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SUBSTANTIVE REVIEW

Burden of Depression in Outpatient HIV-Infected adults in Sub-Saharan Africa; Systematic Review and Meta-analysis

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Abstract

Despite the substantial burden of HIV in Africa, and the knowledge that depression causes worse HIV outcomes, the burden of depression in people living with HIV in Africa is unknown. We searched Pubmed and four other databases using key terms: depression, Africa, HIV, and prevalence from 2008 to 2018. We summarized depression prevalence by country. We estimated the burden of depression using our prevalence data and 2018 UNAIDS HIV estimates. Our search yielded 70 articles across 16 African countries. The overall prevalence of major depression in those HIV-infected using a diagnostic interview was 15.3% (95% CI 12.5–17.1%). We estimate that 3.63 million (99.7% CI 3.15–4.19 million) individuals with HIV in Sub-Saharan Africa have major depression and provide country-level estimates. We estimate that 1.57 million (99.7% CI 1.37–1.82 million) DALYs are lost among people with depression and HIV in Sub-Saharan Africa. There is a significant burden of depression in Africans with HIV. Further work to screen for and treat depression in Sub-Saharan Africa is needed to improve HIV outcomes and achieve the 90-90-90 UNAIDS goals.

Keywords HIV · Depression · Sub-Saharan Africa · Prevalence · Burden of disease

Resumen

A pesar del problema sustancial del VIH en África y el conocimiento de que la depresión causa peores resultados en pacienes con VIH, se desconoce el impacto especifico de la depresión en las personas que viven con el VIH en África. Se realizaron búsquedas en Pubmed y otras cuatro bases de datos utilizando términos clave: depresión, África, VIH y prevalencia desde 2008 hasta 2018. Resumimos la prevalencia de depresión por país. Estimamos el impacto de la depresión utilizando nuestros datos de prevalencia y las estimaciones de VIH de ONUSIDA para 2018. Nuestra búsqueda indetifico 70 artículos en 16 países africanos. La prevalencia general de depresión en las personas infectadas por el VIH durante entrevista de diagnóstico fue del 15,3% (IC del 95% CI 12,5–17,1%). Estimamos que 3.63 millones (99.7% CI 3.15–4.19 millones) de personas con VIH en África Subsahariana sufren de depresión y proporcionamos estimaciones a nivel país. Estimamos que se pierden 1,57 millones (IC del 99,7%, 1,37–1,82 millones) de AVAD entre las personas con depresión y VIH en el África subsahariana. La depresión tiene un impacto significativo en los africanos con VIH. Se necesitan más estudios para detectar y tratar la depresión en África subsahariana con el fin de mejorar los resultados del VIH y alcanzar los objetivos 90-90-90 de ONUSIDA.

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Background

Depression is estimated to cause 2.2 million excess deaths globally in 2010 from suicide or worsening of comorbid diseases [1]. Depression is significantly more common in people living with HIV, where the prevalence estimates range widely from 13 to 78% compared with 5% prevalence in the general population [2, 3]. Persons with HIV and depression are less likely to achieve good antiretroviral therapy (ART) adherence, more likely to have clinical progression regardless of adherence behavior [4], and more likely to develop virologic failure [2, 5].

Despite the known worse outcomes and quality of life, depression in HIV is often overlooked in clinical practice [6, 7]. One study in the USA showed that only half of those depressed carried the diagnosis [8]. The diagnosis of depression is even less common in low-resource countries. A Nigerian studied showed that no patients with depression carried the diagnosis [9]. There are many reasons for this including busy clinics, limited resources for mental health practitioners, and a difference in the expected versus actual presentation of depression in people living with HIV [6, 10, 11].

To improve screening and diagnosis of depression, a better understand of the burden of depression is needed, particularly in sub-Saharan Africa which has the most substantial burden of HIV [12]. The countries in sub-Saharan Africa are low and middle income, underscoring the need for quantifiable data to justify spending resources on mental health care [6]. Given the dearth of mental health practitioners in sub-Saharan Africa, a long term commitment to training and retaining professionals or ways to task-shift would be required to improve the situation [13].

While there have been some global estimates of depression in HIV [2, 3], there are a paucity of data from Africa with just one multi-country survey done [14] and several single-country, often single health center studies [15–22]. To date, there has been one review on depression prevalence in people living with HIV in Arica 23. This analysis presented the prevalence of depression by the MINI international neuropsychiatric interview (MINI) or other diagnostic interview and presented depressive symptoms using depression screening tools by tool. However, through limiting the inclusion criteria by diagnostic tool, the number of studies and countries included is limited.

Additionally, this review prior review did not provide country or region level data nor provide the burden of depression. Given that the ministry of health in each country makes spending decisions on an individual basis, we wanted to provide depression prevalence and burden among those HIV-infected by country and region. We also present both the prevalence of major depression as well as depressive symptoms, as the diagnosis of major depression is more precise, but a depressive symptom screening tool is most likely to be the only metric used in HIV clinics. We hope this will better inform country-level resource allocation for mental health services.

Our objective was to perform a systematic review and meta-analysis of the prevalence of depression in those with HIV in Africa to estimate the burden of depression, using multiple metrics, among persons HIV-infected by country in Africa.

Methods

Systematic Search

The current systematic review and meta-analysis were conducted following the preferred reporting items of systematic reviews and meta-analyses (PRISMA) guidelines. Medline/Pubmed was searched using the terms HIV and Africa and Depression, and limited to articles in English involving human adults. This resulted in the following search string ((“depressive disorder”[MeSH Terms] OR (“depressive”[All Fields] AND “disorder”[All Fields]) OR “depressive disorder”[All Fields] OR “depression”[All Fields] OR “depression”[MeSH Terms]) AND (“hiv”[MeSH Terms] OR “hiv”[All Fields]) AND (“africa”[MeSH Terms] OR “africa”[All Fields])) AND “humans”[MeSH Terms] AND English [24] AND “adult”[MeSH Terms].

Additionally, Scopus, Web of Science, Embase, and African Journals Online were searched using the same terms HIV, depression, and Africa. The dates of all searches were limited to 2008–2018. We compared the articles between searches and eliminated duplicates.

Inclusion/Exclusion Criteria

Included articles: (1) measured depression in humans using standardized and validated diagnostic interviews, screening tools, or psychological distress tools (there were no restrictions on severity of depression or treatment history), (2) included adult outpatients living with HIV, (3) were conducted in Africa, and (4) were valid cross-sectional or cohort studies, which presented numbers for depression prevalence (number depressed and total evaluated).

Articles were excluded if they were: (1) peripartum depression studies, (2) pediatric studies, (3) qualitative studies, (4) unpublished data, conference abstracts, or case reports, (5) multiple reports from the same data set (only the most recent study was included as it was felt to be the most up-to-date estimate of prevalence), (6) those with sub-populations such as HIV-TB co-infection, and (7) those at HIV testing it would be challenging to distinguish adjustment

disorder from depression. These articles were excluded as there was a recent review on peripartum depression [25], and as depression presentation and screening is very different in children. Articles that were case–control studies or interventions, which do not give the number of those screened, were excluded. We excluded articles with the sub-population of just women as most studies over-represented women; however, we included articles with only older adults as they are generally under-represented in studies.

We allowed a wide range of depression tools to have broad applicability and cover many countries across the continent. We parsed the prevalence by the diagnostic method to standardized interviews that diagnosed major depressive disorder, screening tools specific for depressive symptoms, and tools measuring general psychological distress. All prevalence numbers are point prevalences.

Data Extraction and Statistical Analysis

The first author (SL) extracted data using a standardized data extraction spreadsheet from included studies to evaluate study characteristics and risk of bias systematically. When there were concerns about study generalizability (i.e., risk of bias of selected, non-generalizable populations), the first author discussed the concerns with other authors (DB and NN), and a consensus was reached.

From each selected article, we extracted data on each study population, country, year, and study design. Additionally, we assessed the prevalence data presented, the depression scale(s) utilized, sample size, inclusion criteria, CD4 counts, ART status, and any control groups used. Duplicate references were identified and removed. Descriptive comparisons were compiled using Microsoft Excel. We performed a quantitative analysis using Microsoft Excel and IBM SPSS. We generated maps via GunnMap [26].

We calculated the weighted prevalence by summing the number of depressed participants and dividing by the total number of participants in each study or group of studies, using numerical counts from each article. The studies were organized by country and demographic factors. We examined the prevalence comparing a diagnostic interview and a depression screening tool in the countries that used both. Next, we evaluated the prevalence of depression by ART status. The ART status was recorded as a binary variable (i.e., on ART or not). We then calculated a weighted risk difference and relative risk, both with confidence intervals. The CD4 count mean or median versus prevalence were graphed for each study, and the Pearson r^2 correlation coefficient calculated using Microsoft Excel 2016. Next, we looked at studies that compared those with HIV and controls. We also noted those studies with comparisons to HIV negative people at HIV testing, where data were available.

Evaluation for Bias

Next, we evaluated if our use of articles with different tools altered the prevalence of depression. We graphed a funnel plot to assess for publication bias of prevalence by the size of the study. We also generated scatter plots of the prevalence by year. Finally, we graphed the prevalence by the screening or diagnostic method.

The Burden of Depression in Absolute Numbers

Next, we estimated the burden of overall depressive symptoms among HIV-infected persons in sub-Saharan Africa. We used 2018 UNAIDS estimates for the number of HIV-infected adults 15 and older in sub-Saharan Africa, and by country [27]. These were accessed on December 1, 2018, and are UNAIDS data for the calendar year 2017. We used standard β distributions for binomial data of estimate of depressive symptoms, and normal distribution for estimates of HIV prevalence with 95% confidence intervals for countries with data and 99.7% confidence intervals (3 standard deviations) for countries without published data using the depression prevalence from that region: Southern, East, and West/Central Africa. Using Microsoft Excel 2016, we randomly selected a value for each parameter within the appropriate distribution and used the combination of these values to estimate the number of HIV-infected persons with depression symptoms. Using 20,000 iterations, we obtained empirical distributions corresponding to posterior distributions calculated by Monte Carlo simulations for each country and region. These distributions were used to generate a point estimate (posterior mean) and Monte Carlo confidence intervals for the 99.7% confidence intervals. We used the estimated burdens to calculate the country-specific prevalence, the regional, and overall prevalence of depression in people with HIV in sub-Saharan Africa.

Review of Burden of Depression Measures

We next evaluated the general metrics of the burden of disease. We looked at which of the studies had follow-up data. We assessed what articles had measured disability-adjusted life years (DALY) or quality-adjusted life years (QALY), ART adherence, and viral suppression rates.

The Burden of Depression in Disability-Adjusted Life Years (DALYs)

Finally, we calculated the DALYs from our data. First, we found the studies which used PHQ-9 and presented the data by the severity of depression. We used this to calculate the

prevalence of moderate and severe depression amongst those depressed. We then used the disability weights from those used in the Global Burden of Disease 2013 study to calculate DALYs associated with moderate to severe depression [28]. Specifically, the disability weight for mild depression was 0.145 (95% CI 0.099–0.209), for moderate depression was 0.396 (95% CI 0.267–0.531), and severe depression was 0.658 (95% CI 0.477–0.807).

Results

Search Outcomes

We completed our search on the prevalence of depression in HIV in Africa on August 4, 2018. Our PubMed search yielded 496 articles, our Scopus search yielded 602 articles, our Web of Science search yielded 691, Embase yielded 592 articles, and African Journals Online yielded 7 articles for a total of 2388 articles. In removing duplicates, we subjected each of the 1258 articles to each of the selection criteria with a title evaluation, of which 690 articles were excluded, leaving 568 articles. We reviewed the abstracts and removed 310 based on inclusion/exclusion criteria. Then, we reviewed the full texts of the remaining 258 and removed 189 more articles. Full search details are displayed in Fig. 1.

Our search to quantify the prevalence of depression in HIV-infected persons in Africa resulted in 70 articles, which we read and abstracted data per our criteria. We found two articles from Botswana [29, 30] five from Cameroon [18, 31–33] eight from Ethiopia [22, 34–40] one from Ivory Coast, [41] three from Kenya [42–44] one from Lesotho [45] two from Malawi [46, 47] fourteen from Nigeria [9, 15, 48–59] two from Rwanda [60, 61] fourteen from South Africa [21, 62–74] two from Tanzania [19, 75] two from The Gambia [76, 77] nine from Uganda [78–84] two from Zambia [85, 86] two from Zimbabwe [87, 88] and a multi-country paper with data from Kenya, Namibia, and Tanzania [14]. The search revealed that the investigators used a variety of depression scales. We divided studies into those

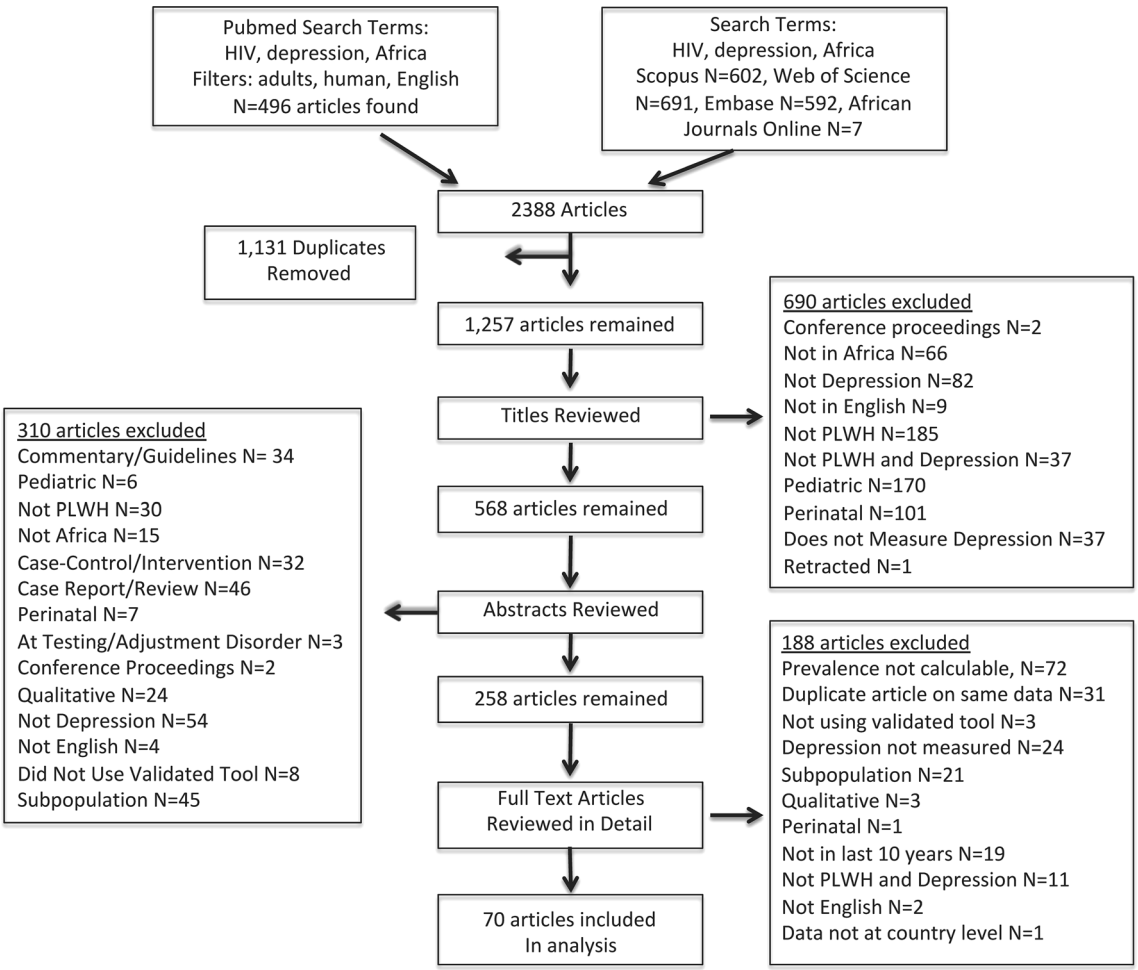


Fig. 1 Burden of Depression Search Strategy. Note: Search performed in August 2018

who measured depression using standardized, diagnostic interviews, studies using a depression-specific screening tool, and, finally, studies using a tool measuring generalized psychological distress. We provide full details of the articles in Supplemental Table 1 and the details on depression tools in Supplemental Table 2. We graphed depression prevalence by each article in Supplemental Fig. 1.

Prevalence of Depression

The prevalence of depression by country among HIV-infected persons was calculated using a diagnostic interview, a depression-specific screening tool, or general psychological distress (Supplemental Tables 3–5). We found that the mean weighted prevalence of major depression was 16.8% (95% CI 15.9–17.7%) using a diagnostic interview. The prevalence of depressive symptoms was 25.5% (95% CI 24.9–26.0%) using a depression screening tool, and the prevalence of general psychological distress was 33.1% (95% CI 31.9–34.4%). This data of weighted prevalence by country and diagnostic method is displayed via a map in Fig. 2.

We next compared the prevalence of major depression and depressive symptoms in HIV-infected individuals using different depression tools within the same population. Specifically, we wanted to compare the prevalence of depression in countries, which was found using both a screening tool and a diagnostic interview. We found two cohorts from Nigeria and South Africa, which used both methods [9, 51, 58]. In Nigeria, the prevalence of major depression by diagnostic interview was 23.9% (110/460) versus 24.8% (114/460) prevalence of depressive symptoms by screening tool. In South Africa, the prevalence of major depression by diagnostic interview was 13.5% (63/465) versus 44.7% (208/465) prevalence of depressive symptoms by screening tool. The weighted average prevalence for those countries was 16.3% (151/925) by interview compared to 34.8% (322/925) by screening tool.

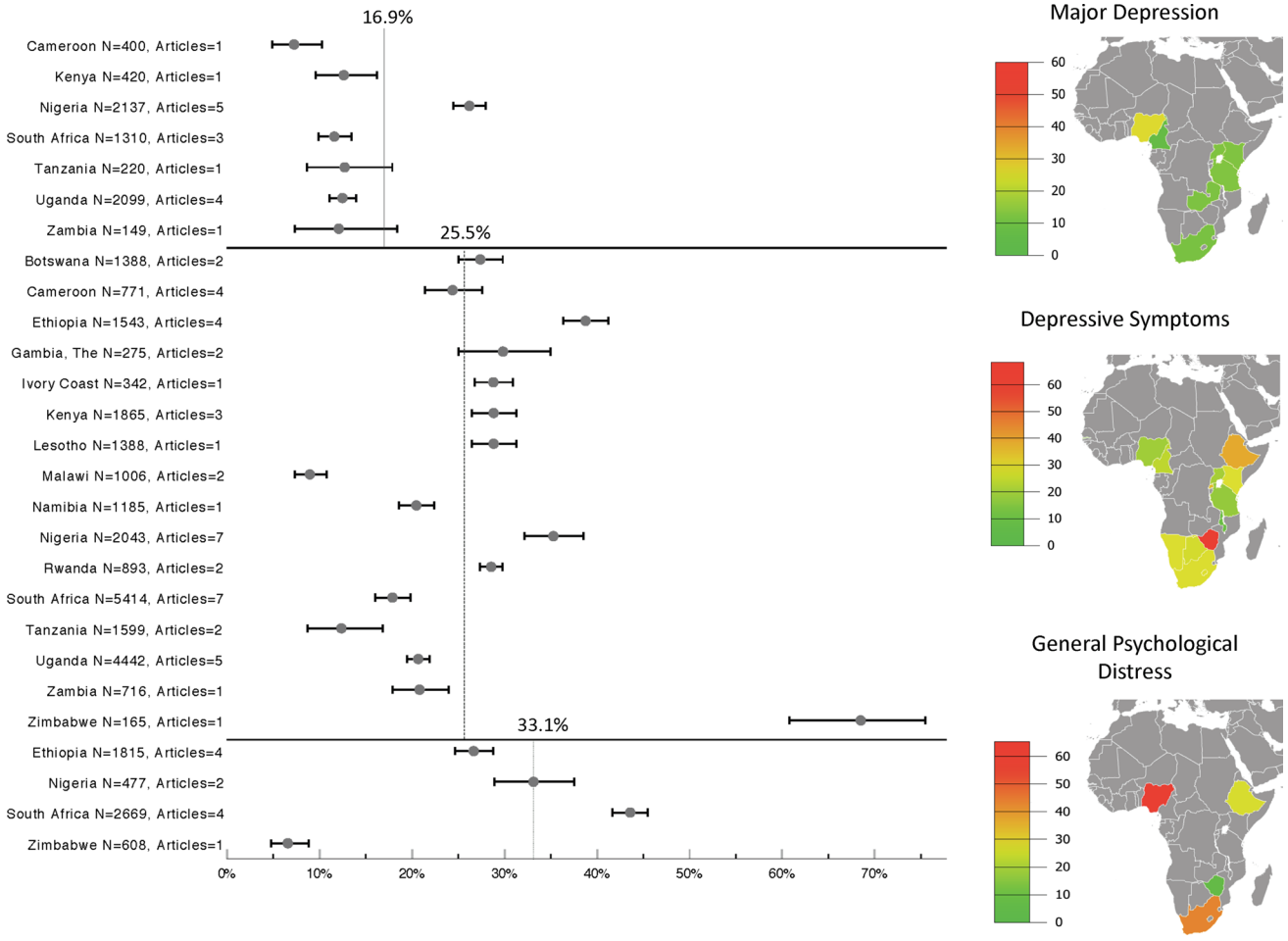


Fig. 2 Prevalence of Depression in Africans Living with HIV by Country. Note: Major depression as defined by a standardized, diagnostic interview; Depressive symptoms as defined by a depression-specific screening tool; Generalized psychological distress as defined by a psychological distress screening tool. Error bars are the 95%CI

Thus, there is an 18.5% (95% CI 14.6–22.4%) higher prevalence of depressive symptoms compared to major depression diagnosis by diagnostic interview.

Next, we compared the prevalence of depressive symptoms by ART status and CD4 count. Those not on ART had a prevalence of 28.8% (846/2942) [42, 61, 71, 76, 79, 89], compared with those on ART of 26.5% (3475/13097) prevalence of depressive symptoms [9, 14–16,18–21, 30, 32, 33, 36, 37, 41, 45, 51, 53, 54, 58, 60, 65, 68, 69, 75, 77, 80–84, 86, 87]. The relative difference was 8.7%, weighted absolute difference was 2.3% (95% CI 0.5–4.1%; $p=0.011$), more depression for those not on ART. We examined the relationship between the prevalence of depressive symptoms and CD4 count, which can be seen in Supplemental Fig. 2. The overall correlation was very weak and non-significant ($R^2=0.00075$ for mean CD4 and $R^2=0.026$ for median CD4 count) [14, 18, 29, 30, 37, 41, 44, 61, 67, 68, 71, 73, 75, 77–79, 81, 84].

We next characterized differences in prevalence of depression by biological sex among 17 studies providing distribution by sex. In those studies using diagnostic interviews, men had a 12.9% (145/1121) prevalence of major depression while 17.7% (450/2547) of women had major depression (relative difference 36.6%, absolute difference: 4.8% 95% CI 2.3–7.2%; $p<0.001$) [52, 54, 64, 78, 89]. In the studies that used a depression screening tool men had a 23.5% (776/3296) prevalence of depressive symptoms while women had a prevalence of 31.1% (1606/5169) (relative difference 32.0%, absolute difference: 7.6%, 95% CI 5.7–9.5%; $p<0.001$) [9, 14, 18, 29, 32, 33, 44, 45, 55, 57, 67, 79]. Overall, in this HIV-infected African population, women had more major depression and depressive symptoms than men.

We then wanted to understand the prevalence of major depression and depressive symptoms in those with HIV compared to the background prevalence of depression in the HIV-negative general population. This extra depression in the HIV-infected population is termed "excess depression." To this end, we evaluated seven studies with control groups to find excess depression in those with HIV compared to controls from the general population [21, 33, 51, 80, 85, 87, 90, 91]. There were studies that used diagnostic interviews from Nigeria [51] and Uganda [88], and studies that used a depression screening tool from Malawi [71], South Africa [91], Zambia [85], Zimbabwe, [87] and Cameroon [33]. Those studies utilizing diagnostic interviews showed the prevalence of major depression in those with HIV was 30.0% compared with 18.1% in HIV-negative controls for a relative increase of 65.7% and an absolute difference of 11.9% (95% CI 7.3–16.6%). Those studies utilizing screening tools found a prevalence of depressive symptoms of 27.8% in those with HIV and 13.5% in HIV-negative controls for a relative increase of 206% and an absolute difference of 14.3% (95% CI 11.8–16.9%). Thus, depressive symptoms are two-fold more common in HIV-infected African adults than in general African populations.

Next, we assessed whether there was a potential publication bias based on the size of the study. Thus, we graphed the prevalence data in funnel plots, which show a funnel pattern, consistent with minimal bias, seen in the Supplemental Fig. 3a and 3b for diagnostic interview and depression screening tool. Next, we graphed the prevalence of depression by diagnostic method, by year of data collection, and by year of publication Supplemental Fig. 4. Overall there does not seem to be a relationship between prevalence and method or date. As such, there seems again to be minimal bias.

The Burden of HIV-associated Depression in Absolute Numbers

The burden of depression and depressive symptoms in absolute numbers was estimated using our prevalence data and found to be 3,626,000 (99.7% CI 3,152,000–4,189,000) people living with HIV in Sub-Saharan Africa for major depression (Table 1) and 6,376,000 (99.7% CI 5,565,000–7,386,000) individuals HIV-infected with depressive symptoms (Table 2). The calculated estimates are based on the prevalence by country. Where country-specific data was lacking, we estimated the burden using regional averages. From these estimates, we mapped the burden of major depression and depressive symptoms (Fig. 3).

Descriptive Assessment of the Effects of HIV-associated Depression

We characterized other measures of the effects of depression, including DALYs, ART adherence, or viral suppression, and found the data to be scarce. None of the 70 articles presented DALYs or QALYs. Eight articles addressed baseline ART adherence with two finding no association between depression and adherence [61, 92], while six found depression was negatively associated with adherence [20, 22, 48, 69, 75, 88]. Only, two of the 70 articles evaluated the relationship between depression and HIV viral load with neither finding a statistically significant relationship between more depressive symptoms and more virologic failure on ART [75, 77].

Disability-Adjusted Life Years (DALYs) Lost Due to Major Depression

Finally, to better understand the burden of disability from depression in Africans with HIV, we calculated DALYs. We found five papers from Nigeria [49, 50, 58], Cameroon [31], and Uganda, [83] which used PHQ-9 to estimate the severity of depression. We estimated 18.5% of individuals had mild depression (95% CI 16.6–20.6%), 8.4% had

Table 1 Estimated burden of major depression in those with hiv in sub-saharan africa using data from systematic review and UNAIDS 2008–2018

Country	Estimated prevalence (%)	Mean estimate of major depression	Confidence interval of estimate	Disability adjusted life-years (Daly)s
Eastern and Southern Africa				
Angola	12.1	34,000	(21,000–49,000)	15,000
Botswana	12.2	44,000	(28,000–65,000)	19,000
Ethiopia	12.5	69,000	(45,000–98,000)	30,000
Kenya[a]	12.6	177,000	(130,000–232,000)	77,000
Lesotho	12.0	36,000	(22,000–52,000)	16,000
Malawi	12.6	116,000	(72,000–169,000)	50,000
Mozambique	12.1	239,000	(142,000–361,000)	104,000
Rwanda	12.4	26,000	(18,000–36,000)	11,000
South Africa[a]	12.0	825,000	(699,000–961,000)	360,000
Tanzania[a]	12.7	165,000	(112,000–229,000)	72,000
Uganda[a]	12.5	150,000	(130,000–172,000)	65,000
Zambia[a]	12.1	133,000	(80,000–196,000)	58,000
Zimbabwe	12.1	143,000	(89,000–210,000)	62,000
Regional sub-total	12.4	2,243,000	(2,045,000–2,521,000)	972,000
Western and Central Africa				
Cameroon[a]	7.3	34,000	(22,000–49,000)	15,000
Côte d'Ivoire	24.5	113,000	(71,000–160,000)	49,000
Dem. Republic Congo	24.5	83,000	(60,000–110,000)	36,000
Ghana	24.5	69,000	(52,000–88,000)	30,000
Guinea	24.5	27,000	(20,000–35,000)	12,000
Mali	24.5	29,000	(21,000–39,000)	13,000
Nigeria[a]	27.8	804,000	(527,000–1,095,000)	348,000
Regional Sub-Total	24.7	1,383,000	(1,019,000–1,754,000)	599,000
Sub-Saharan Africa total	15.3	3,626,000	(3,152,000–4,189,000)	1,572,000

[a]Country burden calculated from prevalence data identified from systematic review. Other countries' burdens were calculated using regional mean for major depression and 99.7% confidence interval (i.e. 3 standard deviations)

Only the 20 countries with the highest prevalence of depression are listed. A full listing of all countries is provided in Supplemental Table 6

moderate depression (95% CI 7.1%–9.9%), and 1.4% had severe depression (95% CI 0.8–2.1%). Since our data used the cutoff of major depression, we only calculated DALYs for moderate to severe depression. We estimated that the DALYs lost from major depression were 1.57 million (95% CI 1.37–1.82 million) across Sub-Saharan Africa among people living with HIV (Supplemental Table 6).

Discussion

We estimated the prevalence of major depression in people living with HIV in Sub-Saharan Africa to be 17%, the prevalence of depressive symptoms to be 26%, and the prevalence of psychological distress to be 33%. This prevalence of depression is substantial, given the limited mental health resources and the large number of those with HIV in Africa. These prevalence rates are up to twofold higher than in non-HIV populations in Africa [33, 46, 51, 80, 85, 87, 91]. Above and beyond improving the quality of life of people with HIV, treatment of depression is vital given depression in HIV is known to cause worse HIV outcomes [4, 5].

There are significant differences in the prevalence of depression in HIV-infected individuals between different African countries. The prevalence of major depression ranged from 7% in Cameroon [93] to 28% in Nigeria [15, 51, 52, 54, 59]. Reasons for this difference could be social and political, or highlight differences in specific diagnostic methods. It is also possible that those sampled as controls in these studies had been impacted by HIV more than the general sub-Saharan African population and thus had higher rates of depression.

We found that the absolute prevalence of depressive symptoms was similar between those participants on ART and those not on ART. This consistency is likely because of changing guidelines for the CD4 cut-offs to start ART. Given that the studies were mostly cross-sectional, the longitudinal changes over time were not assessed. However, two studies

Table 2 Burden of depressive symptoms in those with HIV in Sub-Saharan Africa using data from systematic review 2008–2018

Country	Estimated prevalence (%)	Mean estimate of depressive symptoms	Confidence interval of estimate
Eastern and Southern Africa			
Angola	27.1	76,000	(47,000–106,000)
Botswana[a]	27.3	101,000	(88,000–116,000)
Eswatini	26.8	51,000	(46,000–57,000)
Ethiopia[a]	38.7	213,000	(165,000–262,000)
Kenya[a]	28.8	403,000	(340,000–469,000)
Lesotho[a]	28.7	86,000	(77,000–96,000)
Malawi[a]	9.0	87,000	(70,000–105,000)
Mozambique	26.9	538,000	(421,000–660,000)
Namibia[a]	28.4	54,000	(47,000–62,000)
Rwanda[a]	35.2	74,000	(65,000–84,000)
South Africa[a]	29.1	2,007,000	(1,814,000–2,205,000)
Tanzania[a]	17.9	232,000	(203,000–264,000)
Uganda[a]	20.7	248,000	(223,000–274,000)
Zambia[a]	20.8	229,000	(191,000–271,000)
Zimbabwe[a]	68.5	822,000	(713,000–932,000)
Regional sub-total	29.4	5,304,000	(4,851,000–5,955,000)
Western and Central Africa			
Cameroon[a]	24.5	115,000	(93,000–138,000)
Dem. Republic Congo	19.1	65,000	(47,000–85,000)
Ivory Coast[a]	29.8	137,000	(89,000–190,000)
Ghana	18.9	53,000	(41,000–68,000)
Nigeria[a]	16.6	480,000	(312,000–654,000)
Regional sub-total	19.1	1,072,000	(785,000–1,358,000)
Sub-Saharan Africa total	27.0	6,376,000	(5,565,000–7,386,000)

[a]Country burden calculated from prevalence data identified from systematic review. Other countries' burdens were calculated using regional mean for major depression and 99.7% confidence interval (i.e. 3 standard deviations)

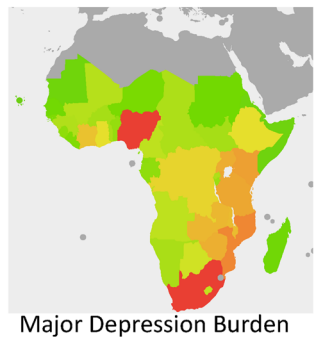
Only the 20 countries with the highest prevalence of depression are listed. A full listing of all countries is provided in Supplemental Table 6

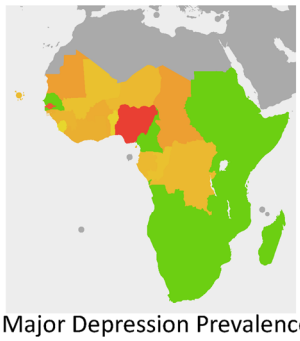
did longitudinal assessments. Specifically, Kinyanda showed that depression decreased as individuals initiated ART, and Chan showed that population-level rates of depression over time declined as people initiated ART earlier [79, 89].

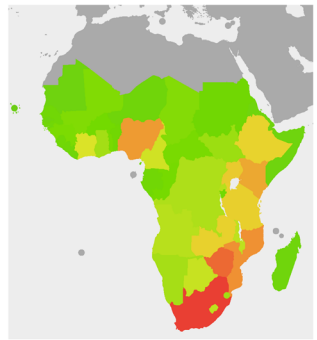
Depression appeared to affect women more than men, with women having one-third higher prevalence of both major depression and depressive symptoms compared to men. This difference in prevalence has been shown in other settings [94]. There is some thought that hormones may be involved in this difference [95]. Our data show a smaller disparity between men and women than in different contexts, although most of the other data originated in western countries [96]. Further work is needed to know if this difference is related to HIV or social factors.

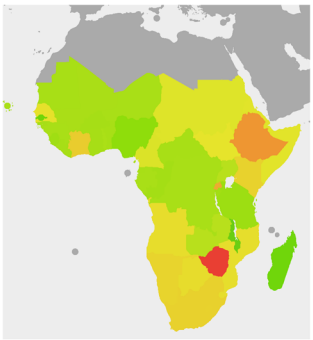
We looked at several metrics of the burden of depression, including markers related to disability, adherence, and viral suppression. Our search found a paucity of data. DALYs were not reported in the articles we found, so we calculated them and found 1.57 million DALYs lost among people living with HIV in sub-Saharan Africa. Our calculation is likely a conservative estimate as the DALY estimate does not include those with sub-clinical or mild depression. We could not find a clear link between depression and viral suppression; however, virologic testing has only been available in Africa for a limited time [97]. The relationship between viral suppression and depression is an area of needed further study. A study from the USA has found this link between depression and more virologic failure [98].

We compiled as many articles as possible, but some countries have no data or a paucity of data. Many different depression tools were used. While these tools have been validated, the cutoff for depression is not identical between different diagnostic methods [99–102]. We evaluated the validity of combining the prevalence using various tools by generating a scatter plot; the prevalence was not significantly altered by the tool used. The lack of significance suggests that combining prevalences using different methods was reasonable. We also completed a funnel plot for both









Country	Prevalence of Major Depression	Buden of HIV-Associated Depression	Prevlence of Depressive Symptoms	Burden of HIV-Associated Depressive Symptoms
Angola	12%	34,000	27%	76,000
Botswana	12%	44,000	27%	101,000
Cameroon	7%	34,000	25%	115,000
Côte d'Ivoire	25%	113,000	30%	137,000
Democratic Republic of the Congo	25%	83,000	19%	65,000
Eswatini	12%	23,000	27%	51,000
Ethiopia	13%	69,000	39%	213,000
Ghana	25%	69,000	19%	53,000
Guinea	25%	27,000	19%	21,000
Kenya	13%	177,000	29%	403,000
Lesotho	12%	36,000	29%	86,000
Malawi	13%	116,000	9%	87,000
Mali	25%	29,000	19%	23,000
Mozambique	12%	239,000	27%	537,000
Namibia	12%	23,000	28%	54,000
Nigeria	28%	804,000	17%	480,000
Rwanda	12%	26,000	35%	74,000
South Africa	12%	825,000	29%	2,007,000
Tanzania	13%	165,000	18%	233,000
Uganda	13%	150,000	21%	248,000
Zambia	12%	133,000	21%	229,000
Zimbabwe	12%	143,000	69%	822,000

Fig. 3 Prevalence of Depression in Africans Living with HIV by Country in Absolute Numbers. Note: Major depression as defined by a standardized, diagnostic interview; Depressive symptoms as defined by a depression-specific screening tool

major depression and depressive symptoms, which did not show significant publication bias despite using various tools. We estimated the burden of depression in those with HIV using regional averages. However, more accurate data would require more research to survey the prevalence of depression in many more countries.

Overall, this work reveals a substantial burden of depression in those with HIV in Africa. As governments, nonprofits, and international commissions work to reach the 90-90-90 goals [103], interventions for depression and mental illness broadly are needed. Those with depression are known to have a higher risk of acquiring HIV [104], and a lower rate of linkage to HIV care that those without depression [91]. Those with HIV-associated depression are also less likely to achieve good ART adherence [2], more likely to develop virologic failure [5], and are more likely to have HIV progression, independent of ART adherence, than those without depression [4].

While this review highlights the need for more screening to diagnose depression, screening alone is insufficient to improve depression care in resource-limited settings without more work on how best to treat depression in this setting. Our prior systematic review on depression interventions in sub-Saharan Africa showed many pilot and feasibility studies had been done; however, we found limited efficacy studies [105]. High-quality clinical trials are needed to evaluate the effectiveness of antidepressant medications in these settings, given the paucity of data [106]. While psychotherapy has been shown to improve symptomatology in those with depression and HIV [107], further work adapting psychotherapy to local settings is needed. Finally, implementation studies will be required to fully integrate depression care in HIV primary care if we hope to end the epidemic of HIV in sub-Saharan Africa [47,108–110].

Limitations

A variety of validated depression tools have been used to quantify the prevalence of depression and depressive symptoms, and some inter-scale variation is likely. More agreement in depression scales would have made comparing data simpler. The prevalence by study and country varied significantly. The studies with a cross-sectional design using populations of convenience may not be fully representative of a country's general population. Also, many favored urban areas, given the ease in sampling. ART status was measured as a binary state (on or off ART by study), but virologic outcomes were generally unknown. Among studies included, all but one used depression tools validated in Africa.

Conclusion

Depression in those with HIV in Africa is more prevalent than those uninfected with HIV, and this work better characterizes the prevalence by country and region. We found a prevalence of major depression of 15% in HIV-infected Africans. The overall burden of major depression in those with HIV in Sub-Saharan Africa was 3.6 million. More attention to interventions for mental illness will be needed to achieve control of HIV in Sub-Saharan Africa.

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