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Alcohol use and alcohol-related consequences are associated with not being virally suppressed among persons living with HIV in the Rakai region of Uganda

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Abstract

Background: Alcohol use is common among persons living with HIV (PWH) in Uganda and associated with poor HIV care outcomes; findings regarding the relationship between alcohol use and viral suppression (VS) have been inconclusive.

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APM drafted the manuscript. All authors provided input and have approved the final manuscript.

Declaration of Competing Interest

The authors report no declarations of interest.

Methods: Data from two rounds (2017–2020) of the Rakai Community Cohort Study, an open population-based cohort study in the Rakai region, Uganda, were analyzed. Two alcohol exposures were explored: past year alcohol use and alcohol-related consequences. Multivariable models (GEE) were used to estimate associations between alcohol exposures and VS for the overall sample and stratified by sex, adjusting for repeated measurement. Causal mediation by ART use was explored.

Results: Over half (55 %) of participants (n = 3823 PWH) reported alcohol use at baseline; 37.8 % of those reporting alcohol use reported alcohol-related consequences. ART use and VS at baseline significantly differed by alcohol use with person reporting alcohol use being less likely to be on ART or VS. Alcohol use was significantly associated with decreased odds of VS among women but not men (adj. OR 0.72 95 % CI 0.58–0.89, p = 0.0031). However, among males who use alcohol, experiencing alcohol-related consequences was significantly associated with decreased odds of VS (adj. OR 0.69 95 % CI 0.54–0.88, p = 0.0034). The relationships between both alcohol exposures and VS were not significant in models restricted to persons on ART.

Conclusions: We provide sex-stratified estimates of associations between two alcohol measures and VS in the context of current HIV treatment guidelines. This study confirms that alcohol use is adversely associated with VS but ART use mediates this pathway, suggesting that initiation and retention on ART are critical steps to addressing alcohol-related disparities in VS.

Keywords

Uganda; Alcohol; HIV care continuum; Viral suppression; Treatment adherence

1. Introduction

More than half (52.6 %) of Uganda's citizens ≥15 years consume alcohol, and its use is a major public health concern (WHO, 2018). Among those who drink alcohol, 56.9 % have consumed at least 60 g (six drinks) or more of unmixed alcohol on at least one occasion in the past 30 days (WHO, 2018) and per capita annual consumption is 50 % higher than the average individual for the WHO Africa region (9.5 liters compared to 6.3 liters) (WHO, 2018). Rates of alcohol use disorder and physical alcohol dependence are nearly twice that of the overall African region (WHO, 2018). In Uganda there are also pronounced differences in alcohol use by gender: men are more likely to consume alcohol and engage in heavy drinking. Two-thirds of men (68.8 %) who use alcohol report engaging in heavy episodic drinking (defined as at least 60 g of pure alcohol on at least one occasion in the past 60 days) while only one-third of women (32.6 %) who drink alcohol report this same behavior (WHO, 2018). Men in Uganda are also more likely to report experiencing consequences related to their alcohol use, such as drinking on the job (Wagman et al., 2020). These gendered differences in alcohol drinking patterns are culturally ingrained and socially enforced (Breuer et al., 2019; Wolff et al., 2006).

There is overlap between the disease burden of alcohol use and of HIV, another prevalent public health issue in Uganda. National prevalence of HIV in Uganda is 6.2 % (Ugandan Ministry of Health, 2018) and prior research found an estimated 32.7 % of PWH had a biomarker related to unhealthy drinking, Phosphatidylethanol (PEth) ≥ 50 mg/mL

(Magidson et al., 2019). In Rakai, a district in southwestern Uganda, population ~500,000 (Uganda Bureau of Statistics, 2017), HIV prevalence exceeds the national average at 7.9 % (Ugandan Ministry of Health, 2018), including a prevalence as high as 42 % in the fishing communities that lie along the shores of Lake Victoria at the district border (Chang et al., 2016). Overall, 57 % of PWH residing in the district and participating in a previous survey reported past year alcohol use (Rakai Health Sciences Program, 2014).

Alcohol use is a widely recognized risk factor for HIV infection (Fisher et al., 2007; Rehm et al., 2012) and a robust global evidence base suggests that among PWH, alcohol use adversely impacts engagement in HIV care and antiretroviral treatment (ART) outcomes throughout the HIV care continuum (Rehm et al., 2017). Some studies have found a relationship between any level of alcohol use and non-adherence to ART (Hendershot et al., 2009) while others have found threshold effects among heavy drinkers (Samet et al., 2004). Some of this non-adherence is intentional, driven by fears of “alcohol-ART interaction intoxication” beliefs (Kalichman et al., 2013) but doses are also unintentionally forgotten or missed (Hendershot et al., 2009). While the existing literature has consistently found an association between alcohol use and decreased engagement and retention in the HIV care continuum (Azar et al., 2010; Kahler et al., 2017; Vagenas et al., 2015; Wandera et al., 2015), findings on the relationship of alcohol use and viral suppression (VS) have been mixed (Williams et al., 2016).

Ability to achieve VS can be directly affected by alcohol use through biological mechanisms. For example, through the shared metabolic pathway between alcohol use and ART medications (Hahn and Samet, 2010). The relationship between VS and alcohol use may also be mediated by treatment adherence (Baum et al., 2010; Williams et al., 2016). A recent paper by Puryear et al. examined associations between alcohol use and heavy drinking on VS (using a cut-off of <500 viral copies/mL) in a large sample from 28 East African study sites (Puryear et al., 2020). Among all PWH, regardless of ART use, they found a significant association between any alcohol use and VS. While this study included a very large population-based sample (118,923), and rigorous alcohol use measures and virologic outcomes, the data was collected prior to the rollout of universal test-and-treat programs in Uganda, a policy which aims to test all individuals at risk for HIV infection and initiate those with a positive test onto ART immediately.

Early initiation and correct and consistent use of ART can prevent HIV disease progression through the achievement of an undetectable viral load (viral suppression). Accurate measurement of VS is also important to HIV prevention efforts because VS significantly diminishes the likelihood of HIV transmission (Cohen et al., 2016). In 2014, the Joint United Nations Programme on HIV/AIDS (UNAIDS) unveiled its current fast-track framework: the 95–95-95 targets. This framework aims to achieve 95 % coverage of the following by 2030: (1) 95 % of those infected aware of their status, (2) 95 % of PWH who are aware of their status receiving ART and (3) 95 % of those on ART achieving VS.

The present study fills a gap in knowledge regarding the relationships between alcohol use and VS by exploring associations using data from two consecutive rounds of the Rakai Community Cohort Study (RCCS) in Uganda. Achieving VS in Rakai is important because

this is one of many regions in the world with a heavy burden of both HIV and alcohol use and our findings can inform potential avenues of intervention in other regions. The results are especially critical to support Uganda's National HIV strategic prevention efforts due to the district's high HIV prevalence. We propose three broad hypotheses. First, we predict that alcohol use will be positively associated with not being VS. Second, there will be sex differences in alcohol use that may result in differential impacts on VS. Third, we hypothesize that not being VS will be associated with reporting past year alcohol-related consequences (e. g., waking up with shaky hands the morning after drinking). In addition to our hypothesis driven research questions, we also explore the role of current ART use as a potential mediator of the relationship between our two alcohol exposures and VS. This will be the first study in Rakai to focus on VS in data collected *after* the rollout of universal test-and-treat in the district in 2016.

2. Materials and methods

2.1. Study design and data collection

The design and data collection methods of the RCCS have been described in detail previously (Wawer et al., 1998). Briefly, the RCCS is an open cohort longitudinal HIV surveillance study in its 20th continuous round of data collection, (started 1994). The RCCS is conducted across 40 communities in Rakai and neighboring districts. A household census proceeds each round of the survey in order to identify eligible participants. Following the census, residents between the ages of 15 and 49 years who are present and provide written informed consent are invited to participate in the RCCS survey, which covers sociodemographic and behavioral characteristics and health care utilization. HIV rapid testing is performed and post-test HIV counseling, referral to care and ART treatment initiation are provided.

The present study included data collected during RCCS survey rounds 18 (August 2016-May2018) and 19 (June 2018-March 2020) until Uganda declared a national lockdown in response to the COVID-19 pandemic. Of the 40 RCCS communities, 34 were surveyed in both rounds 18 and 19 (prior to lockdown) and these 34 communities were included in the current analysis. Survey round 18 is herein referred to as the baseline study visit.

Ethical approval for the RCCS has been granted by the Johns Hopkins School of Public Health's institutional review board (IRB), Columbia University's IRB, Western IRB, the Uganda Virus Research Institute's Research and Ethics Committee and the Uganda National Council for Science and Technology.

2.2. Measures

All measures were collected at both baseline and follow up; generalized estimating equations (GEE) were used to adjust for within subject correlations from repeated measures.

2.2.1. Primary independent variables—Our primary independent variable of interest was "any alcohol use", a dichotomous variable measured by the question, "Have you drunk any alcohol in the past year, for instance, beer, wine, waragi or other spirits, or home-made beer?" Our second major independent variable of interest was the number of alcohol-related

consequences experienced in the past 12 months. Individuals were asked "In the past 12 months, when you drank alcohol, did you ever have/get the following… (1) unsteady gait; (2) fell over; (3) got angry; (4) got violent/got into a fight; (5) had difficulty speaking; (6) forgot some of the things that you did or that happened while you were drinking; (7) had shaking hands the next morning; (8) felt ashamed of something that you did while drinking. These items were designed to capture aspects of harmful alcohol use and proxies of alcohol dependence as described in our previous research (Wagman et al., 2020). Two of these items (items 4 and 7) were adapted measures from the Michigan Alcoholism Screening Test, a validated alcoholism screening tool (Selzer, 1971) while the remaining items were developed specifically for use in the RCCS. To assess harmful alcohol use, two items were created that were comparable to items in the Alcohol Use Disorders Identification Test (AUDIT): items 6 (blackouts) and 8 (guilt after drinking) (Babor et al., 2001, 1992). Items 3 and 4 assess alcohol-related aggression. Items 1, 2, 5 and 7 assess proxies of alcohol dependence using criteria from the International Classification of Diseases (WHO, 1993). Responses to each of these questions were tallied into a new variable, "number of past year consequences experienced" and based on the distribution of this variable, a dichotomous variable "no consequences vs. any consequences" was created.

2.2.2. Dependent variable—Our outcome variables of interest was VS, which was collected as a continuous variable, viral load, and dichotomized per Ugandan ministry of health guidelines for VS, defined as a viral load ≤1000 viral copies per mL of blood (PEPFAR, 2016).

2.2.3. Covariates—Sociodemographic covariates included sex (male, female), community type (agricultural, fishing, trade), marital status (currently married, previously married, never married), education (no formal education, primary school or higher), employment (defined as the primary occupation of bar/restaurant worker, fishermen, trade/shopkeeper, agriculture/housework, other), religion (Christian, Muslim, other/no religion), age, and household socioeconomic status (an index based on dwelling attributes divided into tertiles for low, middle, high). As a study focused on alcohol use, we also controlled for other substance use, and specifically use of one or more drugs (marijuana, amphetamines, aero fuels ["glue"], mayirungi [a leaf that is chewed with stimulant properties], and/or heroin collapsed into any/no past year drug use) in the past 12 months. "Current ART use" was a dichotomous variable measured by a yes/no response to the question, "Are you currently taking antiretrovirals?"

2.3. Data analysis

All analyses were conducted in SAS studio (SAS Institute Inc., 2021). Data were inspected for errors, omissions, and data outside the limit ranges. Baseline sociodemographic and independent variables of interest were analyzed to characterize the analytic sample overall and explore differences by participant sex. Descriptive analysis included frequencies for dichotomous and categorical variables, measures of central tendency for continuous outcomes and stratified bivariate analysis of covariates by sex using $\chi 2$ analysis and 2 sample T-test. Multicollinearity was assessed by examining the intercorrelations between the predictor variables in the model as well as the tolerance and variance inflation

factor (VIF). VIF and tolerance for independent variables with all three outcome models and intercorrelations between independent variables suggested that there was little multicollinearity between variables. All VIF were approximately 1, no tolerance values were <0.1 and no correlations were >0.7.

We encountered a negligible number of missing observations for VS (0.44 % of observations missing this outcome), as well as one of our covariates, household SES (1.2 %) at follow-up. The source and impact of missing data was not explored further for these variables, given the small proportion of missing observations.

To test our hypotheses, correlates of VS were examined, using multivariable logistic regression models. GEE were built using the proc genmod function in SAS and the logit link and binomial distribution adjusting for correlations from within person observations at the two visits. In order to identify potential bias due to loss-to-follow-up, sociodemographic and drug use covariates identified a priori from the literature were compared for participants that were retained at follow-up and those that were not. This was done for the overall sample as well as for men and women separately. Any variables that were statistically significantly different by retention status using an alpha of 0.05 were included as covariates in multivariable models. We also examined potential covariates by testing associations between these same sociodemographic and drug use variables and VS. Covariates were included in multivariable analysis if they differed by retention status and/or were significantly associated with VS using a p-value of < 0.05. We ran models among all PWH regardless of ART use and among only those that reported current ART use. A stratified analysis by sex was also conducted to explore differences in VS by this variable. Finally, all multivariable models were rerun among persons who use alcohol, this time with our other main independent variable of interest, past year alcohol-related consequences (no consequences vs. any consequences), to evaluate associations between alcohol-related consequences and the outcomes. VS was analyzed among all PWH to best capture the absolute associations between alcohol use and viral load; it was also analyzed among persons reporting current ART use to understand if these variables were associated among those reporting they were currently on treatment and facilitate interpretation of the results in the context of the third 95–95-95 target. We also performed mediation analyses to explore if current ART use mediated pathways between alcohol use and alcohol-related consequences and VS.

The mediation analyses were performed prospectively using the approach described by Vanderweele [31]. Causal mediation models were estimated in SAS using the PROC CAUSALMED function. To explore the pathway from alcohol use to VS mediated by current ART use, a model was estimated for VS at follow-up with alcohol use at baseline as the exposure and current ART use at follow-up as the mediating variable. To explore the pathway from alcohol-related consequences to VS mediated by current ART use, a model was estimated for VS at follow-up with alcohol related-consequences at baseline as the exposure and current ART use at follow-up as the mediating variable. Models were adjusted using baseline measurements of the same covariates from the multivariable GEE models. All models also adjusted for current ART use and VS values at baseline. Beta estimates and ninety-fifth percentile bootstrap bias corrected confidence limits were obtained.

3. Results

3.1. Descriptive characteristics of the sample at baseline

Table 1 describes relevant baseline characteristics for the total sample as well as the characteristics of males and females separately, with all differences across the sexes being statistically significant. A total of 3283 people and 5277 visits contributed to the analysis. Just over half of the sample (55 %) reported past year alcohol use at baseline, including 72 % of men and 44 % of women. Among persons who use alcohol, 38 % reported experiencing any alcohol-related consequences in the past 12 months, with significantly higher rates for men (42 %) than women (31 %). Regarding demography, over half of study participants resided in the fishing communities with only 6% from trade communities. Housework (47.3 %) and fishing (46.1 %) were the most common professions among women and men, respectively. Past year drug use was uncommon, but men were much more likely to report this behavior than women (11 % versus 1%, respectively). Men were more likely to be married than women (66 % versus 55 %). Three quarters (79.2 %) participants reported current ART use at baseline with a greater proportion of women reporting ART use than men (82.1 % vs 79.2 %, $p < 0.0001$). A similar proportion (79.7 %) were VS at baseline; women were more likely to be VS than men (84 % vs 73.2 %, <0.0001).

Fig. 1 shows the proportion of persons who were VS at baseline, overall, and by alcohol use status. Overall, 79.9 % of PWH were VS at baseline. A greater proportion of persons who did not report alcohol use in the past year (84.3 %, 95 % CI 82.3%–86.1%) were VS than those who did (76.0 %, 95 % CI 73.9%–77.9%) ($p < 0.0001$). Persons reporting no past year alcohol use had higher rates of current ART use than those who did not report alcohol use (83.4 % vs. 75.8 %, $p < 0.0001$; data not shown). Among those reporting current ART use at baseline, rates of VS were higher at 93 % (95 % CI 92.0%–94.0%) overall. Again, a greater proportion of persons who did not report alcohol use in the past year (93.8 %, 95 % CI 92.3%–95.1%) were VS than those who did (92.4 % 95 % CI 90.1%–93.8%); however, this difference was not statistically significant ($p = 0.15$).

3.2. Multivariable analysis of alcohol use on VS

Tables 2 present multivariable analysis of the association between past year alcohol use and VS among all PWH. These data are presented for the full sample, and then for men and for women separately. All analyses are adjusted for covariates that were significantly associated with VS in bivariate analysis and/or were associated with retention at follow-up. Past year alcohol use was significantly associated with VS (OR 0.73 95 % CI 0.62–0.87 $p = 0.0004$), as hypothesized. However, when stratifying by sex, only women showed a significant lower odds ratio for this relationship.

Table 3 presents the same multivariable analysis presented in Table 2, but the sample is restricted to only those who reported current ART use. After adjusting for covariates, among those currently on ART, past year alcohol use was not significantly associated with VS, overall (OR 0.97 95 % CI 0.74–1.27 $p = 0.8164$) or in sex stratified analysis.

3.3. Multivariable analysis of alcohol use consequences on VS

Tables 4 summarize multivariable analysis results of the association between past year experiences of alcohol-related consequences and VS among individuals in the sample who reported alcohol use in the past12 months (regardless of ART use). These data are presented for the full sample, and then for men and for women separately. All analyses are adjusted for covariates that were significantly associated with VS in bivariate analysis and/or were associated with retention at follow-up. Experiencing past year alcohol-related consequences was significantly associated with lower odds of VS (OR 0.69 95 % CI 0.57–0.85, p = 0.003); when stratified by sex, this finding was only statistically significant for men.

Table 5 presents the same multivariable analysis presented in Table 4, but the sample is restricted to only those who reported current ART use. After adjusting for covariates, among those currently on ART, past year alcohol related consequences were not significantly associated with VS, overall (OR 0.75 95 % CI 0.54–1.03 p = 0.0764) or in sex stratified analysis.

3.4. Analysis of mediation by current ART use for any alcohol use and VS

In the overall sample, a significant natural indirect effect (NIE) was observed (β = 0.01, 95 % CI 0.00–0.02, p = 0.0193); in sex stratified analysis, the indirect effect was no longer significant among women (β = 0.01, 95 % CI −0.01–0.01, p = 0.5215) or men (β = 0.00, 95 % CI −0.00–0.01, p = 0.0704).

3.5. Analysis of mediation by current ART use for alcohol-related consequences and VS

Among persons who use alcohol, no significant indirect effects were observed, overall (β = 0.00, 95 % CI −0.01–0.02, p = 0.6399) or in sex stratified analysis (β = 0.00, 95 % CI −0.01–0.02, p = 0.5622 and β = 0.01, 95 % CI −0.01–0.02, p = 0.7515 among women and men, respectively).

4. Discussion

The present study fills important gaps in the existing literature regarding the relationship between alcohol use and HIV care outcomes in Uganda using an objective measure (VS) in a large generalizable prospective cohort. It is the first to explore associations between alcohol use and VS in Uganda in the context of current HIV treatment guidelines. We provide estimates for the association between two alcohol use measures and VS among all PWH to capture absolute associations; we also provide estimates for these same associations among persons currently on ART for ease of interpreting our findings in the context of the 95–95-95 fast-track targets. Prospective mediation analysis by current ART use was also performed. Finally, we explored sex differences in the relationship between alcohol use and VS through stratified anaylsis. We found that alcohol use and alcohol-related consequences were significantly associated with not being VS; however, when restricting to those currently on ART, the relationship between our alcohol use measures and VS was no longer significant. The analysis confirmed many, but not all our hypotheses, including finding clinically significant differences in viral load (i.e., the achievement of VS) by alcohol use status and observing sex specific differences in our results. Significant inverse associations

between alcohol-related consequences and VS were driven by the relationship between these variables in men while significant inverse associations between any alcohol use and VS were driven by the relationship between these variables in women. These findings have important public health implications and address existing gaps in understanding the effects of alcohol use on VS in the era of universal test and treat.

When studying the relationship between alcohol use and VS (regardless of current ART use), we found that those reporting any alcohol use were significantly less likely to be VS. When restricting to persons currently on ART, the relationship was no longer significant. Participants who reported alcohol use in our sample were significantly less likely to currently be on ART; differences in ART coverage by alcohol use status may have driven the differences in viral suppression observed when not restricting to those currently on ART. Alcohol use is associated with both delayed initiation of ART as well as non-adherence (Hendershot et al., 2009; Monroe et al., 2016; Patsis et al., 2020). However, current ART regimens are more forgiving of missed doses and this could also explain high rates of VS among all participants on ART (Gordon et al., 2015). We relied on self-reported ART use, a measure subject to measurement error due to social desirability bias which may have resulted in nondifferential misclassification of ART use status and biased our estimates towards the null. Future work should utilize objective measures of ART adherence to limit this potential source of bias.

Our findings are consistent with Puryear et al. (2020), who observed a significant association between VS and alcohol use when looking in their overall sample, but not when controlling for ART use (Puryear et al., 2020). Prior studies have found that ART use mediated the relationship between alcohol use and VS (Baum et al., 2010; Hahn and Samet, 2010). For any alcohol use, we observed a significant natural indirect effect which suggests mediation by ART use; however, among persons who use alcohol, ART use did not mediate the relationship between experiencing consequences and VS (i.e., no significant indirect effect). Additional research is warranted to further disentangle the relationship between alcohol use, ART use, and VS, preferably using objective measures for both alcohol use and ART use.

In sex stratified analysis, only women who used alcohol in the past year had statistically significant lower odds of VS. It is possible that the lack of significant association between alcohol use and VS among men is a product of the alcohol use measure itself not being sensitive enough to detect differences in patterns of alcohol use (e.g., hazardous alcohol use) that may differentially impact VS. Ideally, alcohol use is measured by a validated scale that allows for differentiation of drinking behaviors, such as the Alcohol Use Disorder Identification Test (AUDIT) to detect problematic alcohol use (Babor et al., 1992). In Uganda, persons who drink tend to drink heavily (WHO, 2018), so our measure is more sensitive in this context than others, but this variable still captures a wide range of alcohol use behaviors from very low risk (e.g. ceremonial drinking on special occasions) to very high risk (e.g. regular binge drinking). The lack of precision regarding alcohol use behaviors captured by this variable may have reduced our ability to detect a significant association if the relationship between alcohol use and VS is strongest among those in the heaviest drinking categories, as has been observed in previous studies (Baum et al., 2010; Miguez et al., 2003; Puryear et al., 2020).

Among persons who use alcohol, those reporting at least one past year alcohol-related consequence were significantly less likely to be VS than those reporting none. When stratified by sex, this relationship was only significant among men. Several previous studies have found that individuals in the heaviest drinking categories are the least likely to achieve VS, and a recent biomarker study in Uganda found that men are more likely than women to underreport unhealthy levels of drinking (Magidson et al., 2019). If this extends to reporting of alcohol-related consequences, men in our sample may have actually experienced a greater number of consequences than reported which would bias our estimates towards the null. Furthermore, our finding related to the relationship between alcohol-related consequences and VS (which was significant among all PWH but not mediated by ART use) suggests that other unmeasured confounders (e.g., mental health) may be the key to better understanding this pathway.

In Uganda, men are not only more likely than women to drink, they are also more likely to consume hazardous amounts of alcohol, a trend seen globally (WHO, 2018). These gendered differences in alcohol consumption are most pronounced in societies with greater gender inequality (Wilsnack et al., 2009). The lack of significant association between alcohol-related consequences and VS among women may be a product of different gendered patterns of drinking. Social norms around alcohol use in Uganda dictate gendered differences in where and how one can consume alcohol. Prior work in Rakai has found that it is less socially acceptable for women to consume alcohol than men (Breuer et al., 2019); furthermore men in more rural (i.e., traditional) areas of Uganda have agency to consume alcohol outside of the household at drinking establishments (Wolff et al., 2006). Still, we found that women who reported any past year alcohol use were statistically significantly less likely to be VS, suggesting differences in VS by alcohol use status. Women who report any level of alcohol use in Rakai may have less heterogeneity in their drinking behaviors than men (i.e., they may mostly be low level users) or they may be underreporting their alcohol-related consequences for social desirability, diminishing differences between our categories of persons who use alcohol.

Although the prevalence of other drug use in Uganda is low and only a small proportion of participants in our study reported use of drugs other than alcohol this covariate was significant in some models and an important potential confounder in the relationship between alcohol use and VS. A recent systematic review of factors associated with alcohol use disorder among PWH in sub-Saharan Africa found that khat chewing (a commonly used amphetamine in the region) as well as non-adherence to ART were both strongly positively associated with alcohol use disorder (AUD) in PWH (Necho et al., 2020). In our sample, nearly all drug use was reported by persons who also reported alcohol use (88 %, results not shown). Although drug use is uncommon in this setting, its overlap with alcohol use and associations with AUD, non-adherence to ART medication and VS indicate it is an important topic to address in alcohol use interventions in this setting.

This analysis identified alcohol use as an important barrier to achieving VS in Uganda. It provides timely estimates for VS in an area heavily impacted by the HIV epidemic and explores differences in the relationship between alcohol and VS by sex. These findings have important implications for public health planning because alcohol use is a modifiable

risk behavior that can be targeted for behavior change. Despite data collection occurring in the era of universal test and treat, we observed differences in current ART use status, suggesting persons who use alcohol were not initiating ART at the same rate as persons who reported no alcohol use. Research with patients as well as providers exploring reasons for this difference in ART use is needed. The negative association between alcohol use and VS and the fact current ART use mediated this relationship suggests that interventions to address alcohol use among PWH should occur as early in the care and treatment cascade as possible (i.e., at the point of HIV testing) to facilitate immediate uptake and adherence to treatment. Our recent qualitative work in the region suggests that immediately after receipt of HIV test results is an optimum time to screen for and intervene on harmful drinking (Miller et al., 2021). Participants indicated such an intervention would be acceptable and that people's willingness to implement lifestyle changes immediately after receiving their results offers a unique window of susceptibility to behavior change. Counseling around the harms of alcohol use is already discussed by healthcare providers once an individual is engaged in routine HIV care, so this would involve extending alcohol-related counseling by introducing it at an earlier stage in the continuum: time of diagnosis. Among men who consume alcohol we observed lower odds of VS among those experiencing consequences related to their alcohol use, suggesting that men who consume enough alcohol to experience these consequences should be a priority population for alcohol interventions. Current ART use did not mediate this relationship and more work is needed to understand what other variable may be influencing the relationship between alcohol-related consequences and VS among men. More rigorous alcohol measures in this setting are also needed to clearly distinguish types of drinkers and further identify highest priority populations.

To date there is limited evidence available regarding the effectiveness of interventions to address alcohol use among PWH and even fewer studies looking at this problem in Africa (Sileo et al., 2020, 2021). Additional work is needed to adapt and pilot effective interventions to reduce risky alcohol consumption or treat alcohol use disorders from other settings. Findings from prior work suggests a balance needs to be struck between not overburdening the primary healthcare system (i.e., limiting the additional time and effort an integrated intervention demands of health care providers) while also ensuring intervention dose is large enough to be effective.

This study had several limitations related to variable availability. All our outcomes and risk factors except for viral load were self-reported measures, subject to bias. Validated measures for harmful and hazardous alcohol use were not available and the included alcohol use variables may not have been sensitive enough to identify differences in VS by patterns of alcohol use in our study sample. In addition, variables from important domains that may confound the relationship between alcohol use and our HIV outcomes of interest (such as measures of impulsivity (Patton et al., 1995) and mental health (Radloff, 2016; Spitzer, 1999) were not available, which may result in unmeasured (and therefore uncontrolled) confounding in our analysis. We were also not able to control for time since diagnosis in our models. RCCS is an open cohort study; although HIV tests are performed at each visit, there is no way of knowing if the oldest available test on file for an individual in the RCCS dataset is their first positive test. Finally, the associations reported in this paper should be interpreted with caution; they are odds ratios and may not approximate the relative risk. Furthermore,

the primary analysis is not prospective, and causality cannot be inferred from our results. However, the mediation analysis was prospective. Despite these limitations, our study had a number of strengths including the large sample size, use of virologic outcomes and the timeliness of the presented findings which reflect current treatment guidelines and protocol.

This study confirms that alcohol use is adversely associated with VS, but the relationship was no longer significant when restricting to persons on ART. ART use mediated the pathway between any alcohol use and VS, suggesting that initiation and retention on ART are critical steps to addressing alcohol-related disparities in VS. In the era of test and treat, treatment is offered at time of diagnosis, presenting an opportune time to intervene on alcohol use to improve uptake and retention of ART and VS. Among persons who use alcohol, experiencing alcohol-related consequences is also associated with not being VS. Alcohol consumption should be a target of intervention among PWH in Uganda, especially those recently diagnosed as HIV-positive to improve their own health as well as regional HIV care continuum outcomes. The use of objective measures and validated measures for alcohol use and ART adherence in future studies are also needed to explore if a dose-response relationship between alcohol use and VS exists.

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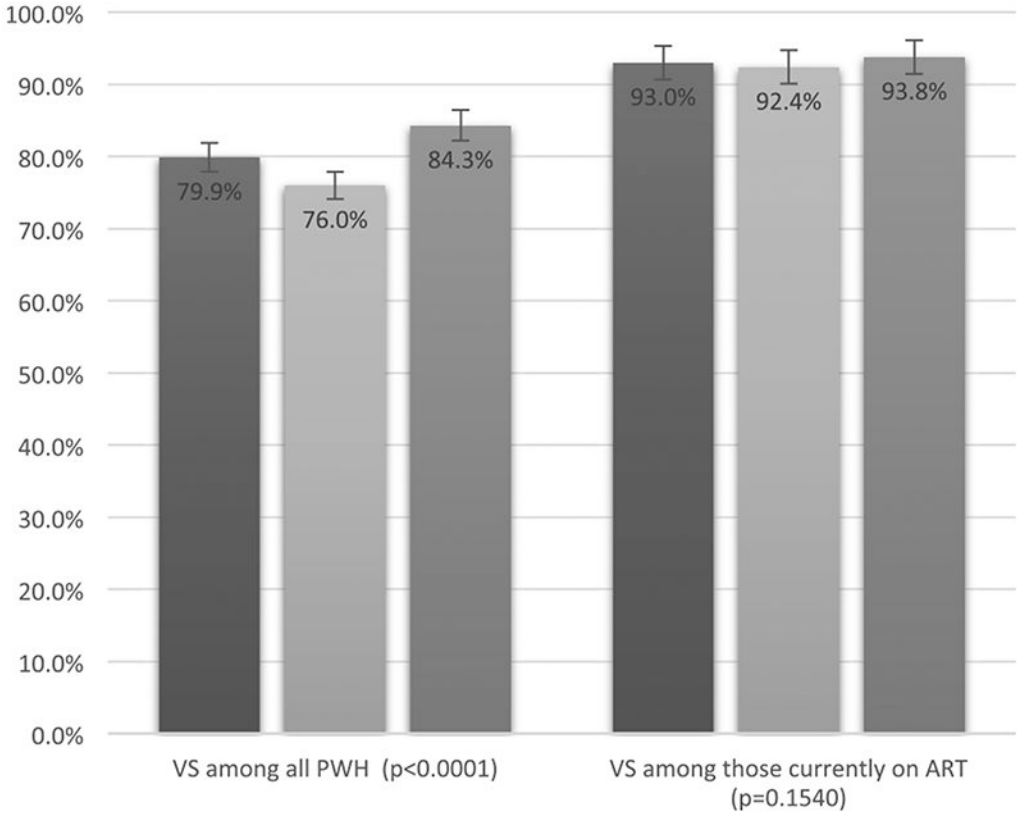

Fig. 1.

Proportion Of PWH Virally Suppressed at Baseline, by Past Year Alcohol Use Status.

Darkest grey = overall.

Lightest grey = persons who use alcohol.

Medium grey = persons who do not use alcohol.

Table 1

Baseline (round 18) characteristics of PWH participating of the Rakai Community Cohort Study, overall and stratified by sex.

Characteristic		Overall (n = 3283)	Men (n = 1310)	Women (n = 1973)	P-value for Chi^2	Chi^2
Past year alcohol use					<0.0001	258.7
	Yes	1816 (55.3 %)	949 (72.4 %)	867 (43.9 %)		
	No	1467 (44.7 %)	361 (27.6 %)	1106 (56.1 %)		
Alcohol-related consequences *					<0.0001	32.1
	None	1127 (62.2 %)	532 (58.2 %)	595 (68.7 %)		
	Any	685 (37.8 %)	414 (43.8 %)	271 (31.3 %)		
Mean Age (SD)		34.5 (7.5)	36 (7.0)	33.6 (7.6)	<0.0001	t = 9.9
Current ART Use					<0.0001	24.1
	Yes	2601 (79.2 %)	982 (75.0 %)	1619 (82.1 %)		
	No	682 (20.8 %)	328 (25.0 %)	354 (17.9 %)		
Residence					<0.0001	62.3
	Agrarian	1305 (39.8 %)	439 (33.5 %)	866 (43.9 %)		
	Trade	200 (6.1 %)	54 (4.12 %)	146 (7.4 %)		
	Fishing	1778 (54.2 %)	817 (62.4 %)	961 (48.7 %)		
Education					<0.0001	18.8
	No School/Primary	1036 (31.6 %)	470 (35.9 %)	566 (28.7 %)		
	Secondary or above	2247 (68.4 %)	840 (64.1 %)	1407 (71.3 %)		
HH SES					0.0003	16.1
	High	1631 (50.3 %)	595 (46.9 %)	1036 (52.5 %)		
	Middle	579 (17.9 %)	219 (17.2 %)	360 (18.3 %)		
	Low	1033 (31.9 %)	456 (35.9 %)	577 (29.2 %)		
Occupation					<0.0001	154.2
	Housework	1209 (36.8 %)	276 (21.1 %)	933 (47.3 %)		
	Trade/shopkeeper	556 (16.9 %)	146 (11.2 %)	410 (20.8 %)		
	Bar/Restaurant worker	268 (8.2 %)	collapsed into "other" *	261 (13.2 %)		
	Fisherman	605 (18.4 %)	604 (46.1 %)	collapsed into "other" *		
	Other	645 (19.7 %)	284 (21.7 %)	369 (18.7 %)		

Characteristic		Overall (n = 3283)	Men (n = 1310)	Women (n = 1973)	P-value for Chi^2	Chi^2
Religion					0.0005	15.2
	Christian	2891 (88.1 %)	1188 (90.7 %)	1703 (86.3 %)		
	Muslim	370 (11.3 %)	113 (8.6 %)	257 (13.0 %)		
	None/Other	22 (0.7 %%)	9 (0.7 %)	13 (0.7 %)		
Any Drug Use **					<0.0001	171
	Yes	165 (5.0 %)	146 (11.2 %)	19 (1.0 %)		
	No	3118 (95.0 %)	1164 (88.9 %)	1954 (99.0 %)		
Marital Status					<0.0001	43.1
	Currently Married	1956 (59.6 %)	867 (66.2 %)	1089 (55.2 %)		
	Previously Married	1124 (34.2 %)	363 (27.7 %)	761 (38.6 %)		
	Never Married	203 (6.2 %)	80 (6.1 %)	123 (6.2 %)		

*Only individuals reporting past year alcohol use were asked about past year consequences related to their alcohol use.

**due to small cell sizes these categories were collapsed into “other” in the sex stratified analysis.

***3.7 % reported marijuana use, 0.1 % reported amphetamine use, 0.03 % reported aerofuels, 2.3 % reported amayirungi use and 0.4 % reported heroin use.

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Table 2

Multivariable GEE of the Relationship between Past Year Alcohol Use and Viral Suppression among PWH.

	Overall* (n = 3283)				Men** (n = 1310)				Women*** (n = 1973)			
	B	**SE**	**OR (95 % Cl)**	**P value**	**B**	**SE**	**OR (95 % Cl)**	**P value**	**B**	**SE**	**OR (95 % Cl)**	**P value**
Past Year Alcohol Use												
Yes	−0.31	0.09	0.73 (0.62–0.87)	0.0004	−0.24	0.13	0.79 (0.61–1.08)	0.0698	−0.32	0.11	0.72 (0.58–0.89)	0.0031
No	–	–	1.00	–	–	–	1.02	–	–	–	1.00	–

*adjusted for visit no, marital status, HH SES, occupation, sex, drug use, residence.

**adjusted for visit no, marital status, HH SES, drug use.

***adjusted for visit no, marital status, age, occupation.

Table 3

Multivariable GEE of the Relationship between Past Year Alcohol Use and Viral Suppression among Participants Reporting Current ART Use.

	Overall* (n = 2601)				Men** (n = 982)				Women*** (n = 1619)			
	B	**SE**	**OR (95 % Cl)**	**P value**	**B**	**SE**	**OR (95 % Cl)**	**P value**	**B**	**SE**	**OR (95 % Cl)**	**P value**
Past Year Alcohol Use												
Yes	−0.03	0.14	0.97 (0.74–1.27)	0.8164	0.20	0.20	1.22 (0.83–1.81)	0.3171	−0.21	0.17	0.81 (0.58–1.14)	0.2264
No	–	–	1.00	–	–	–	1.02	–	–	–	1.00	–

*adjusted for visit no, marital status, HH SES, occupation, sex, drug use, residence.

**adjusted for visit no, marital status, HH SES, drug use.

***adjusted for visit no, marital status, age, occupation.

Table 4

Multivariable GEE of the relationship between experiencing Alcohol-related Consequences and Viral Suppression among PWH.

	All persons who use alcohol* (n = 1812)				Men** (n = 946)				Women*** (n = 866)			
	B	**SE**	**OR (95 % Cl)**	**P value**	**B**	**SE**	**OR (95 % Cl)**	**P value**	**B**	**SE**	**OR (95 % Cl)**	**P value**
Consequences												
None	–	–	1.00	–	–	–	1.00	–	–	–	1.00	–
Any	−0.37	0.10	0.69 (0.57–0.85)	0.0003	−0.37	0.13	0.69 (0.54–0.88)	0.0034	−0.27	0.17	0.76 (0.54–1.07)	0.1120

* visit no, marital status, HH SES, occupation, sex, drug use, residence.

** visit no, marital status, HH SES, drug use.

*** visit no, marital status, age, occupation.

Table 5

Multivariable GEE of the relationship between experiencing Alcohol-related Consequences and Viral Suppression among Participants Reporting Current ART Use.

	All persons who use alcohol* (n = 1374)				Men** (n = 695)				Women*** (n = 679)			
	B	SE	OR (95 % Cl)	P value	B	SE	OR (95 % Cl)	P value	B	SE	OR (95 % Cl)	P value
Consequences												
None	–	–	1.00	–	–	–	1.00	–	–	–	1.00	–
Any	−0.29	0.16	0.75 (0.54–1.03)	0.0764	−0.10	0.21	0.91 (0.60–1.38)	0.6490	−0.48	0.25	0.62 (0.37–1.01)	0.0569

*adjusted for visit no, marital status, HH SES, occupation, sex, drug use, residence.

**adjusted for visit no, marital status, HH SES, drug use.

***adjusted for visit no, marital status, age, occupation.