Age-varying Associations of Depressive Symptoms and Heavy Episodic Drinking Throughout Adulthood Among People with HIV and Receiving care in Cameroon Within a National "treat all" Policy

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Abstract

Comorbid depression and heavy episodic drinking (HED) may threaten the success of "treat all" policies in sub-Saharan Africa as the population of people with HIV (PWH) ages. We investigated associations between depressive symptoms and heavy episodic drinking (HED) and the extent the relationship differed across ages among PWH receiving HIV care in Cameroon. We conducted a retrospective analysis of 18-60-year-old PWH on antiretroviral therapy in Cameroon from January 2016 to March 2020. Age-varying effect modelling was conducted to assess associations between depressive symptoms and HED across ages and by gender. Prevalence of depression and HED was highest at ages 20 and 25, respectively. After age 25, the magnitude of the association between depressive symptoms and HED was significant and increased until age 30 (aOR: 1.88, 95% CI: 1.48, 2.39), with associations remaining significant until age 55 (aOR: 1.64, 95% CI: 1.17, 2.29). Women had more variability and higher magnitudes of associations between depressive symptoms and HED than men. The interrelationship between depressive symptoms and HED was significant throughout most of adulthood for PWH receiving HIV care in Cameroon. Understanding age and gender trends in these associations can guide integration efforts in HIV care settings.

Keywords Mental health · Alcohol misuse · HIV · Antiretroviral therapy · Adults · Cameroon

Introduction

The expansion of antiretroviral therapy (ART) in the treat-all era has extended the lives of millions living with HIV [1]. In 2019, an estimated 4.46 million people with HIV (PWH) over the age of 50 lived in sub-Saharan Africa (SSA) [2, 3]. Projections estimate that PWH over the age of 50 in SSA will increase by 190%, to approximately 9 million, by 2040 [3]. In 2019, there were nearly 500,000 PWH 15 years of age and older in Cameroon [2]. In 2016, Cameroon implemented a national implementation of a national "treat all" policy, which all PWH are eligible to initiate antiretroviral treatment (ART) as soon as possible after diagnosis [2, 4]. The treat all policy will likely lead to increases in rapid ART initiation and viral suppression, ultimately leading to reduced mortality [4, 5]. As this population ages, co-occurring conditions, such as depression and heavy episodic

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drinking (HED), may become ongoing challenges for HIV care and treatment among PWH.

Depression and HED are common among PWH and could synergistically worsen HIV health outcomes. The syndemic theory posits that co-occurring conditions can synergistically worsen health outcomes more than each condition individually [6]. Approximately 46% of PWH in a Ugandan study screened positive for depressive disorder [7]. In another Ugandan study of PWH, 26% of patients reported clinically significant depressive symptoms [8]. However, prevalence varies depending on the screening tool, with prevalence between 12 and 19% when assessed by diagnostic interview and 13–24% when assessed by screening instruments [9]. Among PWH receiving HIV care in Cameroon, the prevalence of depression is estimated to be 12%, 22%, and 9% among ART non-users, recent ART initiators, and long-term ART initiators, respectively [10]. Alcohol use is also common among PWH in SSA [8, 11, 12]. Approximately 15% of PWH in care in Cameroon report HED of drinking six or more drinks in one sitting, with HED prevalence highest among recent ART initiators compared to those not on ART and long-term ART initiators [13]. Both depression and alcohol use, independently and interdependently, can lead to delays in HIV diagnoses, suboptimal ART adherence, and virological failure [11, 14].

As the population of older PHW continues to grow rapidly, there is an increased need to understand how the relationship between depression and HED changes over the life course of PWH. Depression and HED are thought to be more prevalent in younger age groups. Depression and HED often begin during adolescence or young adulthood [15]. Among adolescents and young adults in Africa, 14–25% had depressive symptoms, and approximately 20% reported HED [15]. Estimates of depression and HED among aging PWH are limited, possibly due to gaps in screening and treatment availability in HIV treatment clinics across SSA [16]. Understanding the potential for dynamic changes in the interrelationship between depression and HED throughout the lifespan will ultimately inform prevention and treatment efforts.

The dynamics of co-occurring depression and HED across the lifespan are likely influenced by gender. Gender relates to socially constructed characteristics, roles, and expectations that are informed by culture and society [17]. Depression is more common among women, with the onset of depression typically occurring earlier in life [18]. Conversely, alcohol use, including problem drinking, is more common among men, including in Cameroon and among PWH [12]. Yet, it remains unclear if the relationship between depression and HED differs by gender or across the life course, particularly within the context of treat all implementation.

We used data from a large cohort of PWH in HIV care and on ART in Cameroon to examine the age-specific effects between depression and HED throughout adulthood, i.e. across ages 18–60 years. We also investigated the extent to which these associations differed by gender.

Methods

We used data from the Central Africa-International epidemiology Databases to Evaluate AIDS (CA-IeDEA) study, a clinical cohort of PWH.[19] The CA-IeDEA research consortium, one of seven regional cohorts within IeDEA (https://www.iedea.org), is funded by the United States National Institutes of Health to investigate the impact, progression and long-term outcomes of the HIV/AIDS epidemic in Central Africa. The CA-IeDEA routinely collects sociodemographic, clinical, and immunological data from the medical records of patients enrolled in HIV care at participating sites in Burundi, Cameroon, Democratic Republic of the Congo (DRC), Republic of Congo (ROC) and Rwanda [19]. In Cameroon, clinical information, including depressive symptoms and alcohol use, is collected directly from the participants. This retrospective analysis includes data from 18-60-year-old PWH on ART at CA-IeDEA Cameroon sites between January 2016 and March 2020. The IeDEA Cameroon sites included were three HIV treatment centers in Bamenda, Limbe, and Yaounde.

CA-IeDEA was approved by the Cameroon National Ethics Committee and the institutional review board (IRB) at the Albert Einstein College of Medicine; this secondary analysis of de-identified data was exempt from IRB review. Informed written consent was obtained from patients actively enrolled in HIV care at study sites before conducting structured interviews with these patients or abstracting data from medical records.

Measures

Depressive symptoms: We ascertained depressive symptoms using the two-item Patient Health Questionnaire (PHQ-2). A score of three or greater on a six-point scale indicated likely major depressive disorder. The PHQ-2 has been used throughout SSA and validated among PWH in Kenya [20].

Heavy episodic drinking: At enrollment into IeDEA Cameroon, participants were asked several questions related to alcohol use using a locally adapted Alcohol Use Disorder Identification Test [21]. Patients were also asked, “During the past three months, what best describes how often the patient has a drink containing alcohol? This includes beer, wine, etc.“ During the first year of data collection, if a patient responded “never” to this question, they were not asked any

additional questions about their alcohol use, including those about HED. Therefore, if a patient responded "never" to this question and thus was missing responses to both questions about HED, we classified that patient as not having engaged in HED. Analysis of data from later years of the study showed that over 99% of patients who indicated they never drank in the past three months and who had non-missing responses to the HED questions did not engage in HED.

We defined HED as a response of more frequently than "never" to either of the following questions: "During the past three months, how often did the patient drink more than three bottles of beer in one sitting" and "During the past three months, how often did the patient drink more than six glasses of other alcoholic drinks (not beer) in one sitting." In Cameroon, beer is served in large bottles (750 mL), approximately the size of two standard alcoholic drinks, and so the question pertaining to beer was scaled accordingly.

Covariates: Most covariates were measured at the same visit as depressive symptoms and HED. These covariates, all self-reported, were gender, age, smoking status (current, former, never), and HIV disclosure. All participants identified as cisgender males or females and are referred to hereafter as "men" and "women." At each visit, respondents were asked if they had disclosed their HIV status to anyone since their last visit. For this analysis, we were interested in if they had ever disclosed their HIV status to anyone; an affirmative response at that visit or any prior visits was considered evidence of "HIV disclosure." The date of ART initiation was abstracted from medical records. Self-reported education (no schooling, primary, secondary, high school or equivalent, or university or equivalent) was not recorded with an indication of which visit it was collected. As such, we did not know when the change occurred for patients who reported changes in education level over time. As this happened in less than 1% of our data, we eliminated all visits for people with multiple recorded levels of education. We included visits with complete covariate data among non-pregnant adults aged 18–60 between January 2016 and March 2020.

Statistical Analysis

We used time-varying effect modeling (TVEM) to assess longitudinal associations between depressive symptoms and HED. Unlike standard methods, which estimate a single point estimate of the association between two variables across time, TVEM estimates a function. TVEM allows for assessing the functional form of the relationship between two variables over some continuous timescale without imposing parametric assumptions [22]. TVEM does, however, assume the change in the relationship over time between the variables of interest is smooth [22]. We used the SAS macro %TVEM accessible from methodology.psu.edu [23]. Results from the TVEM are presented as figures with point estimates and 95% confidence intervals (CIs). We used P-splines with 10 knots and with sandwich standard errors, to relax parametric assumptions [22]. Statistical significance was defined as a 95% CI that excludes the null value.

First, we graphed the prevalence of HED across the life course using an intercept-only TVEM. We then graphed the prevalence of depressive symptoms across the life course. Finally, we modeled the effect (odds ratio [OR]) of depressive symptoms on HED between the ages of 18 and 60 in the entire population and stratified by gender, adjusting for the time-invariant effects of clinic site, smoking status, HIV disclosure, and education level.

Given that we classified the PHQ-2 into a binary, clinically meaningful cut-point, our models may result in a loss of power and be less sensitive to change [24]. Therefore, we conducted a sensitivity analysis to model the effect of the original continuous PHQ-2 score to examine the relationship between depression and HED within the entire population.

Statistical analyses were performed in SAS 9.4 (SAS Institute Inc., Cary, NC).

Results

There were 23,984 visits among 11,668 non-pregnant adults aged 18–60 years on ART between January 2016 and March 2020 (Figure 1). At 21,790 of those visits, depression data were collected. At 21,339 of those visits, alcohol use data were also collected. In addition, all covariates (i.e., gender, clinic site, education, smoking status, HIV disclosure status) were collected at 19,916 visits. These visits were made by 11,470 unique individuals.

Across the 19,916 clinic visits, the median age was 42 (interquartile range: 35–49) (Table 1). Over two-thirds (69%) of participants were women. Approximately 50% of PWH had completed secondary education or higher. Over 60% of PWH reported being employed, while 38% reported being unemployed, a student, or retired. The majority reported never smoking (90%); 3% reported currently smoking and 7% reported formerly smoking.

The prevalence of both depressive symptoms and HED decreased over time across adulthood (Figure 2). The prevalence of depressive symptoms was highest at age 18 and then consistently declined throughout adulthood, from 19% at age 18 to 8% at age 60. For HED, the prevalence increased from 14% at age 20 to 17% at age 25. The prevalence of HED then continued to decrease to 9% by age 60.

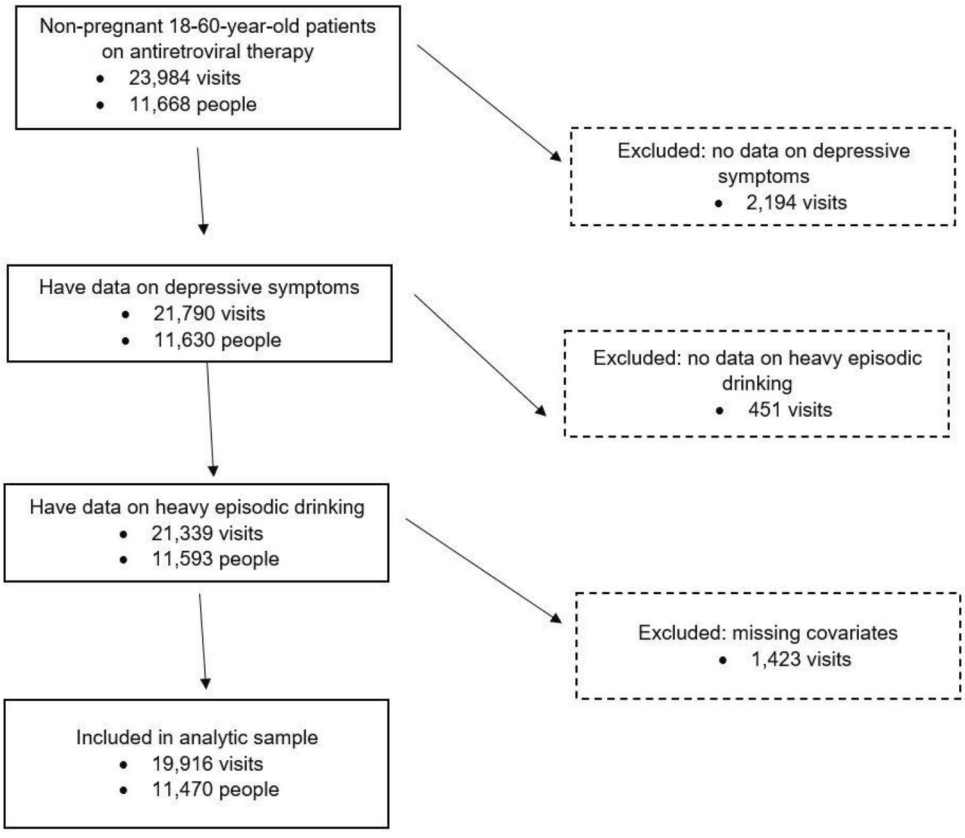

Fig. 1 Participant inclusion flowchart

Depressive symptoms and HED were significantly associated throughout much of adulthood, beginning at age 25 until age 55 (Figure 3). For ages 18 to 24, there was no significant relationship between depressive symptoms and HED, which may be due to a low proportion of 18 to 24 years in the sample. Those with depressive symptoms had 1.60 times the odds of HED (95% CI: 1.19, 2.15; p value < 0.01) compared to those with no depressive symptoms at age 25, adjusting for gender, clinic site, smoking, HIV disclosure, and education. The magnitude of the association between depressive symptoms and HED increased until age 30 (adjusted odds ratio [aOR]: 1.88, 95% CI: 1.48, 2.39; p value < 0.01). After age 30, the magnitude decreased and remained significant through age 55 with an aOR of 1.64 (95% CI: 1.17, 2.29; p value < 0.01).

For men, depressive symptoms and HED were significantly associated through ages 25 to 50 (Figure 4). The odds of depressive symptoms and HED was highest at age 40 (aOR: 1.64, 95% CI: 1.29, 2.09; p value < 0.01). The association approached the null at age 60. The weakest magnitude of the relationship was at age 50, with an aOR of 1.44 (95% CI: 1.04, 2.00; p value 0.03).

Women had more variability and higher magnitudes of associations between depressive symptoms and HED compared to men (Figure 4). The coefficient of the relationship varied substantially across ages for women, with a bimodal distribution peaking at ages 30 and 55. For women, the age with the most substantial aOR was at age 30, 2.07 (95% CI: 1.53, 2.83; p value < 0.01). Women with depressive symptoms had 2.19 times the adjusted odds of HED (95% CI: 1.36, 3.53; p value < 0.01) than those with no depressive symptoms at age 55.

In the sensitivity analysis where PHQ-2 was specified continuously, the trajectories of associations were similar to those in the main analyses. For every 1-unit increase in the PHQ-2 score, the adjusted odds of HED increased throughout much of the age range. PHQ-2 score and HED were significantly associated from age 23–58 in the entire sample (Figure SI). Results for men and women were also similar to the main analysis (Figure SII).

Discussion

In this large sample of PWH receiving HIV care in Cameroon, depressive symptoms and HED were prevalent through the majority of adulthood. Depressive symptoms and HED were significantly associated from ages 25 to 60. Notably, the interrelationship was not significant for adults aged 18–24. Women had more variability and higher magnitudes of association between depressive symptoms and HED throughout adulthood than men. Integrating prevention, screening, and

Table 1 Characteristics of 11,470 people with HIV on antiretroviral treatment at three HIV clinics in Cameroon, 2016–2020

Number of observations		19,916
Number of people		**11,470**
		N (%)
Age		
	18–24 years	655 (3)
	25–34 years	3,738 (19)
	35–44 years	7,438 (37)
	45–54 years	5,948 (30)
	55–65 years	2,137 (11)
Gender		
	Female	13,790 (69)
	Male	6,126 (31)
	Missing	0
Education		
	No schooling	1,462 (7)
	Primary	8,791 (44)
	Secondary	6,210 (31)
	High school or equivalent	1,873 (9)
	University or equivalent	1,580 (8)
	Missing	0
Employment		
	Student	491 (2)
	Employed	12,230 (62)
	Unemployed	6,807 (34)
	Retired	336 (2)
	Missing	52
Smoking status		
	Never	17,999 (90)
	Current	582 (3)
	Former	1,335 (7)
	Missing	0
Depressive symptoms		
	Yes	1,998 (10)
	No	17,918 (90)
Heavy episodic drinking		
	Yes	2,591 (13)
	No	17,325 (87)
Has shared HIV status		
Yes		18,000 (90)
No		1,916 (10)

treatment for both depression and HED is urgently needed in HIV treatment centers in low-resource settings.

Both depression and HED were highly prevalent over adulthood, with possible syndemic implications among this population of PWH receiving care in Cameroon. Generally, prevalence estimates of depression and heavy alcohol use were comparable to pooled prevalence estimates from meta-analyses among PWH in sub-Saharan Africa [25–27]. Within this present study, depression and HED were significantly associated through most of adulthood for men and women living with HIV in Cameroon, potentially leading to suboptimal HIV outcomes. While the nature of this analysis does not allow for the estimation of causal effects of depressive symptoms and HED on HIV outcomes, several pathways can lead to co-occurrence. Depressive symptoms may increase the risk for HED, as internalizing depressive symptoms and "self-medication" may lead to alcohol use and misuse [18, 28]. Additionally, HED has been endorsed as a coping mechanism to deal with negative affect, including depressive symptoms [29]. At the same time, alcohol use can also lead to the onset of depression by exacerbating or inducing related psychological symptoms. This co-occurrence can ultimately delay HIV diagnosis and worsen clinical outcomes. Further longitudinal investigations are needed to determine the synergistic effects of depressive symptoms and HED on HIV outcomes among PWH.

While depression and HED were prevalent among young adults under 25 years of age, the association between depression and HED was not significant. Adolescence and young adulthood are critical transitional periods with increased independence, pressures, and responsibilities [30]. This transitional period, as a result, is often correlated with increased stress which can lead to depressive symptoms and self-coping with alcohol [29]. Indeed, among a sample of university students in South Africa, young adults who reported HED were more likely to report high academic stress [31]. Additionally, those reporting HED were also likely to have depression symptoms. In our sample, depression and HED were not significantly associated among young adults, which was likely due to the limited number of 18 to 24 years in our sample and receiving HIV care. The age distribution in our sample aligns with the current epidemic in Cameroon, with the highest HIV prevalence occurring among those 35 to 39 years of age [32].

Regardless, if left untreated, this interrelationship among young adults may lead to suboptimal HIV care outcomes later in life. Prevention and treatment efforts for depression and HED early in adulthood may potentially influence the trajectories of these co-morbidities for PWH.

Early evidence-based psychotherapies can provide young adults with effective coping strategies to reduce co-occurring depression and HED later in life [33]. Cognitive-behavioral therapy, motivational interviewing, and brief interventions are all evidence-based psychotherapies for depression and HED, which effectively improve HIV care outcomes among PHW in low-resource settings [33, 34]. Effective coping strategies may reduce the potential for unprotected sex, which may lead to HIV transmission, delays in HIV diagnosis, and suboptimal engagement with HIV care and treatment further into adulthood [35]. Targeted depression and HED screening should be aimed at young adults in Cameroon to faciliate timely identification and treatment referral for these co-morbidities, as well as to potentially prevent HIV transmission and suboptimal HIV care outcomes.

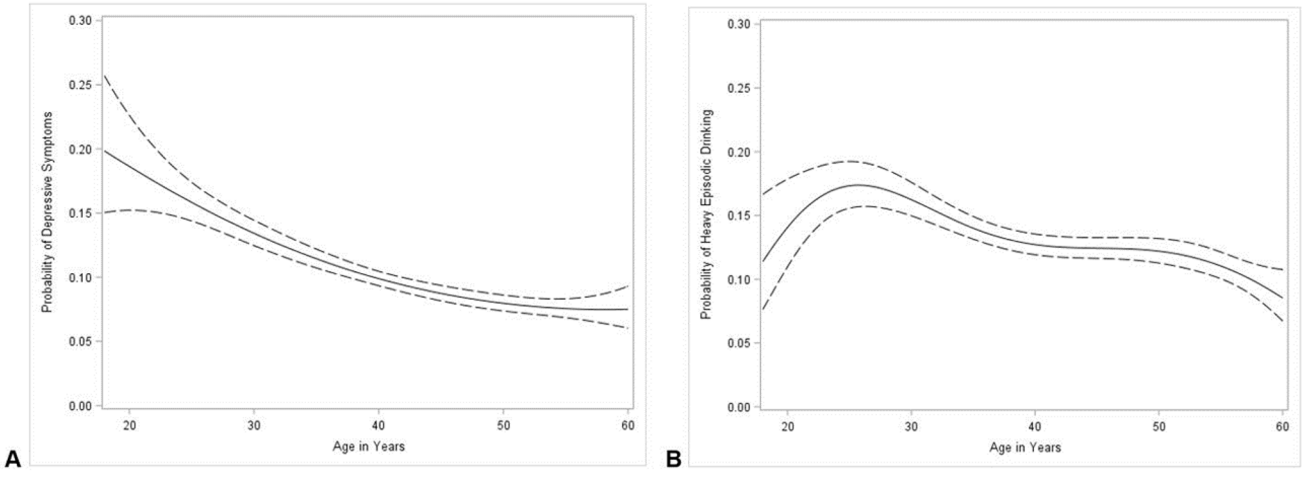

Fig. 2 Prevalence of depressive symptoms (A) and heavy episodic drinking (B) among people with HIV ages 18 to 60 (x-axis) and on antiretroviral treatment in Cameroon, 2016–2020. Solid line represents probability estimates; dashed lines represent 95% confidence intervals

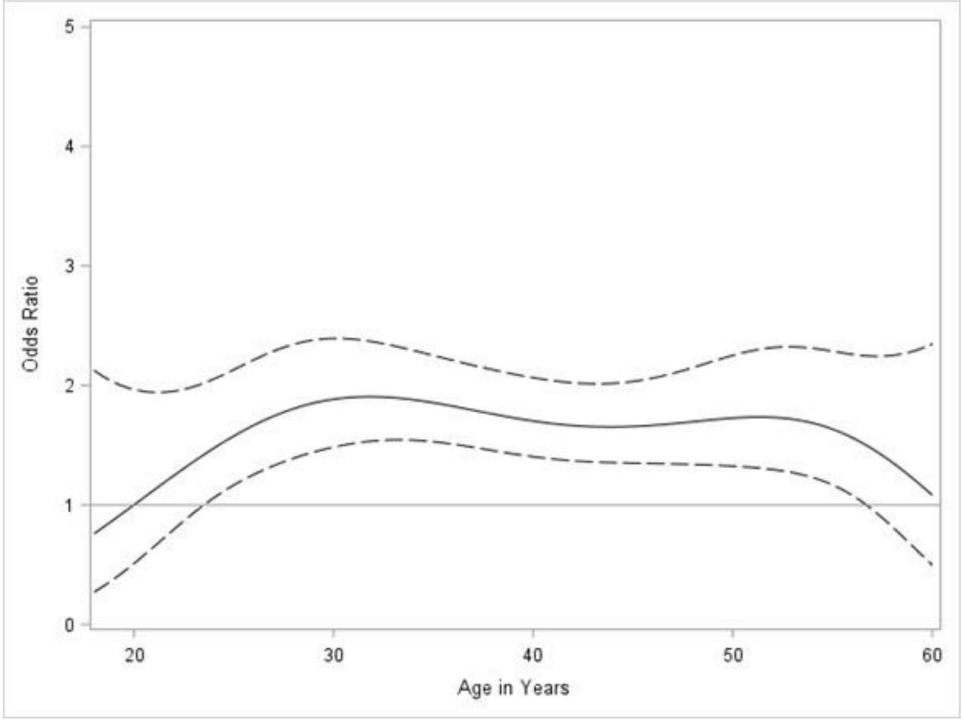

Fig. 3 Time-varying effect modeling showing the association between depressive symptoms and heavy episodic drinking across the age range (18 to 60 years) among adults ages 18 to 60 living with HIV and on antiretroviral treatment in Cameroon, 2016–2020

Women may require gender-tailored approaches to prevent and treat depression and HED to address windows of vulnerability where the interrelationship between these factors is strongest. Women generally experience a higher prevalence of depression, yet a recent study among PWH receiving HIV care in Cameroon found that the prevalence of depression was lower among women than men [36]. Alcohol use among women in SSA has historically been uncommon due to a high prevalence of lifetime alcohol abstinence. Yet, more recently, HED and regular high alcohol consumption are increasing among women in SSA [13]. Gender-specific investigations of lifetime depression and HED among PWH will enhance our understanding of windows to improve HIV diagnosis, ART initiation, and sustained viral suppression in Cameroon and other resource-limited settings.

We were able to investigate the dynamic associations of depression and HED across adulthood by using TVEM. Standard longitudinal models generally yield a single estimate at a specific time point, which is not conducive for evaluating the changing relationships of depression and HED over the adult life. TVEM provides a highly flexible modeling framework that does not make assumptions on the

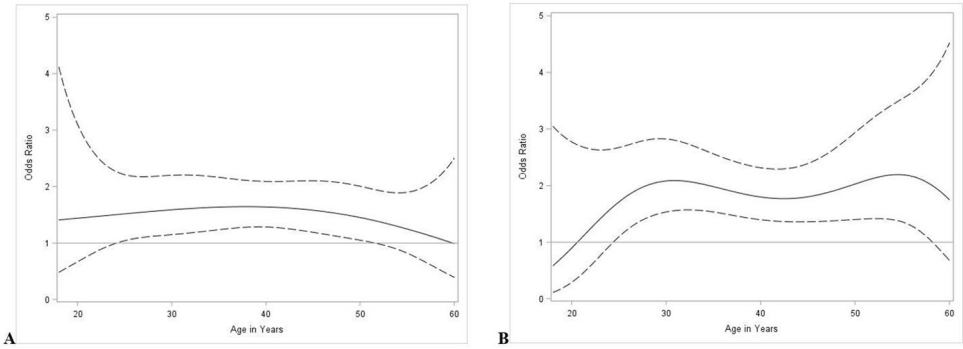

Fig. 4 Time-varying effect modeling showing the association between depressive symptoms and heavy episodic drinking among men (A) and women (B), ages 18 to 60 on antiretroviral treatment living with HIV in Cameroon, 2016–2020. The solid line represents the adjusted odds ratio of the effect of depressive symptoms on heavy episodic drinking, and the dashed line represents the corresponding 95% confidence interval. Odds ratio adjusted on the y-axis for the time-invariant effects of clinic site, smoking, HIV status disclosure, and education

parametric form but instead assesses the functional form of relationships over continuous time [22]. This innovative approach allows for a more nuanced examination of age-related changes for the interrelationship between depressive symptoms and HED. One study strength is our use of a large multicohort sample of PWH in Cameroon. While the high data quality standards within IeDEA make data harmonization feasible across clinics, the cohorts only include PWH receiving HIV care in three regional urban clinics. Both depression and HED can contribute to PWH dropping out of care and treatment, which may lead to underestimating the prevalence of both factors as well as the strength of associations between depression and HED among PWH in Cameroon [37]. Furthermore, our sample may not be generalizable to PWH outside of Cameroon, PWH who receive care at clinics that do not participate in IeDEA, or PWH who receive care in non-urban clinics.

Conclusion

Together, our results underscore a lifelong co-occurrence of depressive symptoms and alcohol use among PWH receiving ART in Cameroon. Thus, sustainable approaches for screening and treatment of both depression and HED are needed to potentially prevent HIV transmission, delays in HIV diagnosis, and suboptimal HIV outcomes for PWH in resource-limited settings.

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Authors' Contributions KEL, MR, and AP conceptualized and designed the study. KEL and MR analyzed the data and wrote up the first draft of the manuscript. MR and AP accessed and verified underlying data. AE, RJ, AD, AA, DN, KA, MY, EWY-P, DN, and AP provided extensive contribution into the manuscript. All authors reviewed and approved the final manuscript.

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Data Availability The dataset contains sensitive information and is not publicly available. However, it could be made available on reasonable request, with approval from the IRB at the Albert Einstein College of Medicine to maintain confidentiality.

Code Availability All analyses were conducted using SAS. SAS code could be made available from the first author (KEL) on reasonable request.

Declarations

Competing Interests The authors have no conflicts of interests to declare.

Ethics Approval The study was approved by the Cameroon National Ethics Committee and the institutional review board (IRB) at the Albert Einstein College of Medicine.

Consent to Participate All participants provided written informed consent.

Consent for publication Not applicable.

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