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Assessing the Interaction between Depressive Symptoms and Alcohol Use Prior to Antiretroviral Therapy on Viral Suppression among People Living with HIV in Rural Uganda

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Abstract

Although there is evidence of individual associations between depressive symptoms and hazardous alcohol use with suboptimal antiretroviral therapy (ART) adherence among people living with HIV (PLWH), few studies have established how the two risk factors may interact to predict viral suppression. We conducted secondary data analyses with two cohorts of Ugandan PLWH (N = 657) to investigate the hypothesized interaction between depressive symptoms (Center for Epidemiological Studies Depression Scale) and hazardous alcohol use (Alcohol Use Disorder Identification Test – Consumption and/or Phosphatidylethanol biomarker) prior to ART initiation with viral suppression (<550 copies/ml). We were unable to detect an interaction between depressive symptoms and hazardous alcohol use prior to ART initiation with viral suppression in the first two years (M = 19.9 months) after ART initiation (p = 0.75). There was also no evidence of a main effect association for depressive symptoms (Adjusted Odds Ratio [AOR] = 0.88, 95% Confidence Interval [CI]: 0.50, 1.55) or hazardous alcohol use (AOR = 1.37, 95% CI: 0.80, 2.33). PLWH with depressive symptoms and/or hazardous alcohol use appear to exhibit similar levels of viral suppression as others in care; further work is needed to determine effects on HIV testing and treatment engagement.

Keywords

Depressive symptoms; hazardous alcohol use; antiretroviral therapy

There are 37 million people living with HIV (PLWH) in sub-Saharan Africa with 1.8 million new infections each year (Elkington, Bauermeister, & Zimmerman, 2010). HIV “universal treatment” guidelines recommend early initiation of first-line antiretroviral therapy (ART), comprised of a non-nucleoside reverse transcriptase inhibitor with two drugs from the nucleotide or nucleoside reverse transcriptase class (e.g., TDF [tenofovir disoproxil fumarate] / 3TC [Lamivudine] / EFV [efavirenz]) to achieve viral suppression and prevent

onward HIV transmission (World Health Organization, 2015). Viral suppression relies on maintaining optimal adherence (defined as taking ≥80% of prescribed doses; Bezabhe, Chalmers, Bereznicki, & Peterson, 2016; Kobin & Sheth, 2011). Thus, identifying modifiable factors associated with suboptimal ART adherence and ongoing viremia is important for secondary HIV prevention intervention development.

Approximately 46% of PLWH in sub-Saharan Africa meet diagnostic criteria for a depressive disorder, and 30% report current alcohol use, both of which may contribute to suboptimal ART adherence (Mills et al., 2006; Nakimuli-Mpungu, Musisi, Katabira, Nachega, & Bass, 2011; World Health Organization, 2014). Meta-analyses show that reporting clinically significant depressive symptoms (Odds Ratio [OR] = 0.58, 95% confidence interval [CI]: 0.55, 0.62; Uthman, Magidson, Safren, & Nachega, 2014) and drinking alcohol (OR= 0.55, 95% CI: 0.49, 0.61; Hendershot, Stoner, Pantalone, & Simoni, 2009) are associated with lower odds of being adherent among PLWH. Depressive symptoms and hazardous alcohol use may also co-occur and jointly influence adherence (e.g., Farley et al., 2010; Malow et al., 2013; Martinez et al., 2008; Sullivan, Goulet, Justice, & Fiellin, 2011). Depressive symptoms and alcohol use may be mutually reinforcing; depressive symptoms can lead to greater alcohol consumption as a means to cope with negative affective states (i.e., self-medication hypothesis; Khantzian, 1997), and alcohol use can increase risk of depression (Boden & Fergusson, 2011; Swendsen & Merikangas, 2000). Further, depressive symptoms (e.g., Cotrena, Branco, Shansis, & Fonseca, 2016) and alcohol use (e.g., Kist, Sandjojo, Kok, & van den Berg, 2014) are both associated with memory and decision-making difficulties that are critical to medication-taking (Johnson, 2002).

To date, there has been only one study to examine how depressive symptoms and alcohol use interact to influence HIV-related outcomes. Fojo et al. (2018) tested the interaction between depressive symptoms (measured via the Patient Health Questionnaire [PHQ]-9) and hazardous alcohol use (score of ≥ 3 in women or ≥ 4 in men on the Alcohol Use Disorders Identification Test-Consumption – [AUDIT-C]) with viral suppression (defined as having all viral load tests in the subsequent year ≤200 copies/mL) among a multi-city sample of PLWH in the United States (N = 14,380). Hazardous alcohol use was associated with a lower likelihood of viral suppression only among participants with moderate or severe depressive symptoms (OR = 0.80, 95% CI: 0.74, 0.87), while no association was apparent for participants reporting low to mild depressive symptoms (OR = 1.00, 95% CI: 0.95, 1.06). We sought to replicate these findings in a sample of PLWH in sub-Saharan Africa where HIV care guidelines are tailored to what is feasible in a low-income country.

We conducted secondary data analyses with two existing cohorts of Ugandan PLWH to investigate the interaction between depressive symptoms and hazardous alcohol use prior to ART initiation with viral suppression (≤ 550 copies/ml) after at least 6 months of ART. We hypothesized that the strength of the association between hazardous alcohol use and viral suppression would be stronger in participants with clinically significant depressive symptoms compared to participants with no or sub-threshold depressive symptoms. We also examined main effects of depressive symptoms and hazardous alcohol use with viral suppression. We hypothesized that individuals reporting clinically significant depressive symptoms prior to ART initiation would have lower odds of being virally suppressed,

compared to those that did not meet the screener cutoff. We also hypothesized that individuals drinking at hazardous levels would have lower odds of being virally suppressed compared to those that were not.

Method

Participants/Procedures

Participants were recruited from the Immune Suppression Syndrome (ISS) Clinic at the Mbarara Regional Referral Hospital (MRRH) as part of two prospective cohort studies to examine alcohol use among Ugandan PLWH: (1) the Biomarker Research of Ethanol Among Those with HIV (BREATH; Hahn et al., 2016), and (2) the Alcohol Drinking Effects on Progression Prior to Treatment (ADEPT; Hahn et al., 2018). Participants in BREATH were randomized to attend quarterly study visits for one year (main cohort) or a single study visit at six months (minimally assessed cohort) in a sub-study of assessment reactivity (Emenyonu et al., 2017). Participants in ADEPT attended visits every six months until ART initiation. All participants completed structured interviewer-administered surveys and underwent phlebotomy at each study visit.

Study eligibility criteria included: aged ≥18 years, fluent in English or Runyakole (the local language) and living within 60 km of the clinic. In BREATH, participants were new to HIV care, and reported alcohol use in the past year at clinic entry or were suspected of alcohol use by their counselor. In ADEPT, participants were not yet eligible for ART, and we over-sampled for PLWH that drank alcohol in the past year to ensure there were an equal number of those drinking at hazardous levels and those that were not. All procedures were approved by the Uganda National Council for Science and Technology (UNCST), and the Institutional Review Boards (IRB) at the University of California, San Francisco (UCSF), and the Mbarara University of Science and Technology.

This study is a secondary data analysis of the BREATH or ADEPT participants with an ART initiation date in ISS Clinic records During BREATH, the ISS Clinic started ART based on a CD4 count of ≤250 cells/mm^3. In ADEPT, the ISS Clinic started ART based on a CD4 count of ≤350 cells/mm^3 until it was revised midway through the project to ≤500 cells/mm^3. Overall, 67% of the ADEPT cohort and 72% of the BREATH cohort initiated ART. The predictor variables were assessed at the last research study visit prior to ART initiation. The primary outcome variable of viral suppression was derived from the earliest viral load result from the ISS clinic record that was at least 6 months post-ART initiation.

Measures

Covariates.—Demographics were collected at baseline research study visits. Items examined as potential covariates to be included in the primary analyses included: age, gender, education, index of household assets, and cohort (BREATH or ADEPT). Clinic variables examined as potential covariates included: time between ART initiation and viral load testing, and CD4 count at the study visit prior to ART initiation.

Predictors.

Phosphatidylethanol (PEth).: PEth is a highly specific and sensitive biomarker of alcohol use (Hahn et al., 2012). We used PEth to augment self-report to mitigate the potential for underreported alcohol use (Bajunirwe et al., 2014). In BREATH, participants were tested for PEth at all study visits. In ADEPT, participants with detectable PEth at baseline or with self-reported alcohol use at any visit were tested for PEth at all subsequent visits. A cutoff of ≥ 50 ng/mL was considered positive for hazardous drinking (Hahn et al., 2016).

Hazardous alcohol use.: The Alcohol Use Disorders Identification Test-Consumption (AUDIT-C) was used to assess self-reported alcohol use in the prior three months at the study visit prior to ART initiation. Cut-offs of ≥ 4 for men and ≥ 3 for women were used to define AUDIT-C positive (Bradley et al., 2007). Hazardous alcohol use was defined as AUDIT-C positive and/or PEth ≥50 ng/mL (Hahn et al., 2016).

Depressive Symptoms.: Center for Epidemiological Studies Depression Scale (CES-D) was used to assess self-reported depressive symptoms for the previous two weeks at the study visit prior to ART initiation. A score of ≥16 on the CES-D indicated clinically significant depressive symptoms (Radloff, 1977).

Outcome: Viral Suppression.—Viral load data came from the first ISS clinic visit after a participant had been taking ART for at least six months. A cut-off of ≤550 copies was used to denote participants with viral suppression. This cutoff was chosen because the limits of detection varied among clinic results, and it was the highest and most common cutoff value.

Data Analysis

Descriptive analyses estimated the prevalence of depressive symptoms, hazardous alcohol use and viral suppression. Bivariate analyses characterized the associations between participant demographic and health characteristics, depressive symptoms, and hazardous alcohol use with viral suppression. Multivariable logistic regression models analyzed likelihood of viral suppression and included terms for clinically significant depressive symptoms, hazardous alcohol use, and the interaction between depressive symptoms and hazardous alcohol use. Models were adjusted for participant gender, age, education level, household asset index, pre-ART CD4 count, time between ART initiation and viral load testing, and study cohort. In the absence of an apparent interaction between depressive symptoms and hazardous alcohol use, an additional model was fitted that included main effects only. To account for missing viral load data ($N = 114$), we used multiple imputation via chained equations (using 40 generated completed datasets). The univariate and bivariate results presented are based on the observed data; the multivariable results presented are based on the imputed dataset. For sensitivity analyses, the multivariable logistic regression analyses were run again after dropping participants for whom the time between ART initiation and viral load testing exceeded two years. Multiple imputation was used to account for any other missing data in this subset of participants.

Results

Descriptive Findings

Overall, 751 participants were in the cohort studies with 94 missing ART initiation dates from the ISS clinic electronic medical records. When participants with an ART initiation date were compared to those with no ART initiation data, the groups did not differ for clinically significant depressive symptoms ($\chi^2 = 0.12$, $p = 0.94$). However, those 94 excluded were more likely to be drinking at hazardous levels compared to those with an ART initiation date (68% versus 45%, respectively; $\chi^2 = 17.07$, $p < 0.01$). Descriptive statistics for the remaining sample ($N = 657$) are shown in Table 1. Approximately 26% ($N = 130$) met the cut-off for clinically significant depressive symptoms, and 45% ($N = 259$) were characterized as drinking at hazardous levels. The majority of the sample (70%; $N = 459$) were virally suppressed (≤550) at first testing six months after ART initiation (median duration since initiation =19.9 months). Participants with missing viral load data (17%; $N = 114$) were somewhat more likely to be positive for hazardous alcohol use compared to those who were not (21% versus 16%).

Unadjusted Analyses

No baseline demographic characteristics were associated with viral suppression. Pre-ART CD4 count was a significant predictor of viral suppression, such that participants with a CD4 count above 500 were more likely to be virally suppressed at later testing (79%) compared to those with a CD4 count between 200–500 (68%) and below 200 (75%). Further, participants who were virally suppressed differed significantly from those that were not virally suppressed in the median number of months between ART initiation and viral load testing (23.3 versus 10.4, respectively; see Table 1), such that longer duration was associated with higher odds of viral suppression.

In the unadjusted logistic regression model, the interaction between depressive symptoms and hazardous alcohol use was not significant ($p = 0.53$; data not shown). In the unadjusted models that examined main effects, the odds of viral suppression were not significantly different for those who screened positive for clinically significant depressive symptoms compared to those who did not (OR = 1.01, 95% CI: 0.51, 1.98, $p = 0.98$). Further, the odds of viral suppression did not differ significantly among participants who were positive for hazardous alcohol use compared to those who were not (OR = 2.63, 95% CI: 0.57, 12.01, $p = 0.21$).

Adjusted Analyses

Primary Analyses.—In the multivariable model controlling for baseline characteristics, CD4 count, and months between ART initiation and viral load testing, the interaction between clinically significant depressive symptoms and hazardous alcohol use was not significant ($p = 0.75$; Table 2). In the multivariable logistic regression model that examined main effects, the odds of viral suppression were not significantly different for those who screened positive for clinically significant depressive symptoms compared to those who did not (Adjusted Odds Ratio [AOR] = 0.88, 95% CI: 0.50, 1.55, $p = 0.65$). Further, the odds of viral suppression did not differ among participants who were positive for hazardous alcohol

use compared to those who were not (AOR = 1.37, 95% CI: 0.80, 2.33, $p = 0.25$; see Table 2).

Sensitivity Analyses.—When multivariable analyses were restricted to participants with viral load data within two years of ART initiation ($N = 313$ based on observed values), the interaction between depressive symptoms and hazardous alcohol use on viral load was not significant ($p = 0.59$). In the multivariable logistic regression model that examined main effects, the odds of viral suppression were not significantly different for those who screened positive for depressive symptoms compared to those who did not (AOR = 0.94, 95% CI: 0.41, 2.14, $p = 0.87$). Further, the odds of viral suppression were not significantly different for those who were positive for hazardous alcohol use compared to those who were not (AOR = 1.69, 95% CI: 0.81, 3.54, $p = 0.16$).

Discussion

In this sample of Ugandan PLWH, the findings did not support the primary hypothesis that the relationship between hazardous alcohol use prior to ART initiation and viral suppression at first clinic testing differs based on whether the participant reported clinically significant depressive symptoms. This is inconsistent with data reported by Fojo and colleagues (2018), which found that hazardous alcohol use was associated with a lower likelihood of viral suppression only for participants with moderate or severe depressive symptoms. However, methodological differences make direct comparisons between the two studies difficult. For example, Fojo et al. (2018) examined viral suppression within one year of the assessment of depressive symptoms and alcohol use. In this study, the assessment of predictor variables and first viral load testing varied considerably (8.3–35.4 months). Thus, it is possible that depressive symptoms and hazardous alcohol use are more detrimental to HIV-related outcomes earlier in treatment, and the strength of the associations may diminish over time.

The current study was also unable to detect a main effect association of depressive symptoms with viral suppression, inconsistent with the broader literature that posits that depressive symptoms are associated with ART nonadherence (see Uthman et al., 2014). However, studies often do not distinguish between clinical levels of depression and the presence of any depressive symptoms. Thus, our more stringent cut-off may have attenuated the magnitude of the association between depressive symptoms and viral suppression. It is also plausible that participants endorsing clinically significant depressive symptoms may have been less adherent to their HIV medications, but not at levels that would have significantly impacted viral suppression. Indeed, newer lines of antiretroviral treatments require only 80% adherence to remain effective (Bezabhe et al., 2016; Kobin & Sheth, 2011). Alternatively, there is evidence that depressive symptoms decrease once PLWH initiate treatment (Manne-Goehler et al., 2019) and that some ART regimens, such as efavirenz, can trigger depressive symptoms as a side-effect. While participants may have reported clinically significant depressive symptoms prior to ART, symptoms could have changed prior to viral load testing, limiting our ability to detect an association with adherence and viremia.

The analysis also did not detect a main effect association between hazardous alcohol use and viral suppression, inconsistent with previous research that has documented a strong negative association between alcohol use and ART adherence (Hendershot et al., 2009). Once more, patients have been shown to reduce their alcohol consumption after ART initiation (Hahn 2016), and this may have mitigated the negative effects on viral load. Another potential explanation is survivor bias—people who drink at hazardous levels may have been ineligible for ADEPT due to low CD4 count, thus leaving a cohort of healthy, care-seeking participants. Further, participants with an ART initiation date were less likely to be characterized as drinking at hazardous levels when compared to those with missing ART initiation data. Therefore, participants drinking at hazardous levels, potentially those with poorer adherence, were disproportionally excluded from the present analyses.

The current findings should be considered in the context of study limitations. First, while both the assessment of alcohol use and viral load utilized biomarkers for objective measurement, depressive symptoms were assessed using a self-report clinical screener for which psychometric evaluation is limited for populations outside the U.S. Therefore, we cannot comment on the association between clinical depression and HIV-related outcomes. Future research would benefit from more objective measurement of depression (e.g., diagnostic clinical interview).

Second, this study is a secondary data analysis. The data were not originally collected to examine associations between depressive symptoms, hazardous alcohol use and viral load. Therefore, the number of study participants that screened positive for both depressive symptoms and hazardous alcohol use ($N = 58$) was low and limited the statistical power of the analyses. There was also a substantial amount of time between the assessment of the predictor variables and viral load testing, limiting our interpretations as both depressive symptoms and alcohol use could have changed in this timeframe. Future research would need to make concerted efforts to recruit PLWH that screen positive for both clinically significant depressive symptoms and hazardous alcohol use and keep the assessment of the primary variables temporally linked, to better ascertain how depressive symptoms may moderate the association between hazardous alcohol use and viral suppression.

The present study also has several methodological strengths. First, we included a biomarker of hazardous alcohol use (i.e., PEth), mitigating the potential of social desirability and recall bias in self-report. Second, this is a prospective study with no temporal overlap between the assessment of the predictor and outcome variables that allowed us to examine temporal sequencing in the association between depressive symptoms, hazardous alcohol use, and HIV-related outcomes. Third, this is the first test of an interaction between depressive symptoms and alcohol use with viral suppression among a sample of Ugandan PLWH. Descriptively, the data showed that participants drinking at hazardous levels were less likely to have ART initiation clinic data available. Therefore, current findings add to an emerging literature that is attempting to examine how clinically significant depressive symptoms and hazardous alcohol use may negatively impact HIV testing and treatment engagement.

References

Bajunirwe F, Haberer JE, Boum Y, Hunt P, Mocello R, Martin JN, . . . Hahn JA (2014). Comparison of self-reported alcohol consumption to phosphatidylethanol measurement among HIV-infected patients initiating antiretroviral treatment in southwestern Uganda. PLoS One, 9(12), e113152.

Bradley KA, DeBenedetti AF, Volk RJ, Williams EC, Frank D, & Kivlahan DR (2007). AUDIT-C as a brief screen for alcohol misuse in primary care. Alcohol: Clinical and Experimental Research, 31(7), 1208–1217.

Derogatis LR, Lipman RS, Rickels K, Uhlenhuth EH, & Covi L. (1974). The Hopkins Symptom Checklist (HSCL): A self-report symptom inventory. Behavioral Science, 19(1), 1–15. [PubMed: 4808738]

Bezabhe WM, Chalmers L, Bereznicki LR, & Peterson GM (2016). Adherence to Antiretroviral Therapy and Virologic Failure: A Meta-Analysis. Medicine (Baltimore), 95(15), e3361. doi:10.1097/MD.0000000000003361

Boden JM, & Fergusson DM (2011). Alcohol and depression. Addiction, 106(5), 906–914. doi:10.1111/j.1360-0443.2010.03351.x [PubMed: 21382111]

Cotrena C, Branco LD, Shansis FM, & Fonseca RP (2016). Executive function impairments in depression and bipolar disorder: association with functional impairment and quality of life. J Affect Disord, 190, 744–753. doi:10.1016/j.jad.2015.11.007 [PubMed: 26606718]

Elkington KS, Bauermeister JA, & Zimmerman MA (2010). Psychological distress, substance use, and HIV/STI risk behaviors among youth. J Youth Adolesc, 39(5), 514–527. doi:10.1007/s10964-010-9524-7 [PubMed: 20229264]

Emenyonu NI, Fatch R, Muyindike WR, Kekibiina A, Woolf-King SE, & Hahn JA (2017). Randomized Study of Assessment Effects on Alcohol Use by Persons With HIV in Rural Uganda. Journal of studies on alcohol and drugs, 78(2), 296–305. [PubMed: 28317511]

Farley J, Miller E, Zamani A, Tepper V, Morris C, Oyegunle M, . . . Blattner W. (2010). Screening for hazardous alcohol use and depressive symptomatology among HIV-infected patients in Nigeria: prevalence, predictors, and association with adherence. J Int Assoc Physicians AIDS Care (Chic), 9(4), 218–226. doi:10.1177/1545109710371133 [PubMed: 20798401]

Fojo AT, Lesko CR, Calkins KL, Moore RD, McCaul ME, Hutton HE, . . . Chander G. (2018). Do Symptoms of Depression Interact with Substance Use to Affect HIV Continuum of Care Outcomes? AIDS Behav. doi:10.1007/s10461-018-2269-0

Hahn JA, Cheng DM, Emenyonu NI, Lloyd-Travaglini C, Fatch R, Shade SB, . . . Samet JH (2018). Alcohol Use and HIV Disease Progression in an Antiretroviral Naive Cohort. J Acquir Immune Defic Syndr, 77(5), 492–501. doi:10.1097/qai.0000000000001624 [PubMed: 29303844]

Hahn JA, Emenyonu NI, Fatch R, Muyindike WR, Kekiibina A, Carrico AW, . . . Shiboski S. (2016). Declining and rebounding unhealthy alcohol consumption during the first year of HIV care in rural Uganda, using phosphatidylethanol to augment self-report. Addiction, 111(2), 272–279. [PubMed: 26381193]

Hendershot CS, Stoner SA, Pantalone DW, & Simoni JM (2009). Alcohol use and antiretroviral adherence: review and meta-analysis. J Acquir Immune Defic Syndr, 52(2), 180–202. doi:10.1097/QAI.0b013e3181b18b6e [PubMed: 19668086]

Johnson MJ (2002). The Medication Adherence Model: a guide for assessing medication taking. Research and theory for nursing practice, 16(3), 179. [PubMed: 12472293]

Khantzian EJ (1997). The self-medication hypothesis of substance use disorders: a reconsideration and recent applications. Harv Rev Psychiatry, 4(5), 231–244. doi:10.3109/10673229709030550 [PubMed: 9385000]

Kist N, Sandjojo J, Kok RM, & van den Berg JF (2014). Cognitive functioning in older adults with early, late, and very late onset alcohol dependence. Int Psychogeriatr, 26(11), 1863–1869. doi:10.1017/S1041610214000878 [PubMed: 24832056]

Kobin AB, & Sheth NU (2011). Levels of adherence required for virologic suppression among newer antiretroviral medications. Annals of Pharmacotherapy, 45(3), 372–379.

Malow R, Devieux JG, Stein JA, Rosenberg R, Jean-Gilles M, Attonito J, . . . Pape JW (2013). Depression, substance abuse and other contextual predictors of adherence to antiretroviral therapy

(ART) among Haitians. AIDS Behav, 17(4), 1221–1230. doi:10.1007/s10461-012-0400-1 [PubMed: 23338563]

Manne-Goehler J, Kakuhikire B, Abaasabyoona S, Bärnighausen TW, Okello S, Tsai AC, & Siedner MJ (2019). Depressive Symptoms Before and After Antiretroviral Therapy Initiation Among Older-Aged Individuals in Rural Uganda. AIDS Behav, 23(3), 564–571. doi:10.1007/s10461-018-2273-4 [PubMed: 30229388]

Martinez P, Andia I, Emenyonu N, Hahn JA, Hauff E, Pepper L, & Bangsberg DR (2008). Alcohol use, depressive symptoms and the receipt of antiretroviral therapy in southwest Uganda. AIDS Behav, 12(4), 605–612. doi:10.1007/s10461-007-9312-x [PubMed: 17968651]

Mills EJ, Nachega JB, Bangsberg DR, Singh S, Rachlis B, Wu P, . . . Cooper C. (2006). Adherence to HAART: a systematic review of developed and developing nation patient-reported barriers and facilitators. PLoS Med, 3(11), e438. doi:10.1371/journal.pmed.0030438

Nakimuli-Mpungu E, Musisi S, Katabira E, Nachega J, & Bass J. (2011). Prevalence and factors associated with depressive disorders in an HIV+ rural patient population in southern Uganda. J Affect Disord, 135(1–3), 160–167. doi:10.1016/j.jad.2011.07.009 [PubMed: 21851986]

Sullivan LE, Goulet JL, Justice AC, & Fiellin DA (2011). Alcohol consumption and depressive symptoms over time: a longitudinal study of patients with and without HIV infection. Drug Alcohol Depend, 117(2–3), 158–163. doi:10.1016/j.drugalcdep.2011.01.014 [PubMed: 21345624]

Swendsen JD, & Merikangas KR (2000). The comorbidity of depression and substance use disorders. Clin Psychol Rev, 20(2), 173–189. [PubMed: 10721496]

Uthman OA, Magidson JF, Safren SA, & Nachega JB (2014). Depression and adherence to antiretroviral therapy in low-, middle- and high-income countries: a systematic review and meta-analysis. Curr HIV/AIDS Rep, 11(3), 291–307. doi:10.1007/s11904-014-0220-1 [PubMed: 25038748]

World Health Organization. (2014). Global status report on alcohol and health, 2014: World Health Organization.

World Health Organization. (2015). Guideline on when to start antiretroviral therapy and on pre-exposure prophylaxis for HIV: World Health Organization.

Table 1

Participant Characteristics and Bivariate Associations with Viral Suppression (≤550 copies)* for BREATH and ADEPT Study Cohorts

	Total Sample	Not virally suppressed (*N*=84)	Virally suppressed (*N*=459)	Missing viral load (*N*=114)
		N (%) or median (IQR)		
Gender				
Female	383 (58.3)	54 (14.1)	277 (72.3)	52 (13.6)
Male	274 (41.7)	30 (11.0)	182 (66.4)	62 (22.6)
Age	32 (26–40)	31 (25–38)	33 (27–40)	29 (25–37)
Education				
Primary or less	435 (66.2)	56 (12.9)	302 (69.4)	77 (17.7)
Secondary or more	222 (33.8)	28 (12.6)	157 (70.7)	37 (16.7)
Household asset index				
Poor	260 (39.6)	37 (14.2)	167 (64.2)	56 (21.5)
Middle	264 (40.2)	33 (12.5)	191 (72.4)	40 (15.2)
High	132 (20.1)	14 (10.6)	100 (75.8)	18 (13.6)
Study cohort				
BREATH cohort	184 (28.0)	21 (11.4)	112 (60.9)	51 (27.7)
BREATH minimally assessed	114 (17.4)	25 (21.9)	74 (64.9)	15 (13.2)
ADEPT	359 (54.6)	38 (10.6)	273 (76.0)	48 (13.4)
Clinically significant depressive symptoms (CES-D positive)^				
No	362 (73.6)	37 (10.2)	268 (74.0)	57 (15.8)
Yes	130 (26.4)	13 (10.0)	95 (73.1)	22 (16.9)
Hazardous alcohol use^ (AUDIT-C positive or PEth ≥50)				
No	313 (54.7)	38 (12.1)	225 (71.9)	50 (16.0)
Yes	259 (45.3)	22 (8.5)	182 (70.3)	55 (21.2)
Depressive symptoms*hazardous alcohol use^				
No depressive symptoms, no hazardous alcohol	204 (41.6)	27 (13.2)	151 (74.0)	26 (12.8)
No depressive symptoms, yes hazardous alcohol	157 (32.0)	10 (6.4)	117 (74.5)	30 (19.1)
Yes depressive symptoms, no hazardous alcohol	72 (14.7)	8 (11.1)	52 (72.2)	12 (16.7)
Yes depressive symptoms, yes hazardous alcohol	58 (11.8)	5 (8.6)	43 (74.1)	10 (17.2)
CD4 count^				
<200	55 (10.2)	4 (7.3)	41 (74.6)	10 (18.2)
200–500	304 (56.1)	38 (12.5)	207 (68.1)	59 (19.4)
>500	183 (33.8)	11 (6.0)	145 (79.2)	27 (14.8)

	Total Sample	Not virally suppressed (*N*=84)	Virally suppressed (*N*=459)	Missing viral load (*N*=114)
		N (%) or median (IQR)		
Months between ART initiation and viral load	19.9 (9.3–32.7)	10.4 (8.3–15.2)	23.3 (9.8–35.4)	-

Note. *N* = 657. Demographic data is taken from study baseline;

* denotes the earliest viral load result after 6 months of antiretroviral therapy (ART);

× denotes data taken from the study visit prior to ART initiation

Table 2

Adjusted Odds Ratios (OR) and 95% Confidence Intervals (CI) for Viral Suppression (≤550)

	Interaction Model[α]		Main Effects Model[β]	
	Adjusted OR (95% CI)	**p-value**	**Adjusted OR (95% CI)**	**p-value**
Depressive symptoms[×] * alcohol use[×]		0.75		
No depressive symptoms, no hazardous alcohol	REF		-	
No depressive symptoms, yes hazardous alcohol	1.31 (0.71, 2.40)		-	
Yes depressive symptoms, no hazardous alcohol	0.81 (0.37, 1.75)		-	
Yes depressive symptoms, yes hazardous alcohol	1.27 (0.54, 2.99)		-	
Clinically significant depressive symptoms (CES-D positive)[×]				0.65
No	-		REF	
Yes	-		0.88 (0.50, 1.55)	
Hazardous alcohol use (AUDIT-C positive or PEth ≥50)[×]				0.25
No	-		REF	
Yes	-		1.37 (0.80, 2.33)	
Gender		0.41		0.43
Female	REF		REF	
Male	0.81 (0.50, 1.33)		0.82 (0.50, 1.34)	
Age	1.02 (0.99, 1.05)	0.13	1.02 (0.99, 1.05)	0.13
Education		0.87		0.87
Primary or less	REF		REF	
Secondary or more	1.05 (0.61, 1.79)		1.05 (0.61, 1.79)	
Household asset index		0.32		0.33
Poor	REF		REF	
Middle	1.44 (0.83, 2.51)		1.44 (0.83, 2.50)	
High	1.52 (0.75, 3.08)		1.51 (0.74, 3.06)	
CD4 count[×]		0.06		0.06
<200	REF		REF	
200–500	1.17 (0.61, 2.24)		1.16 (0.61, 2.23)	
>500	2.16 (0.99, 4.71)		2.15 (0.99, 4.65)	
Months between ART initiation and viral load	1.05 (1.03, 1.08)	<0.01	1.05 (1.03, 1.07)	<0.01
Study cohort		<0.01		<0.01
BREATH cohort	REF		REF	
BREATH minimally assessed	2.28 (1.10, 4.71)		2.25 (1.10, 4.60)	
ADEPT	3.67 (1.93, 6.97)		3.64 (1.92, 6.89)	

Note. $N = 657$ with multiple imputation. Analyses are limited to participants with antiretroviral initiation data;

[×] denotes data taken from the study visit prior to ART initiation;

[α] Multivariable model, including interaction between depression and alcohol use;

[β] Multivariable model, including depression and alcohol use as separate term