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ORIGINAL PAPER

Association Between Alcohol Use, CD4 Count, and Depressive Symptoms Among People with HIV with Viral Load Suppressed in Southwestern Uganda

Alain Favina[1,2] · Robin Fatch[3] · Sowmya R. Rao[4,5] · Gabriel Chamie[3] · Winnie Muyindike[6] · Julian Adong[6] · Nneka I. Emenyonu[3] · Adah Tumwegamire[7] · Christine Ngabirano[7] · Allen Kekibiina[7] · Marson Kara[3] · Brian Beesiga[8] · Adam W. Carrico[9] · Judith A. Hahn[3,10]

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Abstract

Despite the current effective antiretroviral therapy (ART) and viral suppression, depression remains the most prevalent mental health challenge among people with HIV (PWH) in Uganda and worldwide. This study examined the relationship between CD4 cell count and depressive symptoms among PWH on ART with viral suppression, and the potential modification effect of alcohol use on this relationship. We combined baseline data from two longitudinal studies (DIPT (NCT03492216) and ADEPTT (NCT03302299)) conducted between May 2017 and August 2021 across four health facilities in Southwestern Uganda. Eligible participants were adults with suppressed HIV viral load. Depressive symptoms were assessed using the Center for Epidemiologic Studies Depression (CESD) Scale (≥16 considered significant). CD4 + count was measured through blood tests, while alcohol use was measured using both the Alcohol Use Disorders Identification Test - Consumption (AUDIT-C) and the alcohol biomarker phosphatidylethanol (PEth), measured in dried blood spots. Multivariable mixed effects logistic regression models examined associations. Among 908 participants, 14.6% had depressive symptoms. The median CD4 count was 632 cells/mm³ (IQR: 467.5-825.5), and 62.1% had high or very high-risk alcohol use. Overall, no significant association was found between CD4 count and depressive symptoms (aOR: 1.04; 95% CI: 0.97–1.12; $p = 0.26$). Additionally, no evidence of effect modification by level of alcohol use ($p = 0.10$) was found. The prevalence of depressive symptoms is high among PWH with viral suppression. Healthcare providers should assess and manage depression among this population. Further studies should also explore the causes of the depressive symptoms and develop targeted interventions.

Keywords CD4 count · Depression · Alcohol use · People with HIV (PLHIV) · HIV viral suppression

✉ Judith A. Hahn
judy.hahn@ucsf.edu

Alain Favina
favinaalain@gmail.com

[1] Department of Psychiatry, Mbarara University of Science and Technology, Mbarara, Uganda

[2] Research Department, Health Development Initiative, Kigali, Rwanda

[3] Department of Medicine, University of California San Francisco, San Francisco, CA, USA

[4] Department of Global Health, Boston University School of Public Health, Boston, MA, USA

[5] Massachusetts General Hospital Biostatistics Center, Boston, MA, USA

[6] Department of Medicine, Mbarara University of Science and Technology, Mbarara, Uganda

[7] Global Health Collaborative, Mbarara University of Science and Technology, Mbarara, Uganda

[8] Infectious Diseases Research Collaboration, Kampala, Uganda

[9] Department of Health Promotion and Disease Prevention, Robert Stempel College of Public Health and Social Work, Florida International University, Miami, USA

[10] Department of Epidemiology & Biostatistics, University of California San Francisco, San Francisco, CA, USA

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Introduction

Depression among people with HIV (PWH) is a significant problem worldwide and specifically, in sub-Saharan Africa [1–4]. Almost 1 million people (5.1% of the population) in Uganda are living with HIV [5], and previous studies conducted among PWH reported a high prevalence of depression compared to people without HIV [6–10].

Depression in PWH may be linked to immune status; associations between depression and CD4 cell count have been demonstrated over the years among PWH [11, 12]. The mechanisms underlying this suggest immune activation as key. Increased risk for depression may occur from immune dysfunction through stress-responsive pathways like the hypothalamic-pituitary-adrenal (HPA) axis [13]. For example, a recent study using the Mendelian analysis to assess the causal relationship between immune cells and depression found that innate and adaptive immune dysfunction contribute to the pathogenesis of depression [14]. Increased activation of CD4 cells may affect the pathogenesis of depression through a linkage between neuroinflammation and decreased dopamine transmission [14–17]. Additionally, excessive activation is increased among immune non-responders, i.e., those who fail to achieve complete immune reconstitution despite being on ART [18]. The long-term immunological recovery period for PWH can take years, depending on their CD4 count at the initiation of ART [19]. This long period of recovery includes a period of high activity of CD4 cells [20], which may affect the pathogenesis of depression despite being on ART and having a suppressed viral load. However, the association between CD4 count and depression can be bidirectional, with previous studies demonstrating that depression can predict CD4 cell count among PWH through direct biological and indirect behavioral mechanisms [12, 21, 22]. Depression contributes to the CD4 decline biologically through the HPA axis dysregulation, increased inflammatory cytokines, and impaired immune function [12, 21], while it also involves poor adherence through behavioral mechanisms that lead to poor viral suppression [22].

Many prior studies examining the relationship between CD4 cell count and depression were conducted in heterogeneous samples, with some including individuals with unsuppressed viral loads [11, 23]. As the use of ART improves and more people attain viral suppression more quickly [24, 25], more people are living with HIV with suppressed viral load. It is therefore important to reevaluate the association between CD4 count and depressive symptoms among people with suppressed viral load. The hypothesis for this study was that there is a negative association between CD4 cell count and depression among.

persons with viral suppression. Moreover, since depression is one of the most prevalent mental health challenges among PWH in Uganda, understanding the association between CD4 count and depressive symptoms could stimulate further research into the causes of depression in PWH, particularly among those with viral suppression. This analysis aimed to gain further insight into the association between CD4 count and depressive symptoms among PWH on ART with viral suppression. We also sought to evaluate the potential effect modification of alcohol use, which at high levels may contribute to an increased risk for depression and alter the relationship between CD4 count and depressive symptoms.

Methods

Study Design

The current analysis used the baseline data from two longitudinal studies of the Uganda-Russia-Boston Alcohol Network for Alcohol Research Collaboration on HIV/AIDS (URBAN ARCH) Consortium [26–29]. The two studies were: The Drinkers Intervention to Prevent Tuberculosis (DIPT, NCT03492216) and the Alcohol Drinkers Exposure to Preventive Therapy for Tuberculosis (ADEPTT, NCT03302299). The DIPT study was a randomized controlled trial (RCT) of economic incentives to promote reduced alcohol consumption and increased isoniazid (INH) adherence, while the ADEPTT cohort study was a one-arm trial aimed at examining the safety and tolerability of INH preventive therapy in people co-infected with HIV and TB, including both persons who drank alcohol and those who abstained from alcohol use [26–29]. The baseline data collection tools used in both studies were similar, and recruitment took place from May 2017 to August 2021.

Study Setting

In both DIPT and ADEPTT, participants were recruited from the Southwestern region of Uganda. DIPT participants were recruited from two rural (Rugazi Health Center IV and Ruhoko Health Center IV) and two semi-urban (Mbarara City Council (MCC) and Mbarara Regional Referral Hospital Immune Suppression Syndrome (ISS)) HIV clinics. ADEPTT participants were recruited from the Mbarara Regional Referral Hospital ISS HIV clinic.

Study Participants

We limited this analysis to participants with viral suppression (HIV RNA < 200 cells/mm^3) at baseline [30]. Inclusion

criteria for participants in both studies were age ≥ 18 years; living with HIV; prescribed ART for at least 6 months; being fluent in Runyankole (the local language) or English; living within 2 h travel time or 60 km of the study site with no plans to relocate outside the catchment area; a positive tuberculin skin test (≥ 5 mm induration), no history of active TB or use of TB preventive therapy; and alanine aminotransferase (ALT) and aspartate aminotransferase (AST) elevations ≤ 2 times the upper limit of normal. The latter restriction was due to safety concerns since the studies were giving isoniazid, which can be hepatotoxic. Additionally, people were eligible for the ADEPTT study if they reported current alcohol use (prior 3 months) or abstaining from using alcohol for at least the past year. For the DIPT study, additional eligibility criteria included recent risky alcohol use, defined as a self-reported AUDIT-C score of ≥ 3 for women and ≥ 4 for men (modified to assess the prior 3 months), and a positive result for recent alcohol use on a urine ethyl glucuronide (EtG) dipstick test. Additional details of the study participants in both studies are available [26–28].

Data Collection Procedures

The Computer Assisted Survey Information Collection (CASIC) system was used for the structured interviewer-administered survey. The participants were interviewed in Runyankole or English, depending on the participant's language of preference. In addition, blood specimens were collected at the baseline visit and tested for CD4 cell count and phosphatidylethanol (PEth, an alcohol biomarker), as described below. The collection of specimens was performed after the interview.

Variables and Measurement

Outcome Variable

The outcome variable in this analysis was depressive symptoms (yes/no), assessed via the Center for Epidemiologic Studies Depression (CESD) Scale [31]. Two previous studies have evaluated the psychometric properties of the CESD in Uganda among pregnant women with HIV and people living with HIV [32, 33]. Although these studies were conducted in another local language (Luganda), which is different from Runyankole, the CESD tool showed good discriminatory ability, construct validity, and reliability. The Cronbach's alpha from the two studies were 0.92 and 0.90, respectively [32, 33]. In this study, the Cronbach's alpha was 0.90. People with a score of 16 and above were considered to have significant depressive symptoms [32, 34, 35].

Independent Variable

CD4 count: Blood samples were collected and tested at the Mbarara University of Science and Technology (MUST) Clinical Research Laboratory and at the Infectious Diseases Research Collaboration (IDRC) Regional Research Laboratory using the BD FACS Presto (TM), PIMA POC CD4 test system (Alere Inc., Waltham, MA), and GeneXpert® Dx System. The CD4 count was examined as a continuous variable. Additionally, the variable was later categorized into three groups for an exploratory analysis: (i) < 200 cells/mm^3, (ii) 200-<500 cells/mm^3, (iii) ≥ 500 cells/mm^3.

Covariates

Covariates were considered in the model to adjust for potential confounding and improve the precision of the estimate between the CD4 count and depressive symptoms. The covariates included in this analysis were assessed using a questionnaire and included participant age, gender, marital status, and spouse HIV status, level of education, employment status, religion, ART adherence in the past 30 days, and general health status. The ART adherence in the past 30 days was assessed using the following self-reported question: "How have you been at taking your anti-HIV medication in the past 30 days?". The participants rated their adherence to treatment by choosing among the following options: excellent, very good, good, fair, poor, or very poor. This is a 5-point Likert scale tool named the Self-Rating Scale Item (SRSI), which is made up of one question to assess medication adherence over the past 30 days [36]. In this analysis, it was dichotomized as good/fair/poor/very poor versus excellent/very good. The general health status of the participant was assessed using the first question of the Medical Outcomes Study-HIV (MOS-HIV) Health Survey that asked: "In general, would you say your health is excellent, very good, good, fair, or poor?" The MOS-HIV has been used before as a validated measure of general health in Uganda [37]. We dichotomized responses as good/fair/poor versus excellent/very good.

Alcohol use was assessed using both the AUDIT-C and PEth, a biomarker of alcohol consumption in the prior 2–3 weeks [38]. The cutoffs used for medium risk alcohol use via the AUDIT-C were ≥ 3 for women or ≥ 4 for men, and ≥ 6 for high/very high risk alcohol use for both women and men [39, 40]. For PEth, dried blood spot (DBS) cards were tested for the PEth homologue 16:0/18:1 with a limit of quantification of 8 ng/mL at the United States Drug Testing Laboratories, Inc., in the USA. Consistent with previous studies, we employed a cutoff of PEth ≥ 50 ng/ml to indicate medium-risk alcohol use and a cutoff of PEth ≥ 200 ng/ml to indicate high/very high-risk drinking [41–43].

To determine the level of alcohol use, we combined the AUDIT-C and PEth measures as follows: "no/low risk alcohol use": AUDIT-C negative (< 3 for women and < 4 for men) and PEth < 50 ng/ml; "medium risk": AUDIT-C ≥ 3 for women or ≥ 4 for men and AUDIT-C < 6, or PEth ≥ 50 and < 200 ng/ml; "high/very high risk": AUDIT-C ≥ 6 or PEth ≥ 200 ng/ml. If someone fell into two different categories, the higher category was used for the combined level of alcohol use variable. Considering that neither of the above measures for alcohol use is 100% sensitive, combining them can improve overall sensitivity [44].

Data Analysis

Data analysis was conducted using the baseline data from these studies and was limited to participants with CD4 data who were virally suppressed (<200 copies/ml). Participant characteristics were described using proportions and frequencies for the categorical variables, and the median and interquartile range (IQR) for the continuous variables (i.e., age and CD4 count).

The bivariate associations between participant characteristics and the outcome (depressive symptoms) were assessed using Chi-squared tests for categorical variables and Kruskal-Wallis tests for the two continuous variables. The following variables, in addition to CD4 count, were selected a priori for inclusion in the multivariable model: age, gender, marital status, spouse HIV status, education, religion, general health status, alcohol use, and ART adherence. We assessed collinearity among these variables using Spearman correlations and found all correlations to be <0.40; as such, we included all covariates selected a priori in our multivariable models. Bivariate and multivariable mixed effects logistic regression models were used to examine associations with depressive symptoms, and accounted for clustering by study site. We considered a two-sided p-value<0.05 as significant. Additionally, we assessed possible effect modification of alcohol use by including an interaction term between CD4 count and level of alcohol use in the multivariable model. We considered a p-value<0.10 as significant for the interaction term and planned to present models stratified by alcohol use if a significant interaction was observed. As an exploratory analysis, we also assessed CD4 count as a categorical variable, rather than a continuous variable, in the multivariable model.

Ethical Consideration

DIPT and ADEPTT protocols were approved by different ethical approval committees including (i) the institutional review board of the University of California, San Francisco (UCSF); (ii) the institutional review board of Boston University; (iii) the Mbarara University of Science and Technology Research Ethics Committee (MUST-REC); (iv) the Makerere University School of Medicine Research Ethics Committee (SOMREC), and (v) the Ugandan National Council for Science and Technology (UNCST). All participants provided written informed consent prior to enrollment in the studies.

Results

In total, 680 participants were enrolled in the DIPT study, and 301 participants in the ADEPTT study. From the 981 participants in both studies, two participants were excluded from this analysis because they were missing CD4 counts. An additional 71 participants were excluded because they were not virally suppressed ($n=45$) or were missing viral load results ($n=26$). In total, 908 PWH were included in this analysis, with a median age of 40 years (IQR: 32–47) (Table 1). One hundred thirty-three participants (14.6%) reported depressive symptoms. The majority of participants were men (63.2%) and married (61.5%), with primary school as their highest level of education (63.1%). The median CD4 count was 632.0 (IQR: 467.5–825.5). Most (62.1%) participants had high/very high-risk alcohol use, and 80.7% had very good or excellent ART adherence.

Bivariate Associations with Depressive Symptoms

In the bivariate analysis, we found no significant difference in the median CD4 cell count between people with and without depressive symptoms (median CD4 cell counts: 662.0 and 630.0, respectively; p-value=0.407) (Table 2). Among all participants, 65.2% of those with depressive symptoms were classified as having high/very high-risk alcohol use, compared to 61.6% of those without depressive symptoms ($p=0.695$). A higher proportion of participants with depressive symptoms were unmarried compared to those without depressive symptoms (48.1% versus 36.8%, $p=0.014$).

Adjusted Association Between CD4 Count and Depressive Symptoms

In the main multivariable model, there was no evidence of an association between CD4 count and depressive symptoms (adjusted Odds Ratio (aOR) per 100 cells/mm^3: 1.04 (95% Confidence Interval (CI) 0.97–1.12) (Table 3). Age was associated with depressive symptoms in the multivariable model. In the exploratory model including CD4 count as a categorical variable, there was no evidence of an association between CD4 count and depressive symptoms ($p=0.44$).

Table 1 ADEPTT and DIPT study participant characteristics at study enrollment, among those with HIV viral load < 200 copies/ml

	N (%) or median (IQR) (*N* = 908)
Participant sex	
Female	334 (36.8%)
Male	574 (63.2%)
Age (median (IQR))	40.0 (32.0–47.0)
Married	
No	349 (38.5%)
Yes	558 (61.5%)
Spouse HIV status	
HIV-negative	157 (28.1%)
HIV-positive	373 (66.7%)
Don't know status	29 (5.2%)
Marital status/Spouse HIV status	
Not married	349 (38.5%)
Married, HIV- spouse	157 (17.3%)
Married, HIV+ spouse	372 (41.0%)
Married, spouse status unknown	29 (3.2%)
Education	
No formal education	130 (14.3%)
P1-P7	573 (63.1%)
S1-S6	165 (18.2%)
Tertiary/Vocational/University	40 (4.4%)
Job	
Self-employed, business	329 (36.2%)
Paid employment	149 (16.4%)
Agriculture	405 (44.6%)
Unemployed/student	25 (2.8%)
Religion	
Protestant/Anglican	448 (49.3%)
Catholic	391 (43.1%)
Muslim	46 (5.1%)
Other	23 (2.5%)
Depressive symptoms	
No	775 (85.4%)
Yes	133 (14.6%)
CD4 count (median (IQR))	632.0 (467.5–825.5)
CD4 count	
<200 cells/mm3	19 (2.1%)
200-<500 cells/mm3	245 (27.0%)
>=500 cells/mm3	644 (70.9%)
Alcohol use: self-report and PEth	
No/low risk alcohol use	156 (17.3%)
Medium risk alcohol use	186 (20.6%)
High/very high-risk alcohol use	560 (62.1%)
ART adherence, past 30 days	
Good/fair/poor/very poor	175 (19.3%)
Excellent/very good	733 (80.7%)
General health: excellent/very good?	
Good/fair/poor	438 (48.2%)
Excellent/very good	470 (51.8%)
Participant language for questionnaire	
Runyankole	859 (94.6%)
English	49 (5.4%)

We found no evidence of effect modification by level of alcohol use ($p = 0.10$).

Discussion

We did not find an association between CD4 cell count and depressive symptoms in this study of PWH with viral suppression. The lack of association may be due to the recency of the studies included here, which recruited participants after the implementation of the "test and treat" strategy in recent years in Uganda [45], whereby ART is initiated immediately following HIV diagnosis. This may have resulted in higher CD4 counts at treatment initiation [46]. The majority of participants, i.e., 71%, in this study had CD4 cell counts ≥ 500 cells/mm^3 and reported very good or excellent ART adherence and general health. These parameters are linked to better physical and mental health among PWH [3, 47]. In addition, majority of participants were engaged in income-generating activities, which are known to have a protective impact against depression [48]. The clinical significance of our main finding is that depression is still prevalent among PWH even in the context of viral suppression. In this era of early ART initiation and high ART adherence, CD4 cell count may no longer be one of the main predictors of depressive symptoms. Health care providers should therefore prioritize exploring and addressing psychosocial factors such as alcohol use to more effectively manage depressive symptoms in this population.

The prevalence of depressive symptoms in this study was comparable to findings from other studies among PWH in Nigeria (14.2% in 2014) [49] and one study in Uganda (14% in 2017) [50]. However, the prevalence of depressive symptoms in this study was about half lower compared to a systematic review of the prevalence of depression among PWH (28.2%) [51]. These findings suggest that early ART initiation may be having an effect on depression reduction in Uganda [52] and globally [53].

The results of no association between CD4 count and depression contrast previous studies in which alcohol use had a bidirectional association with mental health, such that alcohol use causes poor mental health and vice versa, an effect most pronounced among PWH [54–60]. Although uncommon, our findings may be due to the indirect benefits of broad access to care for PWH. The majority of PWH in this study were adhering well to treatment, which included regular visits to the facility for medication refill and counseling, and may have influenced the lower levels of depression symptoms observed in this study. In addition, PWH in this study may be using alcohol use as a normal behavior since it is culturally and socially accepted in Uganda [61], and not in relation to depression or coping mechanisms.

Table 2 Participant characteristics, by depressive symptoms, among those with HIV viral load < 200 copies/ml

	CES-D >= 16		
	No	Yes	*p*-value (chi2/k-wallis)
N	775 (85.4%)	133 (14.6%)	
Participant sex			0.86
Female	286 (36.9%)	48 (36.1%)	
Male	489 (63.1%)	85 (63.9%)	
Age (median (IQR))	40.0 (33.0–47.0)	37.0 (32.0–45.0)	0.06
Married			0.01
No	285 (36.8%)	64 (48.1%)	
Yes	489 (63.2%)	69 (51.9%)	
Is spouse HIV+?			0.73
HIV-negative	138 (28.2%)	19 (27.5%)	
HIV-positive	328 (66.9%)	45 (65.2%)	
Don't know status	24 (4.9%)	5 (7.2%)	
Marital status/spouse HIV status			0.09
Not married	285 (36.8%)	64 (48.1%)	
Married, HIV- spouse	138 (17.8%)	19 (14.3%)	
Married, HIV+ spouse	327 (42.2%)	45 (33.8%)	
Married, spouse status unknown	24 (3.1%)	5 (3.8%)	
Education			0.03
None	107 (13.8%)	23 (17.3%)	
P1-P7	484 (62.5%)	89 (66.9%)	
S1-S6	145 (18.7%)	20 (15.0%)	
Tertiary/vocational/University	39 (5.0%)	1 (0.8%)	
Religion			0.07
Protestant/Anglican	395 (51.0%)	53 (39.8%)	
Catholic	321 (41.4%)	70 (52.6%)	
Muslim	38 (4.9%)	8 (6.0%)	
Other	21 (2.7%)	2 (1.5%)	
CD4 count (median (IQR))	630.0 (467.0–825.0)	662.0 (492.0–851.0)	0.41
CD4 count			0.40
<200 cells/mm3	18 (2.3%)	1 (0.8%)	
200-<500 cells/mm3	210 (27.1%)	35 (26.3%)	
>=500 cells/mm3	547 (70.6%)	97 (72.9%)	
Alcohol use: self-report and PEth			0.70
No/low risk alcohol use	134 (17.4%)	22 (16.7%)	
Medium risk alcohol use	162 (21.0%)	24 (18.2%)	
High/very high-risk alcohol use	474 (61.6%)	86 (65.2%)	
ART adherence, past 30 days			0.14
Good/fair/poor/very poor	143 (18.5%)	32 (24.1%)	
Excellent/very good	632 (81.5%)	101 (75.9%)	
General health: excellent/very good?			0.36
Good/fair/poor	369 (47.6%)	69 (51.9%)	
Excellent/very good	406 (52.4%)	64 (48.1%)	

These results should be interpreted with consideration of the limitations. This study was a secondary analysis of data originally collected for other research aims, and we used only baseline data for the analysis. Therefore, the actual direction of causality between the variables included in the study could not be determined, and some of the relationships may be bidirectional. Additionally, any unmeasured confounding may also distort the relationship. Although combining self-report and Peth in assessing alcohol use was used to improve overall sensitivity, the two tools can have discrepancies, with the self-report being potentially affected by social desirability. Additionally, while people with ALT and AST elevations ≤ 2 times the upper limit of normal were excluded from the analysis due to safety concerns, it is important to note that these liver enzymes can be linked to alcohol and could have removed some participants from the analysis. Lastly, self-reported variables have potentially been impacted by social desirability bias. For example, the

Table 3 Unadjusted and Adjusted Odds Ratios (OR) and 95% Confidence Intervals (CI) for depressive symptoms (CESD≥16), ADEPTT and DIPT study participants at baseline with HVL<200 copies/mL (n=908)

	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI) (n=902)	p-value	Adjusted OR (95% CI) (n=902) (exploratory)	p-value
CD4 count (per 100 cells/mm3)	1.04 (0.98, 1.12)	0.21	1.04 (0.97, 1.12)	0.26	–	
CD4 count		0.40				0.44
<200 cells/mm3	1.00		–		1.00	
200–499 cells/mm3	3.31 (0.42, 25.99)		–		3.08 (0.39, 24.58)	
≥500 cells/mm3	3.74 (0.48, 28.85)		–		3.49 (0.44, 27.45)	
Gender		0.91		0.24		0.28
Woman	1.00		1.00		1.00	
Man	0.98 (0.66, 1.45)		1.33 (0.83, 2.15)		1.30 (0.81, 2.08)	
Age (per 1 year)	0.98 (0.96, 1.00)	0.08	0.98 (0.96, 1.00)	0.04	0.98 (0.96, 1.00)	0.04
Marital status, spouse HIV status		0.08		0.30		0.32
Not married	1.00		1.00		1.00	
Married, HIV- spouse	0.60 (0.34, 1.04)		0.67 (0.37, 1.20)		0.66 (0.37, 1.19)	
Married, HIV+ spouse	0.61 (0.40, 0.93)		0.67 (0.43, 1.05)		0.69 (0.44, 1.07)	
Married, spouse HIV status unknown	0.88 (0.32, 2.43)		0.93 (0.33, 2.66)		0.95 (0.33, 2.71)	
Education		0.06		0.07		0.07
No formal education	1.00		1.00		1.00	
Primary	0.76 (0.45, 1.28)		0.69 (0.40, 1.19)		0.69 (0.40, 1.20)	
Secondary	0.52 (0.26, 1.02)		0.49 (0.24, 1.00)		0.49 (0.24, 1.00)	
Tertiary/Vocational/Uni	0.10 (0.01, 0.81)		0.10 (0.01, 0.83)		0.10 (0.01, 0.82)	
Religion		0.17		0.10		0.11
Protestant/Anglican	1.00		1.00		1.00	
Catholic	1.52 (1.02, 2.26)		1.64 (1.08, 2.49)		1.62 (1.07, 2.45)	
Muslim	1.62 (0.71, 3.67)		1.57 (0.68, 3.64)		1.54 (0.66, 3.58)	
Other	0.77 (0.17, 3.38)		0.66 (0.15, 3.00)		0.65 (0.14, 2.95)	
General health status		0.08		0.15		0.13
Good/fair/poor	1.00		1.00		1.00	
Excellent/very good	0.71 (0.48, 1.04)		0.73 (0.48, 1.19)		0.72 (0.48, 1.10)	
Alcohol use		0.53		0.66		0.63
No/low risk alcohol use	1.00		1.00		1.00	
Medium risk alcohol use	0.86 (0.45, 1.67)		0.80 (0.41, 1.58)		0.80 (0.41, 1.57)	
High/very high-risk alcohol use	1.1 (0.65, 2.01)		1.02 (0.55, 1.88)		1.03 (0.56, 1.91)	
ART adherence, past 30 days		0.04		0.15		0.18
Good/fair/poor/very poor	1.00		1.00		1.00	
Excellent/very good	0.62 (0.39, 0.97)		0.70 (0.43, 1.14)		0.72 (0.44, 1.17)	

adherence measure used one self-reported question, which can be questionable. However, previous studies have demonstrated the validity of the single-item self-rating adherence scale [62]. Strengths of the study include the use of validated tools to assess depressive symptoms and alcohol use, as well as an objective biomarker (PEth) to measure alcohol use.

In summary, while the results of this study suggest no evidence of an association between CD4 cell count and depressive symptoms among PWH with suppressed viral load, depressive symptoms are still prevalent. These results suggest that health providers should be aware that PWH, although virally suppressed, are still at risk for depression. Further studies should focus on other areas of research in addressing depression among PWH.

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Declarations

Ethics Approval and Consent to Participate All procedures conducted in the two studies included in this analysis were performed in accordance with the 2013 Declaration of Helsinki. Ethical approvals were

obtained as described in the Methods section. Both studies involved human participants, and all of them provided written informed consent prior to enrolment.

Competing Interests The authors declare no conflicts of interest.

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References

1. Hoare J, et al. Global systematic review of common mental health disorders in adults living with HIV. Curr HIV AIDS Rep. 2021. https://doi.org/10.1007/s11904-021-00583-w.
2. Chukwuorji JC, et al. Addressing the unmet mental health needs of people living with HIV: a scoping review of interventions in sub-Saharan Africa. AIDS Care. 2023;35(11):1677–90.
3. Dessauvagie AS, et al. The prevalence of mental health problems in sub-Saharan adolescents living with HIV: a systematic review. Glob Mental Health. 2020;7:e29.
4. Boakye DS, et al. Mental health burden among females living with HIV and AIDS in sub-Saharan Africa: a systematic review. PLOS Glob Public Health. 2024;4(2):e0002767.
5. UAC. Uganda Aids Commission: 2024 Uganda HIV and AIDS Factsheet: based on data ending 31st December 2023. 2024. https://drive.google.com/file/d/1awjU7HeaheWFNhl1gDlKIcN7daKWJQ7s/view Accessed 15 Sept 2024.
6. Ndagire R, et al. HIV viral load suppression among people with mental disorders at two urban HIV clinics in Uganda: a parallel convergent mixed methods study using the social ecological model. AIDS Res Ther. 2023;20(1):68.
7. Kinyanda E, et al. Risk of major depressive disorder among older persons living in HIV-endemic central and southwestern Uganda. AIDS Care. 2016;28(12):1516–21.
8. Kinyanda E, et al. Incidence and persistence of major depressive disorder among people living with HIV in Uganda. AIDS Behav. 2017;21:1641–54.
9. Psaros C, et al. The factor structure and presentation of depression among HIV-positive adults in Uganda. AIDS Behav. 2015;19:27–33.
10. Pei J-H, et al. Prevalence of suicidal ideation, suicide attempt, and suicide plan among HIV/AIDS: a systematic review and meta-analysis. J Affect Disord. 2021;292:295–304.
11. Bernard C, Dabis F, de Rekeneire N. Prevalence and factors associated with depression in people living with HIV in sub-Saharan Africa: a systematic review and meta-analysis. PLoS ONE. 2017;12(8):e0181960.
12. Taniguchi T, et al. Depression severity is associated with increased risk behaviors and decreased CD4 cell counts. AIDS Care. 2014;26(8):1004–12.
13. Bekhbat M, et al. HIV and symptoms of depression are independently associated with impaired glucocorticoid signaling. Psychoneuroendocrinology. 2018;96:118–25.
14. Xue H, Chen J, Fan W. Assessing the causal relationship between immune cell traits and depression by Mendelian randomization analysis. J Affect Disord. 2024;356:48–53.
15. Alvarez-Mon MA, et al. Expansion of CD4 T lymphocytes expressing interleukin 17 and tumor necrosis factor in patients with major depressive disorder. J Personal Med. 2021;11(3): 220.
16. Foley ÉM, et al. Peripheral blood cellular immunophenotype in depression: a systematic review and meta-analysis. Mol Psychiatry. 2023;28(3):1004–19.
17. Goodkin K, et al. The comorbidity of depression and neurocognitive disorder in persons with HIV infection: call for investigation and treatment. Front Cell Neurosci. 2023;17: 1130938.
18. Zhao J, et al. Mitochondrial functions are compromised in CD4 T cells from ART-controlled PLHIV. Front Immunol. 2021;12: 658420.
19. Palella F Jr, et al. CD4 cell count at initiation of ART, long-term likelihood of achieving CD4 > 750 cells/mm3 and mortality risk. J Antimicrob Chemother. 2016;71(9):2654–62.
20. Mudra Rakshasa-Loots A, et al. Neuroinflammation in HIV-associated depression: evidence and future perspectives. Mol Psychiatry. 2022;27(9):3619–32.
21. Rivera-Rivera Y, et al. Impact of depression and inflammation on the progression of HIV disease. J Clin Cell Immunol. 2016;7(3):423.
22. Huang B, et al. Depressive symptoms and HIV viral suppression: a systematic review and meta-analysis. AIDS Behav. 2025;29(3):870–83.
23. Nakimuli-Mpungu E, et al. Prevalence and factors associated with depressive disorders in an HIV+ rural patient population in southern Uganda. J Affect Disord. 2011;135(1–3):160–7.
24. Pathela P, et al. Initiating antiretroviral treatment for newly diagnosed HIV patients in sexual health clinics greatly improves timeliness of viral suppression. AIDS. 2021;35(11):1805–12.
25. Zhao B, et al. Antiretroviral therapy initiation within 7 and 8–30 days post-HIV diagnosis demonstrates similar benefits in resource-limited settings. Aids. 2022;36(12):1741–3.
26. Chamie G, et al. Financial incentives for reduced alcohol use and increased isoniazid adherence during tuberculosis preventive therapy among people with HIV in Uganda: an open-label, factorial randomised controlled trial. Lancet Global Health. 2023;11(12):pe1899–e1910.
27. Muyindike WR, et al. Alcohol use and HIV suppression after completion of financial incentives for alcohol abstinence and isoniazid adherence: a randomized controlled trial. EClinicalMedicine. 2025. https://doi.org/10.1016/j.eclinm.2024.103045.
28. Hahn JA, et al. Safety and tolerability of isoniazid preventive therapy for tuberculosis for persons with HIV with and without alcohol use. Aids. 2023;37(10):1535–43.
29. Lodi S, et al. The Drinkers' Intervention to Prevent Tuberculosis (DIPT) trial among heavy drinkers living with HIV in Uganda: study protocol of a 2× 2 factorial trial. Trials. 2021;22(1):355.
30. Gunn JK, et al. Understanding the risk of human immunodeficiency virus (HIV) virologic failure in the era of undetectable equals untransmittable. AIDS and Behavior. 2021;25(7):2259–65.
31. Radloff LS. The CES-D scale: a self-report depression scale for research in the general population. Appl Psychol Meas. 1977;1(3):385–401.
32. Natamba BK, et al. Reliability and validity of the center for epidemiologic studies-depression scale in screening for depression among HIV-infected and-uninfected pregnant women attending antenatal services in northern Uganda: a cross-sectional study. BMC Psychiatry. 2014;14(1): 303.

33. Hamby T, et al. A psychometric assessment of the factor structure and reliability of the Center for Epidemiological Studies Depression (CES-D) questionnaire in four African nations. BMC Psychiatry. 2026. https://doi.org/10.1186/s12888-026-07803-w.
34. Carleton RN, et al. The center for epidemiologic studies depression scale: a review with a theoretical and empirical examination of item content and factor structure. PLoS ONE. 2013;8(3):e58067.
35. Eaton WW, et al. Center for epidemiologic studies depression scale Review and revision. In: Maruish M, editor. The use of psychological testing for treatment planning and outcomes assessment. London: IEA Publishers; 2004.
36. Feldman BJ, et al. Evaluation of the single-item self-rating adherence scale for use in routine clinical care of people living with HIV. AIDS Behav. 2013;17:307–18.
37. Wu AW, et al. Evidence for reliability, validity and usefulness of the Medical Outcomes Study HIV Health Survey (MOS-HIV). Qual Life Res. 1997;6:481–93.
38. Hahn JA, et al. Phosphatidylethanol (PEth) as a biomarker of alcohol consumption in HIV-positive patients in sub-Saharan Africa. Alcohol Clin Exp Res. 2012;36:854–62.
39. Bradley KA, et al. AUDIT-C as a brief screen for alcohol misuse in primary care. Alcohol Clin Exp Res. 2007;31(7):1208–17.
40. Rubinsky AD, et al. Estimating risk of alcohol dependence using alcohol screening scores. Drug Alcohol Depend. 2010;108(1–2):29–36.
41. Jones J, et al. The detection of 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphoethanol in human dried blood spots. Anal Methods. 2011;3(5):1101–6.
42. Hahn JA, et al. Alcohol use and HIV disease progression in an antiretroviral naive cohort. JAIDS J Acquir Immune Defic Syndr. 2018;77(5):492–501.
43. Ulwelling W, Smith K. The PEth blood test in the security environment: what it is; why it is important; and interpretative guidelines. J Forensic Sci. 2018;63(6):1634–40.
44. Hahn JA, et al. Alcohol interventions for persons with HIV: meta-analysis of randomized controlled trials using phosphatidylethanol and self-report. Drug Alcohol Depend. 2025. https://doi.org/10.1016/j.drugalcdep.2025.112879.
45. Opito R, et al. Treatment outcome of the implementation of HIV test and treat policy at The AIDs Support Organization (TASO) Tororo clinic, Eastern Uganda: a retrospective cohort study. PLoS ONE. 2020;15(9):e0239087.
46. Ssemwanga D, et al. Prevalence of viral load suppression, predictors of virological failure and patterns of HIV drug resistance after 12 and 48 months on first-line antiretroviral therapy: a national cross-sectional survey in Uganda. J Antimicrob Chemother. 2020;75(5):1280–9.
47. Low A, et al. Incidence of opportunistic infections and the impact of antiretroviral therapy among HIV-infected adults in low-and middle-income countries: a systematic review and meta-analysis. Clin Infect Dis. 2016;62(12):1595–603.
48. Mhando F, et al. Microfinance and peer health leadership intervention implementation for men in Dar es Salaam, Tanzania: a qualitative assessment of perceived economic and health outcomes. Am J Men's Health. 2020;14(4): 1557988320936892.
49. Olisah VO, Adekeye O, Sheikh TL. Depression and CD4 cell count among patients with HIV in a Nigerian University Teaching Hospital. Int J Psychiatry Med. 2014;48(4):253–61.
50. Kinyanda E, et al. Major depressive disorder and suicidality in early HIV infection and its association with risk factors and negative outcomes as seen in semi-urban and rural Uganda. J Affect Disord. 2017;212:117–27.
51. Kaggwa MM, et al. Prevalence of depression in Uganda: a systematic review and meta-analysis. PLoS ONE. 2022;17(10):e0276552.
52. Chan BT, et al. Declining prevalence of probable depression among patients presenting for antiretroviral therapy in rural Uganda: the role of early treatment initiation. AIDS Behav. 2015;19:19–26.
53. Rezaei S, et al. Global prevalence of depression in HIV/AIDS: a systematic review and meta-analysis. BMJ Supp Palliat Care. 2019;9(4):404–12.
54. Rukundo GZ, et al. Depression, suicidality, substance-use and associated factors among people living with HIV the COVID-19 pandemic in Uganda. PLoS ONE. 2023;18(5):e0285310.
55. Ghaimo FE, et al. Prevalence and factors associated with alcohol use disorders among people living with HIV attending care and treatment centers at Kilimanjaro, Tanzania: a cross-sectional study. PLoS ONE. 2025;20(2):e0318120.
56. Yang Y, et al. Global prevalence of depressive symptoms among people living with HIV/AIDS: a systematic review and meta-analysis of the past five years. AIDS Care. 2024;36(2):153–64.
57. Duko B, Ayalew M, Ayano G. The prevalence of alcohol use disorders among people living with HIV/AIDS: a systematic review and meta-analysis. Subst Abuse Treat Prev Policy. 2019. https://doi.org/10.1186/s13011-019-0240-3.
58. Sullivan LE, et al. The impact of alcohol use on depressive symptoms in human immunodeficiency virus-infected patients. Addiction. 2008;103(9):1461–7.
59. Sullivan LE, et al. Alcohol consumption and depressive symptoms over time: a longitudinal study of patients with and without HIV infection. Drug Alcoh Depend. 2011;117(2–3):158–63.
60. Palfai T, et al. The influence of depressive symptoms on alcohol use among HIV-infected Russian drinkers. Drug Alcoh Depend. 2014;134:85–91.
61. Ssebunnya J, et al. Social acceptance of alcohol use in Uganda. BMC Psychiatry. 2020. https://doi.org/10.1186/s12888-020-2471-2.
62. Feldman BJ, et al. Evaluation of the single-item self-rating adherence scale for use in routine clinical care of people living with HIV. AIDS Behav. 2013;17(1):307–18.

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