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Depression and Anxiety Symptoms (PHQ-2/GAD-2) Among People Living with HIV Compared to HIV-Negative Adults in Uganda: A Nationally Representative Analysis

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Abstract

Background.

People living with HIV (PLHIV) experience a disproportionate burden of depression and anxiety, but Ugandan evidence on this comorbidity is drawn almost entirely from HIV clinic-based samples, leaving unclear whether the reported excess reflects a true difference associated with HIV status or clinic-selection into care. We aimed to compare PHQ-2 and GAD-2 positive-screen prevalence between PLHIV and HIV-negative adults nationally, and to examine associated sociodemographic factors, using nationally representative population-based survey data from Uganda.

Methods.

We conducted a secondary analysis of the Uganda Population-Based HIV Impact Assessment (UPHIA) 2020–2021, a nationally representative, cross-sectional household survey of adults aged 15–80 years. Positive PHQ-2 and GAD-2 screens (score ≥ 3) were the outcomes. Factors associated with each outcome were examined using multivariable logistic regression with jackknife-based robust variance, adjusted a priori for age, sex, urban/rural residence, and region. A $p < 0.05$ was considered statistically significant.

Results.

Among 25,479 adults with a definitive HIV status, weighted PHQ-2 positive-screen prevalence was 6.68% (95% CI 6.20–7.19) overall, higher among PLHIV than HIV-negative adults (10.83% vs. 6.42%). GAD-2 positive-screen prevalence followed a similar pattern (11.92% vs. 6.28%). In adjusted models, PLHIV had significantly higher odds of a positive PHQ-2 screen (adjusted odds ratio [aOR] 1.43, 95% CI 1.19–1.74, $p < 0.001$) and GAD-2 screen (aOR 1.69, 95% CI 1.35–2.12, $p < 0.001$) than HIV-negative adults. Female sex, older age, and rural residence were independently associated with higher adjusted odds of both outcomes, while several regions, most consistently Mid-Western and South Western, showed significantly lower adjusted odds relative to Central 1: South Buganda.

Conclusions.

In this nationally representative Ugandan sample, PLHIV had significantly higher odds of depression and anxiety symptoms than HIV-negative adults, independent of age, sex, residence, and region, indicating that the excess mental health burden reported in Ugandan HIV clinic-based studies reflects, at least in part, a genuine difference associated with HIV status rather than clinic-selection alone. These findings support integration of routine mental health screening into HIV care in Uganda and highlight substantial regional variation in mental health burden meriting further investigation.

Introduction

Depression and anxiety disorders are among the leading causes of disability worldwide. In 2015, an estimated 322 million people, 4.4% of the global population, were living with depression, and a further 3.6% of the global population had an anxiety disorder; together these two conditions rank among the foremost contributors to years lived with disability globally, with depression alone accounting for 7.5% of all years lived with disability [1]. People living with HIV (PLHIV) carry a disproportionate share of this burden. A recent meta-analysis pooling 240 studies estimated global prevalence among PLHIV at 31% for depression and 29% for anxiety, several-fold higher than general-population estimates [2]. Within Africa specifically, a meta-analysis of 34 cross-sectional studies restricted to PLHIV on antiretroviral therapy (ART) found a pooled depression prevalence of 36% [3], and a systematic review of outpatient PLHIV across sub-Saharan Africa similarly reported depression prevalence ranging from 9% to 32% depending on measurement approach and treatment status [4]. An earlier, widely cited meta-analysis established that PLHIV face roughly twice the risk of depressive disorders compared with HIV-negative individuals, a finding that has anchored two decades of subsequent research into the psychiatric burden of HIV infection [5].

The clinical significance of this comorbidity extends well beyond symptom burden itself. Depression among PLHIV is bidirectionally linked to the HIV care cascade: a Ugandan case-control study found that PLHIV with lifetime depressive disorders had significantly poorer adherence to antiretroviral therapy than those without [6], a relationship replicated across low-, middle-, and high-income settings and consistent with mechanistic pathways involving impaired treatment engagement, reduced self-efficacy, and the cognitive and motivational symptoms of depression itself. Anxiety symptoms, though less extensively studied than depression in HIV populations, frequently co-occur with depressive symptoms and share overlapping risk factors, including HIV-related stigma, disclosure concerns, and the chronic psychosocial burden of a lifelong diagnosis.

Ugandan evidence on depression and anxiety among PLHIV is extensive but drawn almost entirely from clinic-based samples recruited at HIV treatment centres, where instrument validation work has also been concentrated: the Patient Health Questionnaire (PHQ) was validated for detecting major depressive disorder among HIV-positive individuals attending Ugandan HIV clinics [7], and a separate validation of the Luganda-translated PHQ-9 and PHQ-2 was conducted in rural primary care facilities in eastern Uganda [8]. Comparatively little is known about the general Ugandan population outside HIV care settings using the same brief screening instruments. A mobile phone-based national survey conducted during the first wave of the COVID-19 pandemic measured PHQ-2 and GAD-2 scores among Ugandan adults broadly and found substantial psychological distress associated with pandemic-related hardship [9], while a large population-based study translating and validating the GAD-7 in Luganda and Runyoro found a comparatively low prevalence of likely anxiety disorders (1.5%) using a stricter clinical cut-off [10]. None of these studies, clinic-based or general-population, has directly compared PLHIV with HIV-negative adults using identical measurement instruments and a nationally representative sampling design.

Whether the elevated depression and anxiety burden reported in Ugandan HIV clinic-based studies reflects a true excess associated with HIV status itself, or instead reflects selection into HIV care settings, referral patterns, or measurement differences across studies, remains unresolved in the absence of nationally representative data using a common instrument. This study used data from the Uganda Population-Based HIV Impact Assessment (UPHIA) 2020–2021, a nationally representative household survey, to address this gap. Using the validated PHQ-2 and GAD-2 ultra-brief screening instruments [11, 12], previously validated for detecting depressive symptoms among PLHIV and general populations in Uganda and neighbouring settings [7, 8], we compared the prevalence of positive depression and anxiety screens between PLHIV and HIV-negative adults nationally, and assessed sociodemographic factors associated with each outcome, adjusting a priori for age, sex, urban/rural residence, and region.

Methods

Study design

This was a secondary analysis of de-identified public-release data from the Uganda Population-Based HIV Impact Assessment (UPHIA 2020–2021), a nationally representative, cross-sectional, two-stage stratified cluster household survey conducted between February 2020 and March 2021 [13]. Reporting follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist [14].

Survey design and sampling

UPHIA 2020–2021 was implemented by the Uganda Ministry of Health in collaboration with the Uganda Bureau of Statistics, the U.S. Centers for Disease Control and Prevention, and the International Center for AIDS Care and Treatment Programs (ICAP) at Columbia University, with funding from the United States President's Emergency Plan for AIDS Relief (PEPFAR) [13]. A two-stage stratified cluster sampling design generated nationally representative estimates at the national level and by region, urban/rural residence, and sex. Enumeration areas were selected as primary sampling units with probability proportional to size, stratified by Uganda's eleven regions and by urban/rural residence; households were then selected within each sampled enumeration area by systematic random sampling. All resident household members aged 15 years and older who were present or expected to return during the survey visit were eligible for enrolment. Consenting participants completed a structured individual interview covering demographic characteristics, HIV-related history, and mental health screening, including the PHQ-2 and GAD-2. Final individual sampling weights were calibrated to national census population projections, including by age band and sex [13].

Study population and analytic samples

The study population comprised Ugandan adults aged 15–80 years (top-coded at 80) enrolled in the UPHIA 2020–2021 individual interview (n = 26,071). Of these, 25,479 (97.7%) had a definitive HIV status determination and form the base analytic sample for this study; 592 respondents with an indeterminate HIV status were excluded. The analytic sample for the depression outcome comprised 25,263 adults with a non-missing PHQ-2 response (216 missing); the analytic sample for the anxiety outcome comprised 25,160 adults with a non-missing GAD-2 response (319 missing).

Data collection

Consenting household members completed an individual interview covering demographic characteristics, HIV testing history, and a structured mental health module administered by trained interviewers, comprising the two-item Patient Health Questionnaire (PHQ-2) and the two-item Generalized Anxiety Disorder scale (GAD-2), each scored 0–6 based on the frequency of the two constituent symptoms over the preceding two weeks. HIV status was determined using the PHIA testing algorithm applied to venous blood specimens collected during the same household visit.

Variables

The primary outcomes were a positive PHQ-2 depression screen and a positive GAD-2 anxiety screen, each defined as a summed score of 3 or more, the validated cut-off established in the original instrument development and validation studies [11, 12]. This threshold was applied directly to the underlying 0–6 PHQ-2 and GAD-2 sum scores rather than to the UPHIA dataset's internally derived depression/anxiety flag variables, which use a stricter "over three" (i.e., score > 3) threshold; this distinction is noted here to preempt any apparent discrepancy with prevalence figures derived from the internal flag variables. A priori confounders, selected on the basis of established literature rather than bivariable screening, were age (years), sex, urban/rural residence, and Uganda's eleven-category region variable.

Statistical analysis

Analyses were performed in Stata 19.5 SE (StataCorp LLC, College Station, TX, USA). All estimates were weighted using the UPHIA Individual Final Weight, with jackknife (JK1) replicate-weight variance estimation using the 159 individual-level replicate weights provided with the dataset, consistent with UPHIA's survey design. Participant characteristics are reported as weighted proportions or means with 95% confidence intervals. Prevalence differences across groups were assessed using design-based F tests. Factors associated with a positive PHQ-2 or GAD-2 screen were examined using multivariable logistic regression with jackknife-based robust variance, reported as odds ratios (OR). Crude (unadjusted) and adjusted ORs are both reported for HIV status and for each a priori adjustment covariate, with crude estimates from separate univariable models; covariates were pre-specified rather than selected through bivariable screening, consistent with the analytic convention used across this manuscript series. Because the outcomes examined here are not rare (overall prevalence 6–7%,

exceeding 10% among PLHIV), reported odds ratios will diverge somewhat from the corresponding prevalence ratios and should not be interpreted as directly equivalent to relative risk. A $p < 0.05$ was considered statistically significant.

Results

Characteristics of study participants

Of 26,071 adults interviewed in UPHIA 2020–2021, 25,479 (97.7%) had a definitive HIV status determination and form the base analytic sample for this study; 592 respondents with an indeterminate HIV status were excluded (Fig. 1). Weighted HIV prevalence in this sample was 5.82% (95% CI 5.79–5.86), consistent with the estimate previously reported for the same underlying sample (Table 1). PLHIV were substantially older on average than HIV-negative adults (mean 38.07 years, 95% CI 37.38–38.77 vs. 31.73 years, 95% CI 31.67–31.79), more often female (64.96%, 95% CI 62.77–67.09 vs. 51.85%, 95% CI 51.66–52.03), and more often urban-resident (40.20%, 95% CI 32.73–48.16 vs. 32.31%, 95% CI 27.16–37.93) (Table 1). Age-group and sex margins in the Overall column are shown without a confidence interval because UPHIA's final weights are calibrated to fixed national census population totals by age band and sex, leaving negligible residual design-based variance for these marginal distributions; distributions conditional on HIV status retain meaningful sampling variability and are reported with 95% CIs, as are the Overall-column estimates for urban/rural residence and region, which are not subject to this calibration.

Table 1
Characteristics of study participants, overall and by HIV status, UPHIA 2020–2021

Characteristic	Overall, % (95% CI)	HIV-negative, % (95% CI)	HIV-positive, % (95% CI)
Age group			
15–24	39.63*	41.31 (41.10–41.53)	12.48 (10.57–14.68)
25–34	25.29*	25.02 (24.80–25.24)	29.75 (27.04–32.61)
35–44	15.39*	14.64 (14.45–14.83)	27.57 (25.01–30.28)
45–54	9.59*	8.96 (8.82–9.10)	19.81 (17.74–22.05)
55–64	5.54*	5.41 (5.31–5.51)	7.71 (6.35–9.33)
65–80	4.55*	4.67 (4.60–4.74)	2.69 (2.00–3.61)
Mean age, years	32.10	31.73 (31.67–31.79)	38.07 (37.38–38.77)
Sex			
Male	47.39*	48.16 (47.97–48.34)	35.04 (32.91–37.23)
Female	52.61*	51.85 (51.66–52.03)	64.96 (62.77–67.09)
Residence			
Urban	32.77 (27.55–38.46)	32.31 (27.16–37.93)	40.20 (32.73–48.16)
Rural	67.23 (61.54–72.45)	67.69 (62.07–72.84)	59.80 (51.84–67.27)
Region			
Central 1: South Buganda	17.25 (14.71–20.13)	16.82 (14.29–19.70)	24.23 (19.99–29.04)
Central 2: North Buganda	9.60 (7.98–11.50)	9.56 (7.97–11.44)	10.18 (7.96–12.92)
East Central	9.79 (8.64–11.09)	9.94 (8.74–11.28)	7.53 (6.27–9.00)
Kampala	6.62 (5.49–7.97)	6.61 (5.47–7.97)	6.86 (5.53–8.48)
Mid Eastern	9.66 (8.31–11.20)	9.83 (8.47–11.38)	6.96 (4.84–9.93)
Mid North	9.63 (8.12–11.39)	9.44 (8.03–11.06)	12.73 (8.95–17.80)
Mid Western	9.03 (8.19–9.94)	9.06 (8.20–9.99)	8.54 (6.83–10.63)
Northeast: Karamoja	1.57 (1.27–1.94)	1.64 (1.33–2.02)	0.57 (0.37–0.87)
Northeast: Teso	5.47 (4.65–6.43)	5.56 (4.75–6.51)	3.96 (2.44–6.38)

Characteristic	Overall, % (95% CI)	HIV-negative, % (95% CI)	HIV-positive, % (95% CI)
South Western	13.60 (12.03–15.33)	13.53 (11.97–15.25)	14.70 (11.03–19.32)
West Nile	7.77 (6.91–8.71)	8.01 (7.18–8.94)	3.74 (2.12–6.52)

**Age-group and sex margins in the Overall column are calibrated to national census population totals in the UPHIA weighting scheme (design-based standard error < 0.0001 percentage points); reported without a confidence interval as this would misrepresent negligible residual variance as meaningful precision. CI: confidence interval.*

Prevalence of PHQ-2 and GAD-2 positive screens

Overall weighted prevalence of a positive PHQ-2 depression screen was 6.68% (95% CI 6.20–7.19) among 25,263 adults with non-missing PHQ-2 responses, and was significantly higher among PLHIV than HIV-negative adults in crude comparison (10.83%, 95% CI 9.16–12.76 vs. 6.42%, 95% CI 5.94–6.94; design-based F(1,158) = 36.35, P < 0.001) (Table 2). A positive GAD-2 anxiety screen showed a similar pattern: overall prevalence 6.61% (95% CI 6.04–7.22), higher among PLHIV than HIV-negative adults (11.92%, 95% CI 9.73–14.51 vs. 6.28%, 95% CI 5.73–6.88; F(1,158) = 39.90, P < 0.001).

Table 2
Prevalence of PHQ-2 and GAD-2 positive screens, by HIV status, UPHIA 2020–2021

Outcome	Overall, % (95% CI)	HIV-negative, % (95% CI)	HIV-positive, % (95% CI)
PHQ-2 positive (score ≥ 3), n = 25,263	6.68 (6.20–7.19)	6.42 (5.94–6.94)	10.83 (9.16–12.76)
GAD-2 positive (score ≥ 3), n = 25,160	6.61 (6.04–7.22)	6.28 (5.73–6.88)	11.92 (9.73–14.51)

CI: confidence interval. All estimates weighted using the Individual Final Weight with jackknife (JK1) replicate-weight variance estimation (159 replicate weights).

Factors associated with a positive PHQ-2 screen (depression)

In crude models, PLHIV had 77% higher odds of a positive PHQ-2 screen than HIV-negative adults (OR 1.77, 95% CI 1.47–2.14, p < 0.001). After adjustment for age, sex, urban/rural residence, and region, this association attenuated but remained statistically significant (aOR 1.43, 95% CI 1.19–1.74, p < 0.001) (Table 3). Female sex (aOR 1.62, 95% CI 1.41–1.86, p < 0.001) and older age (aOR 1.03 per year, 95% CI 1.03–1.03, p < 0.001) were independently associated with higher adjusted odds of depression. Rural residence was associated with modestly higher adjusted odds (aOR 1.23, 95% CI 1.02–1.49, p = 0.034). Residents of Mid Western (aOR 0.48, p < 0.001), Northeast: Karamoja (aOR 0.55, p = 0.005), and South

Western (aOR 0.57, p < 0.001) showed significantly lower adjusted odds relative to Central 1: South Buganda (Table 3).

Table 3
Crude and adjusted odds ratios for a positive PHQ-2 screen (depression), UPHIA 2020–2021

Covariate	cOR (95% CI)	p-value	aOR (95% CI)	p-value
HIV status				
Negative	*Ref*		*Ref*	
Positive	1.77 (1.47–2.14)	< 0.001	1.43 (1.19–1.74)	< 0.001
Age (per year)	1.03 (1.03–1.03)	< 0.001	1.03 (1.03–1.03)	< 0.001
Sex				
Male	*Ref*		*Ref*	
Female	1.65 (1.44–1.89)	< 0.001	1.62 (1.41–1.86)	< 0.001
Residence				
Urban	*Ref*		*Ref*	
Rural	1.18 (1.00–1.38)	0.049	1.23 (1.02–1.49)	0.034
Region				
Central 1 (South Buganda)	*Ref*		*Ref*	
Central 2: North Buganda	0.97 (0.71–1.33)	0.848	1.00 (0.73–1.38)	0.997
East Central	0.82 (0.56–1.21)	0.317	0.77 (0.53–1.12)	0.175
Kampala	0.75 (0.56–1.01)	0.060	0.94 (0.71–1.26)	0.696
Mid Eastern	0.88 (0.62–1.27)	0.501	0.78 (0.54–1.11)	0.169
Mid North	0.93 (0.69–1.25)	0.625	0.90 (0.66–1.23)	0.507
Mid Western	0.49 (0.34–0.70)	< 0.001	0.48 (0.34–0.69)	< 0.001
Northeast: Karamoja	0.65 (0.44–0.96)	0.031	0.55 (0.37–0.83)	0.005
Northeast: Teso	0.92 (0.69–1.24)	0.600	0.88 (0.65–1.20)	0.416
South Western	0.68 (0.50–0.93)	0.015	0.57 (0.42–0.78)	< 0.001
West Nile	0.73 (0.50–1.07)	0.107	0.69 (0.47–1.01)	0.057

cOR: crude odds ratio, from separate univariable logistic regression models. aOR: adjusted odds ratio, from a multivariable logistic regression model including HIV status, age, sex, urban/rural residence, and region simultaneously. Ref: reference category. All models used jackknife (JK1) replicate-weight variance

estimation (159 replicate weights). CI: confidence interval. Because outcome prevalence exceeds 10% among PLHIV, odds ratios should not be interpreted as directly equivalent to relative risk.

Factors associated with a positive GAD-2 screen (anxiety)

In crude models, PLHIV had roughly double the odds of a positive GAD-2 screen compared with HIV-negative adults (OR 2.02, 95% CI 1.61–2.52, p < 0.001). This association attenuated but remained statistically significant after adjustment (aOR 1.69, 95% CI 1.35–2.12, p < 0.001) (Table 4). Female sex (aOR 1.65, 95% CI 1.44–1.90, p < 0.001) and older age (aOR 1.03 per year, 95% CI 1.02–1.03, p < 0.001) were independently associated with higher adjusted odds of anxiety. Rural residence was not significantly associated with anxiety after adjustment (aOR 1.22, 95% CI 0.99–1.52, p = 0.063). Residents of Mid Western (aOR 0.52, p = 0.008) and South Western (aOR 0.65, p = 0.032) showed significantly lower adjusted odds relative to Central 1: South Buganda (Table 4).

Table 4
Crude and adjusted odds ratios for a positive GAD-2 screen (anxiety), UPHIA 2020–2021

Covariate	cOR (95% CI)	p-value	aOR (95% CI)	p-value
HIV status				
Negative	*Ref*		*Ref*	
Positive	2.02 (1.61–2.52)	< 0.001	1.69 (1.35–2.12)	< 0.001
Age (per year)	1.03 (1.03–1.03)	< 0.001	1.03 (1.02–1.03)	< 0.001
Sex				
Male	*Ref*		*Ref*	
Female	1.69 (1.48–1.94)	< 0.001	1.65 (1.44–1.90)	< 0.001
Residence				
Urban	*Ref*		*Ref*	
Rural	1.23 (1.02–1.49)	0.030	1.22 (0.99–1.52)	0.063
Region				
Central 1 (South Buganda)	*Ref*		*Ref*	
Central 2: North Buganda	1.05 (0.69–1.61)	0.813	1.09 (0.72–1.67)	0.683
East Central	0.99 (0.62–1.58)	0.970	0.94 (0.59–1.51)	0.808
Kampala	0.79 (0.54–1.15)	0.216	0.99 (0.69–1.42)	0.938
Mid Eastern	1.21 (0.78–1.88)	0.393	1.10 (0.71–1.71)	0.664
Mid North	1.32 (0.93–1.87)	0.116	1.30 (0.91–1.87)	0.147
Mid Western	0.52 (0.32–0.83)	0.006	0.52 (0.32–0.84)	0.008
Northeast: Karamoja	0.80 (0.52–1.22)	0.296	0.70 (0.45–1.08)	0.106
Northeast: Teso	1.09 (0.75–1.59)	0.653	1.06 (0.71–1.57)	0.772
South Western	0.76 (0.51–1.11)	0.153	0.65 (0.44–0.96)	0.032
West Nile	0.99 (0.64–1.54)	0.974	0.96 (0.62–1.49)	0.855

cOR: crude odds ratio, from separate univariable logistic regression models. aOR: adjusted odds ratio, from a multivariable logistic regression model including HIV status, age, sex, urban/rural residence, and region simultaneously. Ref: reference category. All models used jackknife (JK1) replicate-weight variance estimation (159 replicate weights). CI: confidence interval. Because outcome prevalence exceeds 10% among PLHIV, odds ratios should not be interpreted as directly equivalent to relative risk.

Discussion

In this nationally representative analysis of UPHIA 2020–2021, weighted prevalence of a positive PHQ-2 depression screen was 6.68% and of a positive GAD-2 anxiety screen was 6.61% among Ugandan adults overall. PLHIV had substantially higher unadjusted prevalence of both outcomes than HIV-negative adults (10.83% vs. 6.42% for depression; 11.92% vs. 6.28% for anxiety), and this excess persisted, though attenuated, after adjustment for age, sex, urban/rural residence, and region (aOR 1.43 for depression; aOR 1.69 for anxiety). Female sex and older age were independently associated with higher odds of both outcomes, rural residence was associated with modestly higher odds of depression, and several regions, most consistently Mid Western and South Western, showed significantly lower adjusted odds relative to Central 1: South Buganda.

Our PLHIV-specific estimates sit toward the lower end of the range reported across outpatient PLHIV samples in sub-Saharan Africa, where a systematic review found depression prevalence spanning 9% to 32% depending on measurement approach and treatment status [4]. Our 10.83% depression and 11.92% anxiety prevalence among PLHIV fall within this range but close to its lower bound, a position consistent with our use of the ultra-brief, two-item PHQ-2 and GAD-2 rather than the longer PHQ-9, GAD-7, or clinician-administered instruments used in most of the studies contributing to that pooled range; briefer screens with a fixed low cut-off tend to be somewhat more conservative than longer symptom inventories at detecting probable caseness.

Several Ugandan and regional studies report considerably higher prevalence than we observed, and the gap is informative rather than merely a discrepancy to be explained away. A meta-analysis pooling 240 international studies estimated depression and anxiety prevalence among PLHIV at 31% and 29% respectively [2], and a Africa-focused meta-analysis restricted to PLHIV on ART found pooled depression prevalence of 36% [3]. Closer to home, a MINI-defined depression prevalence of 17.4% was reported among HIV-positive attendees at Ugandan HIV clinics [7], and a study of slum residents in Kampala during the COVID-19 pandemic found depression and anxiety prevalence of 33.8% and 13.4% respectively using the longer PHQ-9 and GAD-7 [15]. Three factors plausibly explain why our estimates sit below these figures. First, all of these comparator studies drew participants from clinical or acutely stressed settings, HIV treatment centres, urban slum populations during a pandemic, rather than a nationally representative household sample; individuals already engaged in HIV or general health care, or living through concentrated hardship, are likely to have both higher underlying symptom burden and greater propensity to report it. Second, longer instruments such as the PHQ-9 and MINI capture a broader symptom spectrum, including several mild-to-moderate items, than the PHQ-2/GAD-2's fixed two-item, four-point-scale structure. Third, the Kampala slum study was conducted during an acute phase of the COVID-19 pandemic, a period of unusually elevated population-level distress that our survey, conducted February 2020 to March 2021, only partially overlaps.

Conversely, our overall population estimates are higher than at least one comparable Ugandan population-based study using a stricter instrument: a large population-based validation of the GAD-7 in

Luganda and Runyoro found likely-anxiety-disorder prevalence of only 1.5% [10], well below our 6.61% GAD-2 estimate. This gap is readily explained by instrument choice rather than a true difference in population burden: the GAD-7's conventional cut-off of ≥ 10 identifies a narrower, more clinically severe group than the GAD-2's cut-off of ≥ 3 on a 0–6 scale, which is deliberately calibrated as a sensitive first-stage screen rather than a diagnostic threshold. Our estimates are similarly higher than global clinical-diagnosis prevalence of depression (4.4%) and anxiety disorders (3.6%) reported by WHO [1], consistent with the expected pattern that brief screening instruments identify a wider group of individuals with clinically relevant symptoms than formal diagnostic criteria requiring functional impairment and symptom duration.

Our finding that female sex and older age were independently associated with higher odds of depression and anxiety symptoms is consistent with the limited Ugandan evidence available. A study of low-income earners in southwestern Uganda during the COVID-19 lockdown identified women as a population at elevated risk for depression, with age also positively correlated with depressive symptoms [16], and the national mobile-phone survey conducted during the same period found psychological distress most common among women [9]. Plausible mechanisms for the sex association include the disproportionate caregiving and economic-dependency burden carried by Ugandan women, compounded among women living with HIV by HIV-related stigma and disclosure concerns; for the age association, plausible mechanisms include the cumulative psychosocial burden of a longer duration of HIV diagnosis and treatment, alongside age-related increases in comorbid physical illness.

The association we observed between rural residence and higher adjusted odds of depression runs counter to the pattern reported in at least one Ugandan urban-poverty study, where residents of a Kampala slum setting had markedly elevated depression and anxiety prevalence [15]. This is not necessarily a contradiction: that study sampled specifically from a highly disadvantaged urban slum population rather than the full urban population, and is likely to overstate risk among urban residents generally. A nationally representative comparison, as presented here, may instead be capturing genuine rural disadvantage, more limited access to mental health services, greater reliance on subsistence agriculture with attendant food-security and income volatility, and greater physical distance from HIV and general health services, that a slum-focused urban sample cannot detect because it excludes non-slum urban residents from the comparison entirely.

The regional pattern we observed, lower adjusted odds of both outcomes in Mid Western and South Western regions, and lower odds of at least one outcome in Northeast: Karamoja, is, to our knowledge, not directly addressed in existing published Ugandan mental health literature using nationally representative data, and we offer it as a descriptive finding meriting further investigation rather than a fully explained result. Karamoja's lower adjusted odds are particularly counterintuitive given the region's well-documented socioeconomic disadvantage and history of conflict and insecurity; plausible explanations include regional variation in willingness to disclose psychological symptoms to a household survey interviewer, cultural differences in how emotional distress is expressed and recognised, and possible protective effects of strong communal and extended-family support structures

in some rural regions that may buffer individual-level symptom expression even where objective hardship is high. Distinguishing genuine regional variation in mental health burden from regional variation in symptom reporting or stigma will require qualitative and mixed-methods work that this survey cannot provide on its own.

Strengths and limitations

This study's principal strength is its nationally representative design, allowing direct comparison of PLHIV and HIV-negative adults under identical measurement and weighting, a comparison Ugandan clinic-based cohorts cannot make. The PHQ-2 and GAD-2 are validated brief screening instruments with prior use and validation in Ugandan HIV-clinic and general-population settings [7, 8], supporting the appropriateness of their use here. The large sample (n = 25,479) and jackknife (JK1) replicate-weight variance estimation (159 replicate weights) provide precise, design-appropriate estimates, and confounders were pre-specified from the literature rather than selected post hoc.

Several limitations should be considered. First, the PHQ-2 and GAD-2 are screening instruments, not diagnostic tools; a positive screen indicates a high likelihood of clinically significant symptoms but does not constitute a diagnosis of major depressive disorder or generalized anxiety disorder, and our prevalence estimates should be interpreted as screen-positive prevalence rather than diagnosed-disorder prevalence. Second, the cross-sectional design precludes causal inference and temporal sequencing; we cannot determine whether HIV diagnosis preceded depression or anxiety symptoms, or vice versa. Third, both HIV status and depression/anxiety symptoms may be subject to social desirability and disclosure bias, which could differ systematically between regions and between PLHIV and HIV-negative adults in ways this analysis cannot fully account for. Fourth, we used the validated PHQ-2/GAD-2 cut-off of ≥ 3 rather than UPHIA's internally derived “over three” (score > 3) flag variables, a deliberate and documented choice for comparability with the wider clinical literature, but one that will produce somewhat higher prevalence estimates than analyses using the survey's internal flags. Fifth, odds ratios were used throughout in place of this manuscript series' standard prevalence ratio, at the person's request; because outcome prevalence exceeds 10% among PLHIV, reported odds ratios modestly overstate the corresponding prevalence ratios and should not be treated as directly equivalent to relative risk. Finally, this analysis did not examine ART status, ART duration, or viral suppression as potential correlates of depression or anxiety among PLHIV; these are natural extensions for future work using the same dataset.

Conclusion

In this nationally representative analysis of Ugandan adults, PLHIV had significantly higher odds of positive PHQ-2 and GAD-2 screens than HIV-negative adults, independent of age, sex, residence, and region. This indicates that the elevated mental health burden reported in Ugandan HIV clinic-based studies reflects, at least in part, a genuine association with HIV status rather than clinic-selection alone, while our estimates being lower than most clinic-based figures suggests that clinic samples may not

fully represent the mental health burden among all PLHIV, including those not currently engaged in care. Female sex, older age, and rural residence were independently associated with higher odds of these outcomes, and substantial regional variation was observed that is not yet well explained. These findings support integration of routine brief mental health screening into HIV care in Uganda, alongside consideration of community-based screening approaches given that clinic-based samples may understate the population burden, and underscore the value of nationally representative, population-based data as a complement to clinic-based cohort evidence for characterising the true mental health burden associated with HIV in Uganda.

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki. UPHIA 2020–2021 was approved by the Uganda Virus Research Institute Research Ethics Committee, the Uganda National Council for Science and Technology, and the institutional review boards of Columbia University, Westat, and the U.S. Centers for Disease Control and Prevention; all participants provided written informed consent. This secondary analysis used only de-identified public-release data under the PHIA Data Use Agreement, accessed via the PHIA Data Manager at ICAP, Columbia University, no additional individual consent was required.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Author Contribution

M.O.O. conceived and designed the study and performed the statistical analysis. M.O.O. drafted the initial manuscript. A.G.A., A.B.A., A.J., H.I., O.D., and S.M.S. contributed to the literature review, data interpretation, and critical revision of the manuscript for important intellectual content. K.A. supervised

the study and provided critical revision of the manuscript for important intellectual content. All authors reviewed and approved the final manuscript.

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Data Availability

The UPHIA 2020–2021 public-release datasets are available through the PHIA Data Manager (https://phia-data.icap.columbia.edu/) following registration and acceptance of the Data Use Agreement. Analytical code (Stata do-files) is available from the corresponding author on reasonable request.

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Figures

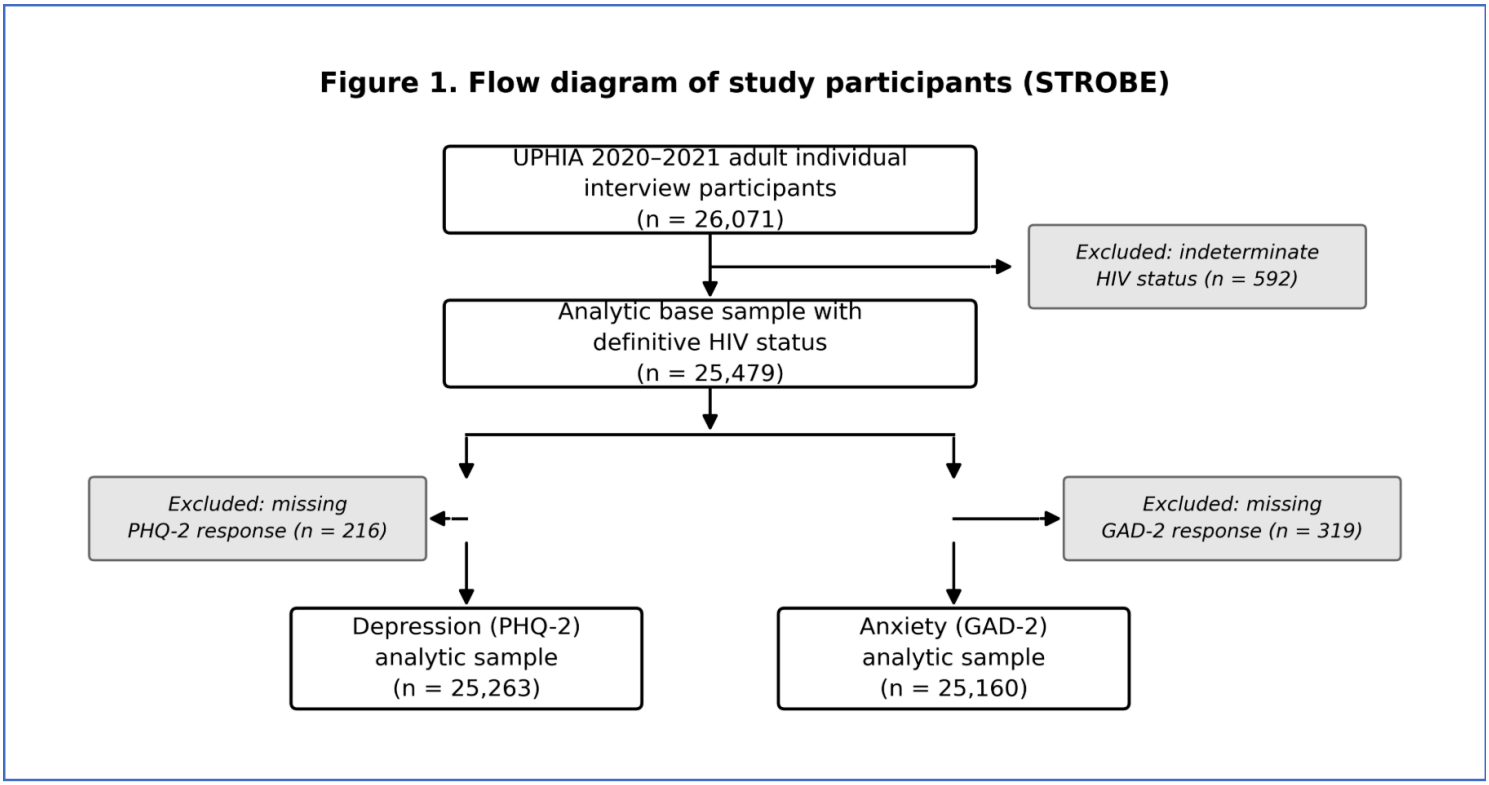


Figure 1

Flow diagram of study participants (STROBE), UPHIA 2020–2021.