversee all aspects of data collection. He provided substantive and editorial feedback on this manuscript.

Susan M. Kiene was the PI on the study in which this data originated (F31MH072547-01), making her the main contributor to designing the research study, acquiring funding support, implementing the study, and overseeing data collection. She contributed to conceptualizing the research questions for this manuscript, writing this manuscript, and provided mentorship in data analysis and writing to the first author.

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Results—Controlling for sociodemographics, each alcohol measure was a statistically significant predictor of non-adherence on a particular day; any drinking compared to no drinking (daytime: AOR = 3.18, 95% CI = 2.25–4.49; evening: AOR = 3.43, 95% CI = 2.13–5.53), consuming more alcohol than one normally consumes (daytime: AOR = 1.06, 95% CI = 1.02–1.11; evening: AOR = 1.10, 95% CI = 1.05–1.15), and drinking at low to moderate risk level (daytime: 4.29, 95% CI = 2.81–6.56; evening: AOR = 4.24, 95% CI = 2.38–7.54) and high to very high risk levels (daytime: AOR = 2.31, 95% CI = 1.56–3.42; evening: AOR = 3.08, 95% CI = 1.91–4.98) were all significantly related to missing ARVs in the daytime and evening.

Conclusions—These data provide support for an event-level relationship between alcohol and non-adherence. Interventions that mitigate alcohol use among people on ARVs or provide strategies to maintain optimal adherence among those who drink are needed.

Keywords

Alcohol; ART; Adherence; HIV/AIDS; Event-level analysis; South Africa

1. INTRODUCTION

In South Africa, a country with one of the highest HIV prevalence globally at 19.1% in the adult population (UNAIDS, 2013), it is estimated that 45% of people living with HIV (PLHIV) were receiving antiretroviral treatment (ART) in 2014, a two-fold increase since 2011 (The World Bank, 2015). However, alcohol, theorized to influence adherence through impaired cognitive functioning (Braithwaite et al., 2008), has been linked to suboptimal treatment outcomes through the mediator of non-adherence (Kader et al., 2014; Malbergier et al., 2014; Molina et al., 2014). Heavy episodic drinking is prevalent in South Africa (World Health Organization (WHO), 2014a, 2014), and PLHIV drink at a higher rate than their HIV negative counterparts (Hargreaves et al., 2002; Mbulaiteye et al., 2000; Zuma et al., 2003). Relatedly, Hendershot et al.'s (2009) meta-analysis of 40 studies reported alcohol drinkers were approximately 50–60% less likely to be adherent compared to non-drinkers.

However, the majority of studies assessing the alcohol-adherence relationship use cross-sectional designs, which only demonstrate global correlations between alcohol and adherence. Global associations can tell us if those who drink, or tend to drink at higher risk levels, are more likely to have poorer adherence in general. There is evidence of a global association between alcohol consumption and poor ARV adherence in South Africa and other sub-Saharan countries (e.g., Kip et al., 2009; Kekwaletswe and Morojele, 2014; Morojele et al., 2014). However, such studies fail to establish if on days when individuals drink alcohol they more likely to miss taking their ARVs compared to days when they do not drink alcohol. Additionally, a global association between alcohol and adherence could be confounded by a number of variables (i.e., gender, socioeconomic status (SES), ART access, personality traits, stress, other substance use; Dewing et al., 2015; Hendershot et al., 2009; Nachega et al., 2004; Parsons et al., 2013; Peltzer et al., 2010; Tucker et al., 2004; Yaya et al., 2014). In contrast, having event-level data from individuals over several weeks provides stronger evidence; it can establish co-occurrence between drinking and non-adherence, and can distinguish the influence of alcohol on adherence across different levels of drinking on a particular day, controlling for potential confounders.

Despite recognition of the need to disentangle the relationship between alcohol use and ARV adherence through event-level data (Hendershot et al., 2009), few studies exist with this aim, all of which are from developed or resource-rich settings (Braithwaite et al., 2008, 2005; Kalichman et al., 2013; Parsons et al., 2008). One such study among PLHIV in the United States (U.S.) found on days when participants drank, they had a 9 times increased likelihood of medication non-adherence (Parsons et al., 2008). No studies to our knowledge have examined the effect of alcohol on adherence beyond a global association in resource-limited settings. Given the distinct patterns of alcohol consumption (World Health Organization, 2014) and ART adherence (Mills et al., 2006) in sub-Saharan Africa compared to developed countries, these findings may not be generalizable across settings. There is a need to replicate the findings of event-level studies in sub-Saharan Africa.

The present prospective cohort study employed daily diary methods sampling PLHIV in South Africa to obtain longitudinal event-level data on daily alcohol consumption and missed ARVs. We test the hypothesis that consuming alcohol on a particular day increases the likelihood that ARVs will be missed that day. We operationalize alcohol consumption in different ways, controlling for relevant covariates, to answer different questions about the relationship between alcohol and ARV adherence: (1) *Does consuming any alcohol on a particular day compared to no alcohol that day influence ARV adherence that day?*; (2) *Does consuming more alcohol than one normally consumes on a particular day influence ARV adherence?*; (3) *Does drinking at different risk levels (low-moderate, high-very high) on a particular day influence ARV adherence compared to no drinking?*

2. METHODS

2.1 Participants and Procedures

The research was part of a larger study assessing the effect of alcohol consumption before sex on unprotected sexual events (Kiene et al., 2008), conducted with 82 PLHIV in South Africa. Participants were recruited from five HIV service organizations in Cape Town, South Africa using a purposeful sampling approach. Eligibility for the parent study required being at least 18 years of age, HIV positive, having vaginal or anal sex, consuming alcohol in the prior 30-days, and having access to a phone. Only one member of a couple was allowed to participate. Of those screened for the original study, two eligible individuals declined participation and five did not meet the eligibility criteria. For the present study, we added the eligibility criteria of ARV use at any time during the 42 day assessment window. The study was approved by U.S. and South African institutional review boards, and all participants provided written, informed consent.

Participants completed questionnaires at the time of enrollment and at the completion of the 6-week study. Event-level data was collected using structured daily phone interviews. Interviewers conducted a structured interview in Xhosa over the phone daily between 1pm and 6pm for 42 days. The interview asked them about things that happened last night (since the interview yesterday until going to sleep) and today (since waking up until now). Participants were compensated with up to 660 Rand if they completed all assessments (about 95 USD at the time) for their participation in the study.

2.2 Measures

At baseline, time-invariant (i.e., variables unlikely to change day-to-day) measures were collected, including sociodemographic information: gender, age, education, SES (self-rated on a 5-point scale dichotomized for analysis): (0) no money for food, enough for food but not enough for other basics (e.g., clothes), or money for food and basics but not for other important things, (1) most important things but not enough for things like children's education, or some money for extra things like eating in restaurants, and marital status; we assessed if participants were on ARVs at baseline (0) or initiated ARVs over the course of the study (1); HIV status disclosure to current partner(s), (yes, no); and validated dimensions of HIV stigma including anticipated stigma (Berger et al., 2001) ($\alpha = 0.77$), enacted stigma (Berger et al., 2001) ($\alpha = 0.86$), and internalized stigma (Kalichman and Simbayi, 2003; Kalichman et al., 2008) ($\alpha = 0.68$). Additional measures collected not relevant to the present study are described elsewhere (Barta et al., 2008; Kiene et al., 2008).

During daily phone interviews, time varying (i.e., measures collected daily over the 42 day study) measures (alcohol consumption, missed ARVs, drug use, stress level) for last night (after yesterday's interview until going to sleep) and for today (since waking up until the time of the interview) were collected. For those time periods (today and last night) participants reported the number of alcoholic drinks consumed (converted to standardized values: 1 drink = 12g of alcohol), how many ARVs were missed, substance use including any dagga (cannabis) use (yes, no) and any Mandrax (Methaqualone) use (yes, no) for each day and night, and the level of stress experienced during each day and night (ranging from 0 "not stressful at all" to 6 "extremely stressful").

Event-level alcohol variables were operationalized in several different ways to answer our research questions. (1) To assess whether any drinking during a particular day or evening influences adherence *today* and *last night*, variables were constructed by dichotomizing consumption into two categories: Any drinking during the time period (1 or more drinks) and no drinking during the time period (0 drinks). (2) To assess the effect of drinking more than the participant normally drinks on adherence we calculated person-centered number of drinks by taking each participant's average number of drinks (separately for day and night) during the study and subtracting it from the number of drinks reported each day and night. By accounting for a participant's "normal" quantity of alcohol, this variable allows us to test whether non-adherence occurs when individuals increase their alcohol consumption beyond their usual levels of consumption. (3) We assess drinking by risk level by creating three categories of drinking for "today" and "last night:" 0 "no drinking," 1 "low to moderate risk drinking," and 2 "high to very high risk drinking" based on the World Health Organization's (WHO) categories for risky drinking by gender (men: no = 0 drinks (0g), low-moderate = 1–5 drinks (1–60g), high-very high = 6 or more drinks (61g or more); women: no = 0 drinks (0g), low-moderate = 1–3.3 drinks (1–40g), high-very high = 3.4 or more drinks (3.4g or more) (Lopez et al., 2000). This variable is used to assess whether alcohol use only affects adherence when the quantity meets standardized thresholds of risky consumption.

The main outcomes were any ARVs missed a) today and b) last night (0 = no ARVs missed, 1 = one or more ARVs missed). Note, we did not use a continuous adherence measure due to

incomplete data on the number of ARVs participants were taking each day, as only 57% of the sample reported being on ARVs at baseline and the remainder of those included in this analysis started ARVs during the study period.

2.3 Analytic Sample and Data Analysis Approach

Data from the daily phone interviews over a period of 42 days resulted in a total of 3,068 possible data points (due to religious holidays, data collection with 10 participants was shortened to 38 days). For the present study, we restricted the analytic sample to those on ARVs at baseline or reporting taking ARVs during the study. Just over forty percent ($n=35$) of the sample did not report being on ARVs at baseline, of which 77% ($n=27$) initiated ART over the course of the study. We therefore excluded 8 participants not on ARVs from the present analysis, resulting in a sample of 74 (52 female, 22 male) who provided 2,718 data points out of a possible 2,861 possible data points.

Using SPSS version 23 (IBM Corp, 2011), we first conducted event-level analysis using generalized estimating equation (GEE) analyses with a binomial distribution and a logit link specified with an autoregressive correlation structure, to account for repeated measurements of participants, to assess the univariate associations between time invariant sociodemographic variables and time-varying variables and the two main outcomes of interest: (1) any ARVs missed today and (2) any ARVs missed last night. In GEE, all data points for each person who has at least two data points can be included; effects of the IVs on the DV are treated as fixed effects and the within-subject correlation structure is treated as a covariate. In most cases, GEE yields results equivalent to mixed modeling (Gardiner et al., 2009). We measured sociodemographic variables including gender, age, education, SES, marital status. We also included three constructs of HIV stigma (anticipated, enacted, internalized), and calculated the mean across all three scales. Finally, taking ARVs at baseline and the average number of drinks across all days and nights were included. Time-varying variables for today and last night included: day (to test for a “time” effect on adherence), stress level, any drinking (yes, no), drinking by risk level (no risk, low-moderate, high-to very high risk). Separate models were run for “today” and “last night.” Other drug use was dropped from the univariate and multivariate analysis due to low prevalence (dagga use: <4% of all days/nights, Mandrax use: <1.5% of all days/nights) in the study sample.

Next, we tested the relationship between each event-level alcohol variable (any drinking, person-centered number of drinks, drinking by risk level) and missed ARVs (today and last night separately), controlling for time-invariant sociodemographic variables found to be significantly associated ($p < 0.10$) with either of the outcome variables in the univariate analysis, or not statistically significant but deemed relevant. In the model assessing person-centered number of drinks only, we control for the average number of drinks per person to disentangle the within-person effect from the between person-effect, as is the recommended practice in this type of analysis (Scientific Software International, 2015). In each model, we also tested for interactions between each alcohol variable and the covariates found significant in univariate associations: gender, age, education, SES, on ARVs at baseline (y/n); we include only those interactions found statistically significant in the multivariate

models. We included “day” in each multivariate model to control for a “time effect” associated with repeated measures. Odds Ratios (OR) from univariate analysis and Adjusted Odds Ratios (AOR) from multivariate analysis with 95% confidence intervals (CI) are presented and used to interpret the effect size of each predictor variable on the outcome variables.

3. RESULTS

All participants were Xhosa-speaking and the average age was 32.87 (SD 6.69, range 22–55). See Table 1 for a detailed description of participant characteristics and descriptive statistics. Completion rates were high; of the possible 2,861 data points, only 5% were missing, resulting in 2,718 data points available for analysis and the range for completion rates by participant was 73–100%.

Of the 2,718 data points collected across participants, optimal adherence was reported: missed ARVs were reported on 5.6% of days and 7.3% of evenings. Across all days 40.0% included any drinking and 58.60% of all evenings included any drinking. The average number of alcoholic drinks consumed in the daytime and in the evening were 1.94 (SD, range 0–6) and 3.53 (SD 3.99, range 1–8), respectively. Looking at averages across all participants, just over half of days included no drinking (59.70%), as opposed to low to moderate (20.10%) and high to very high risk (20.20%). Across all nights, 41.40% of evenings included no drinking, while 18.80% and 39.80% were classified as low to moderate risk and high to very high risk drinking, respectively. Of 153 daytime events where ARVs were missed, 68.60% including drinking, and 83.90% of 199 evening events of missed ARVs included drinking.

3.1. Univariate Analysis

Table 2 displays the findings from univariate logistic regression analyses testing the associations between independent variables and the outcomes of any ARVs missed today and any ARVs missed last night. In sum, predictors ($p < 0.10$) of missed ARVs today included: age, education, average number of drinks, on ARVs at baseline, day (time effect), stress level, and all time-varying alcohol variables. Predictors ($p < 0.10$) of missed ARVs last night included all of the above mentioned variables, with the addition of SES.

3.2. Multivariate Analysis

3.2.1. Does consuming any alcohol compared to no alcohol on a particular day/evening influence ARV adherence that day/evening?—Controlling for time-invariant sociodemographics and day (time effect), those who drank any alcohol today were more than three times more likely to report missing ARVs today compared to those reporting no alcohol use (AOR = 3.18, 95% CI = 2.25–4.9, $p < 0.001$). Those on ARVs at baseline were more likely to report missed ARVs (AOR = 1.71, 95% CI = 0.95–3.06) though only marginally significant ($p = 0.07$). The likelihood of missing ARVs during the daytime also decreased slightly over time (AOR = 0.97, 95% CI = 0.95–0.98, $p < 0.001$). All other main effects of each covariate were no longer statistically significant in the full model (see Table 3).

Controlling for sociodemographics, those who drank any alcohol last night were 3.43 times more likely to report missing any ARVs last night compared to those who did not consume alcohol last night (95% CI = 2.13–5.53, $p < 0.001$). There was a significant time effect, with fewer missed ARVs over time (AOR = 0.97, 95% CI = 0.95–0.99, $p = 0.004$). No other statistically significant main effects or interactions were observed between covariates and any alcohol consumption last night.

3.2.2. Does consuming more alcohol than one normally consumes on a particular day/evening influence ARV adherence that day/evening?—For each additional drink consumed during the daytime more than what the individual usually consumed during the daytime (person-centered), participants were 6% more likely to report missing ARVs today (AOR = 1.06, 95% CI = 1.02–1.11, $p = 0.005$) (see Table 4). This effect was stronger for those with lower SES compared to those with higher SES (interaction: AOR = 0.91, 95% CI = 0.85–0.97, $p = 0.005$). With all other variables entered in the model, the main effect of average number of drinks, representing the between-person effect of alcohol, remained positively associated with missed ARVs today (AOR = 1.99, 95% CI = 1.47–2.69, $p < 0.001$) and time remained negatively associated with missed ARVs today (AOR = 0.96, 95% CI = 0.95–0.98, $p < 0.001$).

Controlling for time-invariant factors, as well as the time varying factor of average number of drinks last night and time effect, for every 1 additional drink last night (person-centered), there was a 10% increased likelihood of reporting missed ARVs last night (AOR = 1.10, 95% CI = 1.05–1.15, $p < 0.001$). The main effect of the individual's average number of drinks last night, representing the between-person effect of drinking, remained statistically significant (AOR = 1.36, 95% CI = 1.14–1.61, $p = 0.001$). The time effect remained negatively associated with missed ARVs last night (AOR = 0.97, 95% CI = 0.95–0.99, $p < 0.001$). No statistically significant interactions were identified.

3.2.3. Does drinking at different risk levels (low-moderate, high-very high) on a particular day/evening influence ARV adherence on that day/evening compared to no drinking?—Controlling for sociodemographic factors, participants reporting low to moderate levels of drinking today were more than four times more likely to report missing ARVs today compared to those reporting no drinking today (AOR = 4.29, 95% CI = 2.81–6.56, $p < 0.001$) and those drinking at high to very high risk levels were more than two times as likely to report missing ARVs today compared to those reporting no drinking today (AOR = 2.31, 95% CI = 1.56–3.42, $p = 0.001$) (see Table 5). The negative time effect on adherence was statistically significant (AOR = 0.96, 95% CI = 0.95–0.98, $p < 0.001$), and individuals on ARVs at baseline were more likely to report missed ARVs today (AOR = 1.71, 95% CI = 0.95–3.08, $p = 0.08$) (borderline significant).

Similarly, in the adjusted models for last night, those who drank at a low to moderate risk level last night were over four times more likely to report missed ARVs last night compared to those reporting no alcohol consumption last night (AOR = 4.24, 95% CI = 2.38–7.54, $p < 0.001$) and those who drank at a high to very high risk level were three times more likely to report missed ARVs last night compared to those reporting no alcohol consumption last night (AOR = 3.08, 95% CI = 1.91–4.98, $p < 0.001$). Time was negatively associated with

missed ARVs last night (AOR = 0.97, 95% CI = 0.96–0.99, $p=0.004$); all other main and interaction effects were not statistically significant.

4. DISCUSSION

This is the first study to our knowledge to examine the event-level association between alcohol use and ARV adherence among PLHIV in a developing country. Among our study sample of PLHIV in South Africa, we found that when participants drank, they were at an increased likelihood of missing ARVs, controlling for relevant confounders. While adherence was high in our sample, drinking occurred during the majority of days and nights in which ARVs were missed. Our findings may point to the negative influence of alcohol on achieving perfect to near perfect adherence-levels (Hendershot et al., 2009; Parsons et al., 2008); despite evidence for lower levels of adherence needed for newer therapies (Bangsberg, 2006; Martin et al., 2008) 95% or greater adherence remains the recommended goal to avoid suboptimal outcomes (Gross et al., 2006; Lima et al., 2008; WHO, 2014b).

Our findings increase our confidence in a direct relationship between alcohol and adherence by linking drinking and missed doses of ARVs to the same 12 hour time period, and by ruling out a number of potential confounders. Sociodemographic factors did not negate the effect of alcohol on adherence, though for daytime drinking and adherence, alcohol had a more negative effect on adherence among those of lower SES. Increasing the sample size for people categorized as high SES ($n=11$ in sample), however, would increase the robustness of this finding. Furthermore, other drug use was reportedly low in our sample (Mandrax < 2%; “dagga” or cannabis use < 4%) and therefore was not assessed; while the low prevalence of other drug use makes it unlikely to account for the alcohol-adherence relationship, it should be explored further in future studies (Hendershot et al., 2009).

Controlling for several relevant confounders, participants in our sample who used alcohol on a particular day were more than three times more likely to miss their ARVs that day, and those who used alcohol on a particular evening were nearly three and a half times more likely to miss taking ARVs than those who abstained from alcohol use that evening. The largest effect was observed when alcohol was used at a low to moderate risk level (men: 1–5 drinks; women: 1–3.3 drinks) compared to those not drinking, suggesting that even low risk drinking can interfere with adherence. Our data also shows that alcohol’s effect on non-adherence is still apparent even after controlling for each person’s normal alcohol consumption (person-centered). For example, when someone drinks 3 drinks more than they normally consume at night, the odds of missing ARVs increases by 30%. Controlling for individual differences is important because one’s tolerance or susceptibility to cognitive impairment likely varies across individuals and may occur even if the magnitude of drinking does not meet criterion for risky drinking (Braithwaite et al., 2008; Hendershot et al., 2009).

In contrast with other studies reporting a “dose-response” relationship between alcohol and non-adherence (Braithwaite et al., 2008, 2005; Hendershot et al., 2009), in our sample the effect size was larger relative to individuals who reported not drinking, for those drinking at the low-moderate than the high-very high risk level. However, the difference between low-moderate to high-very high risk drinking was not statistically significant. Nonetheless, other

studies have reported similar findings (Parsons et al., 2008; Samet et al., 2007, 2004; Sankar et al., 2007; Tucker et al., 2003). It may be possible that heavy drinking is more premeditated, and is associated with greater perceived risk for non-adherence, resulting in more careful planning of taking one's ARVs before drinking. Another explanation is that individuals who drink at lower levels are more likely to intentionally skip doses of ARVs due to greater perceptions of the risk of toxic interactions compared to heavy drinkers, as found by other research (Sankar et al., 2007). Future research should continue to investigate the nature of the incremental relationship between alcohol and adherence, including how perceived toxicity and alcohol-related expectancies differentially affect adherence behavior at different drinking levels.

Prior studies demonstrate an increased effect of alcohol use on non-adherence when the regimen is more complex (Hendershot et al., 2009; Parsons et al., 2008). We were unable to include regimen complexity in our analyses, as part of the sample started ART after baseline. However, we expect all participants were on the recommended first line therapy at the time (i.e., D4T + 3TC + (NVP or [EFV]) (National Department of Health South Africa, 2004); minimal variation may reduce the importance of ARV regimen as a moderator in our sample. Notably, those on ARVs at baseline were more likely to report missed ARVs than those who started ART over the course of the study. Baseline ARV status, however, did not moderate the alcohol—non-adherence relationship. Our null findings between gender and adherence may be partly due an unequal number of men and women enrolled in the study and on ARVs, which would reduce our ability to detect gender differences. Using dichotomous and self-reported assessments of adherence might also have decreased statistical power in our study (Hendershot et al., 2009).

Our daily diary approach is likely to have reduced recall bias inherent in retrospective data collection methods. While a time effect was apparent (participants reported better adherence and less drinking over time), time did not negate nor moderate the alcohol-adherence relationship in the multivariate models. It's likely that daily self-monitoring of adherence and drinking improved these health behaviors over the course of the study, highlighting diary approaches as potentially effective interventions for adherence and alcohol use. Nonetheless, our generalizability may be limited to individuals engaging in self-monitoring behavior. The generalizability of our sample is also limited to individuals who were seeking HIV services in an urban area, had recently consumed alcohol and engaged in sexual activity, and those owning a cell phone, which may be an indicator for higher SES. Generalizability is also limited by the fact that eligibility for ART in South Africa was a CD4 T-cell count of less than or equal to 200 at the time of the study; we did not gather data on the participants' CD4 count or viral load, but patients in our study may have been more immune compromised than patients on ART today. Finally, while our study methodology increases our confidence in a direct alcohol-adherence relationship by linking drinking and adherence to the same time period, it still does not provide evidence for causation, as we cannot fully infer temporality between drinking and missed ARVs. It is possible that ARVs may have been missed before drinking, which could be done intentionally based on misperceptions about toxicity interactions (Kalichman et al., 2009, 2013; Sankar et al., 2007).

The current findings support the event-level negative influence of alcohol use on ARV adherence, and that more support services for PLHIV are needed, as well as interventions that reduce alcohol use among PLHIV struggling with consistent adherence. Two randomized trials among hazardous drinkers in the U.S. found no effect on alcohol reduction (Parsons et al., 2007; Samet et al., 2005), but one did observe significant improvements in adherence rates (Parsons et al., 2007). Given the high rates of drinking in this sample, a more feasible aim may be to help PLHIV who drink with adherence maintenance, rather than to get them to stop drinking all together. Several randomized trials for alcohol-focused ART maintenance are underway in South Africa, with support for efficacy reported to date (Huis in 't Veld et al., 2012; Parry et al., 2014). Future studies should continue to use event-level methodology to understand the pathways in which alcohol and adherence may be linked, and if possible, temporally order the drinking—missed ARVs association.

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Highlights

- All alcohol variables were associated with missed antiretrovirals at the event-level.
- The largest effect was at a low-moderate level compared to no drinking.
- This finding remained controlling for each person's normal alcohol consumption.

Table 1

Participant Characteristics and Descriptive Statistics for Time-Invariant Factors and time-varying measures
N=74

	%	Mean	SD	Range
Time-invariant factors				
Gender				
Female	71.60			
Male	28.40			
Age		32.87	6.69	22.00–55.00
Education				
Secondary or greater	53.60			
Primary or less	46.40			
Socioeconomic status				
Money for basics or more	14.50			
Money for basics or less	85.50			
Marital status				
Married or in a relationship	53.60			
Single	46.40			
Disclosed to partner(s)				
Yes	92.00			
No	8.00			
Total stigma score		1.41	0.55	0.04–2.48
Anticipated HIV stigma		1.50	0.55	0.09–2.78
Enacted HIV stigma		1.42	0.69	0.00–2.67
Internalized HIV stigma		1.22	0.65	0.00–2.67
Average number of drinks today		1.94	0.91	0.00–6.00
Average number of drinks last night		3.53	1.34	1.00–8.00
Time-varying factors				
Stress level today		0.54	1.19	0.00–6.00
Stress level last night		0.54	1.27	0.00–6.00
Days with any dagga (cannabis) use	3.70			
Evenings with any dagga (cannabis) use	3.90			
Days with any mandrax (Methaqualone) use	1.40			
Evenings with any mandrax (Methaqualone) use	1.30			
Days with any drinking	40.30			
Evenings with any drinking last night	58.60			
Days with drinking by risk level				
High to very high	20.20			
Low to moderate risk	20.10			
No risk	59.70			
Evenings with drinking by risk level				
High to very high	39.80			

	%	Mean	SD	Range
Low to moderate risk	18.80			
No risk	41.40			
Days with any missed ARVs	5.60			
Evenings with any missed ARVs	7.30			
Days where ARVs missed and alcohol used	68.60			
Evenings where ARVs missed and alcohol used	83.90			

Note: Proportion of day/evenings of substance abuse includes the total number of reported days/evenings where any substance abuse occurred across all days reported. Time invariant factors were measured during baseline and time-varying factors were measured over 42 daily structured phone interviews.

Results of univariate logistic GEE analysis for predictors of any ARVs missed today and any ARVs missed last night, N=74

Table 2

	Missed ARVs today n=2,202			Missed ARVs last night n=2,202		
	OR (95% CI)	χ^2	p	OR (95% CI)	χ^2	p
Time-invariant factors						
Gender						
Female	1.03 (0.59–1.82)	0.01	0.91	1.14 (0.59–2.19)	0.16	0.69
Male (reference)						
Age	0.96 (0.92–0.99)	4.55	0.03**	0.97 (0.94–1.00)	3.81	0.05 [†]
Education						
Secondary or greater	1.91 (1.09–3.33)	5.18	0.02**	1.56 (0.94–2.58)	2.98	0.08 [†]
Primary or less (reference)						
Socioeconomic status						
Money for basics or more	0.63 (0.32–1.23)	1.84	0.18	0.57 (0.33–0.97)	4.23	0.04**
Money for basics or less (reference)						
Marital status						
Married or in a relationship	0.75 (0.44–1.28)	1.13	0.29	0.85 (0.53–1.39)	0.41	0.52
Single (reference)						
Disclosure	0.80 (0.34–1.88)	0.27	0.60	1.25 (0.58–2.73)	0.32	0.57
Total stigma score	1.00 (0.63–1.59)	0.00	0.10	0.83 (0.56–1.22)	0.95	0.33
Anticipated HIV stigma	0.99 (0.59–1.67)	0.00	0.99	0.82 (0.55–1.22)	0.97	0.32
Enacted HIV stigma	0.97 (0.68–1.37)	0.04	0.84	0.84 (0.62–1.14)	1.19	0.28
Internalized HIV stigma	1.14 (0.77–1.69)	0.41	0.52	0.95 (0.68–1.33)	0.10	0.76
Average number of drinks (across all days)	1.45 (0.99–2.12)	3.74	0.05 [†]	1.22 (1.03–1.45)	5.27	0.02*
On ARVs at baseline						
Yes	1.88 (1.04–3.40)	4.29	0.04*	1.56 (0.93–2.60)	2.84	0.09 [†]
No (reference)						
Time-varying factors						
Day (time effect)	0.96 (0.94–0.97)	26.46	<0.001***	0.97 (0.95–0.98)	16.16	<0.001***
Stress level (person-centered)	1.08 (0.99–1.17)	3.31	0.07 [†]	1.15 (1.04–1.26)	7.94	0.01**

	Missed ARV's today n=2,202			Missed ARV's last night n=2,202		
	OR (95% CI)	χ^2	p	OR (95% CI)	χ^2	p
Any drinking						
Yes	3.19 (2.34–4.35)	53.77	<0.001 ***	3.80 (2.53–5.69)	41.84	<0.001 ***
No (reference)						
Number of drinks (person-centered)	1.08 (1.04–1.12)	14.46	<0.001 ***	1.09 (1.05–1.14)	18.41	<0.001 ***
Drinking by risk level						
High to very high risk	2.83 (2.02–3.97)	36.26	<0.001 ***	3.39 (2.27–5.06)	35.56	<0.001 ***
Low to moderate risk	3.57 (2.40–5.31)	39.57	<0.001 ***	4.68 (2.88–7.60)	38.81	<0.001 ***
No risk (reference)						

Note:

$\hat{\gamma}$
p < .10;

*
p < .05;

**
p < .01.

p < .001;

OR = Odds Ratio; All variables other than time invariant variables were measured both today and last night; Average number of drinks (across all days) = participants' average number of drinks consumed over the 42 events; For any drinking, yes = (1 or more drinks), no = no drinking (0 drinks); Number of drinks (person-centered) = The difference between participants' daily number of drinks and the participant's average number of drinks over the 42 events; Drinking by risk level is based on the WHO's categories for risky drinking by gender (men: no = 0 drinks (0g), low-moderate = 1–5 drinks (1–60g), high-very high = 6 or more drinks (61g or more); women: no = 0 drinks (0g), low-moderate = 1–3.3 drinks (1–40g), high-very high = 3.4 or more drinks (3.4g or more)).²⁹

Results of multivariate logistic GEE analysis assessing the effect of any daytime alcohol use on any ARVs missed today and any evening alcohol use on any ARVs missed last night, controlling for time-invariant sociodemographic factors, N=74

Table 3

	Missed ARVs today n=2,202			Missed ARVs last night n=2,202		
	AOR (95% CI)	χ^2	p	AOR (95% CI)	χ^2	p
Main effects						
Time-invariant factors						
Gender						
Female	1.25 (0.62–2.52)	0.38	0.54	1.37 (0.76–2.47)	1.12	0.30
Male (reference)						
Age	0.98 (0.93–1.01)	2.31	0.13	0.97 (0.93–1.02)	1.41	0.24
Education						
Secondary or greater	1.63 (0.91–2.91)	2.73	0.10	1.52 (0.82–2.82)	1.77	0.18
Primary or less (reference)						
Socioeconomic status						
Money for basics or more	0.70 (0.38–1.31)	1.25	0.26	0.64 (0.34–1.21)	1.91	0.17
Money for basics or less (reference)						
On ARVs at baseline						
Yes	1.71 (0.95–3.06)	3.22	0.07 [†]	1.38 (0.80–2.38)	1.30	0.26
No (reference)						
Time-varying factors						
Day (time effect)	0.97 (0.95–0.98)	14.65	<0.001 ^{***}	0.97 (0.95–0.99)	8.47	0.004 ^{**}
Any drinking						
Yes	3.18 (2.25–4.49)	24.76	<0.001 ^{***}	3.43 (2.13–5.53)	25.41	<0.001 ^{***}
No (reference)						

Note:

[†] p < .10;

* p < .05;

** p < .01.

AOR = Adjusted Odds Ratio; All variables other than demographics were measured both today and last night. For any drinking, yes = (1 or more drinks), no = no drinking (0 drinks).

100
> p

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Results of multivariate logistic GEE analysis assessing the effect of drinking more than normal today and last night (person-centered number of drinks) on any ARVs missed today and any ARVs missed last night, controlling for time-invariant sociodemographic factors, N=74

Table 4

	Missed ARVs today n=2,202			Missed ARVs last night n=2,202		
	AOR (95% CI)	χ^2	p	AOR (95% CI)	χ^2	P
Main effects						
Time-invariant factors						
Gender						
Female	1.24 (0.60–2.54)	0.34	0.56	1.62 (0.90–2.93)	2.58	0.11
Male (reference)						
Age	0.97 (0.93–1.01)	1.80	0.18	0.98 (0.94–1.02)	1.29	0.26
Education						
Secondary or greater	1.28 (0.69–2.38)	0.62	0.43	1.50 (0.82–2.74)	1.76	0.18
Primary or less (reference)						
Socioeconomic status (SES)						
Money for basics or more	0.70 (0.42–1.18)	1.82	0.18	0.75 (0.40–1.41)	0.80	0.37
Money for basics or less (reference)						
On ARVs at baseline						
Yes	1.43 (0.83–2.46)	1.66	0.20	1.27 (0.73–2.21)	0.69	0.41
No (reference)						
Average number of drinks	1.99 (1.47–2.69)	20.03	<0.001	1.36 (1.14–1.61)	11.93	0.001**
Time-varying factors						
Day (time effect)	0.96 (0.95–0.98)	15.78	<0.001	0.97 (0.95–0.99)	10.22	0.001**
Number of drinks (person-centered)	1.06 (1.02–1.11)	7.83	0.005**	1.10 (1.05–1.15)	15.44	<0.001***
Interactions						
SES x number of drinks (person-centered)	0.91 (0.85–0.97)	7.78	0.005**			

Note:

[†] p < .10;

* p < .05;

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AOR = Adjusted Odds Ratio; All variables other than demographics were measured both today and last night. Number of drinks (person-centered) = The difference between participants' daily number of drinks and the participant's average number of drinks over the 42 events.

Table 5

Results of multivariate logistic GEE analysis assessing the effect of drinking by risk level on any ARVs missed today and any ARVs missed last night, controlling for time-invariant sociodemographic factors, N=74

	Missed ARVs today n=2,202			Missed ARVs last night n=2,202		
	AOR (95% CI)	χ^2	p	AOR (95% CI)	χ^2	p
Main effects						
Time-invariant factors						
Gender						
Female	1.37 (0.69–2.72)	0.79	0.37	1.46 (0.81–2.62)	1.57	0.21
Male (reference)						
Age						
Age	0.97 (0.92–1.01)	2.50	0.11	0.97 (0.93–1.02)	1.42	0.23
Education						
Secondary or greater	1.60 (0.90–2.83)	2.57	0.11	1.52 (0.82–2.81)	1.74	0.19
Primary or less (reference)						
Socioeconomic status						
Money for basics or more	0.68 (0.36–1.29)	1.40	0.24	0.63 (0.34–1.18)	2.10	0.15
Money for basics or less (reference)						
On ARVs at baseline						
Yes	1.71 (0.95–3.08)	3.16	0.08 [†]	1.39 (0.80–2.40)	1.35	0.25
No (reference)						
Time-varying factors						
Day (time effect)	0.96 (0.95–0.98)	15.99	<0.001***	0.97 (0.96–0.99)	8.29	0.004**
Drinking by risk level						
High to very high risk	2.31 (1.56–3.42)	17.28	<0.001***	3.08 (1.91–4.98)	21.11	<0.001***
Low to moderate risk	4.29 (2.81–6.56)	45.30	<0.001***	4.24 (2.38–7.54)	24.15	<0.001***
No risk (reference)						

Note:

[†] p < .10;

* p < .05;

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AOR = Adjusted Odds Ratio; All variables other than demographics were measured both today and last night. Drinking by risk level is based on the WHO's categories for risky drinking by gender (men: no = 0 drinks (0g), low-moderate = 1–5 drinks (1–60g), high-very high = 6 or more drinks (61g or more); women: no = 0 drinks (0g), low-moderate = 1–3.3 drinks (1–40g), high-very high = 3.4 or more drinks (3.4g or more).²⁹