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Review article

Epidemiology of depressive disorders in people living with HIV in Africa: a systematic review and meta-analysis
Burden of depression in HIV in Africa

Jean Joel Bigna[a,*], Dahlia Noelle Tounouga[b], Angeladine Malaha Kenne[a,1], Tatiana K. Djikeussi[c,1], Audrey Joyce Foka[b,1], Lewis N. Um[d,1], Serra Lem Asangbeh[e,1], Aurelie T. Sibetcheu[f], Arnaud D. Kaze[g], Marie S. Ndangang[h,1], Jobert Richie Nansseu[c,i]

[a] Department of Epidemiology and Public Health, Centre Pasteur of Cameroon, Yaounde, Cameroon
[b] Faculty of Medicine and Biomedical Sciences, University of Yaoundé I, Yaoundé, Cameroon
[c] Department for the Control of Disease, Epidemics and Pandemics Diseases, Ministry of Public Health, Yaounde, Cameroon
[d] Mfou District Hospital, Ministry of Public Health, Mfou, Cameroon
[e] Department of Clinical Research, National Agency on Research for HIV and Viral Hepatitis, Yaounde, Cameroon
[f] Department of Pediatrics and Specialties, Faculty of Medicine and Biomedical Sciences, University of Yaoundé I, Yaounde, Cameroon
[g] Department of Medicine, University of Maryland Medical Center Midtown Campus, Baltimore, MD, USA
[h] Department of Medical Information and Informatics, Rouen University Hospital, Rouen, France
[i] Department of Public Health, Faculty of Medicine and Biomedical Sciences, University of Yaoundé I, Yaounde, Cameroon

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ABSTRACT

Objective: The burden of HIV infection is higher in Africa where 70% of people living with HIV (PLHIV) resides. Since depression can negatively impact the course of HIV infection, it is therefore important to accurately estimate its burden among PLHIV in the continent.
Methods: We searched multiple databases to identify articles published between January 2000 and February 2018, reporting the prevalence of (major) depressive disorders in PLHIV residing in Africa. We used a random-effects meta-analysis model to pool studies.
Results: Overall, 118 studies (60,476 participants, 19 countries) were included. There was no publication bias. The overall prevalence estimates of depressive disorders and probable major depressive disorders were 36.5% (95% CI 32.3–41.0; 101 studies) and 14.9% (12.1–17.9; 55 studies) respectively. The heterogeneity of the overall prevalence of depressive disorders was significantly explained by screening tool used, period (higher prevalence in recent studies) and distribution in sub-regions. The study setting, site, CD4 cell counts, age, sex, proportion of people with undetectable viral load were not sources of heterogeneity.
Conclusions: This study shows that more than one third of PLHIV face depressive disorders and half of them having major form, with heterogeneous distribution in the continent. As such, depressive disorders deserve more attention from HIV healthcare providers for improved detection and overall proper management.

1. Introduction

To date, the Human immunodeficiency virus (HIV) infection remains one of the major public health concerns the world has ever experienced. In 2016 for instance, there were 36.7 million people living with HIV worldwide, of whom 70.6% were living in Africa [1]. Still in 2016, it is 1.8 million people who became newly infected with the virus globally, with more than two thirds of them originating from sub-Saharan Africa [1]. People living with HIV may experience some comorbid conditions due to their status, among which psychiatric disorders including depression [2]. Depression constitutes one of the most prevalent mental disorders and leading cause of disability worldwide, with > 300 million people affected, being therefore a major contributor to the overall global burden of disease [3]. People with depression can experience a loss of energy, a change in appetite, sleeping more or less, low mood, anhedonia, reduced concentration, indecisiveness,

* Corresponding author at: Department of Epidemiology and Public Health, Centre Pasteur of Cameroon, Rue Henry Dunant; P.O. 1274, Yaounde, Cameroon.
E-mail address: bignarimjj@yahoo.fr (J.J. Bigna).
[1] Contributed equally.

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restlessness, feelings of worthlessness, guilt, hopelessness, and thoughts of self-harm or suicide [4].

The identification of people with depressive symptoms among HIV-infected patients remains challenging since the continent is shaped by multicultural faces, complex psychological and sociological patterns associated with HIV/AIDS [5,6]. Previously published systematic review with meta-analysis reported a high burden and heterogeneous distribution of depressive and major depressive disorders among HIV-infected patients in sub-Saharan Africa [6–8]. Although the entire continent could present some heterogeneity concerning the depression among people with HIV, it would be interesting to present the burden in the entire continent and moreover investigating differences between sub-regions of Africa including the northern part which is different concerning sociocultural aspects. Indeed, previous meta-analyses did not present data by sub-region of the continent. It would be also interesting to investigate if the period of studies, the way of administration (heterogeneous versus self-administration), the setting, and the site of studies can impact the burden of depressive disorders among people with HIV in Africa. Evidence suggest that depression can negatively impact the course of HIV infection including adherence to antiretroviral therapy (ART) [9–11], dysfunction of lymphocytes and alteration of natural killer cells activity [12]; this may lead to detectable viral load, hence contributing to the increase in morbidity and mortality in people living with HIV.

Since the African continent continues to carry the heaviest burden of HIV infection globally [1], it is important to determine the accurate burden of depressive disorders in the entire continent. It is also important to substantially investigate sources of heterogeneous distribution of depressive disorders in HIV-infected patient in the entire continent. Willing to fill this critical gap, we conducted a systematic review and meta-analysis aiming to determine the prevalence of (major) depressive disorders as well as their associated factors among people living with HIV in Africa.

2. Methods

2.1. Data sources and searches

We searched PubMed, EMBASE, Web of Science, Africa Journal Online, and Africa Index Medicus to identify relevant studies published on depression among people living with HIV in Africa, published from January 1, 2000 to February 28, 2018, without any language restriction. The full search strategy in PubMed was published within the study protocol [13]. This search strategy was adapted to fit other databases. To supplement these electronic searches, references of all relevant studies were also screened to identify additional sources. The search in all electronic databases was conducted on March 1st, 2018.

We considered observational studies of people living with HIV throughout the African continent, which reported the prevalence of (major) depressive disorders, or having enough data to compute this estimate. We excluded case series, letters, reviews, commentaries, editorials, and studies without primary data even after two unsuccessful requests addressed to the authors. We also excluded studies of pregnant women. For studies published in more than one report (duplicates), we considered the most comprehensive study that reported the largest sample size.

2.2. Study selection

Two review authors (JJB and AMK) independently screened the titles and abstracts of articles retrieved from the literature search, and all full texts of potentially eligible articles were obtained and further assessed for final inclusion. Disagreements were resolved through discussions between review authors (JJB and AMK) until a consensus was reached, or arbitration by a third review author (JRN).

2.3. Data extraction and quality assessment

We assessed the methodological quality of included studies using an adapted version of the risk of bias tool for prevalence studies, which was developed by Hoy and colleagues [14]. Three pairs of review authors (DNT, AJF, LNU, SLA, TD, and MSN) independently assessed study quality, with disagreements resolved by consensus or arbitration by another review author (JJB). The total score ranged from 0 to 10 with the overall score categorized as follows: 8–10: “low risk”, 5–7: “moderate risk”, and 0–4: “high risk” of bias.

Using a pretested data extraction form, three pairs of review authors (DNT, AJF, LNU, SLA, TD, and MSN) independently extracted relevant information, including first author, publication year and period of participants' recruitment, country of recruitment, site, area, setting, timing of data collection, study design, sampling method, sample size, mean or median age, tool used, CD4 cell count, time since HIV diagnosis infection, proportion on antiretroviral therapy, and sample size. “Depressive disorders” and “probable major depressive disorders (PMDD)” were considered depending on different threshold with the screening tools for self-report or by any healthcare worker or investigator. “Depressive disorders” were defined with the following cut-off: Self-Reported Questionnaire-20 $\geq$15, Patient Health Questionnaire $\geq$5, Mental Health Index-5 $\leq$60, Kessler Depression Scale $\geq$20, Hopkins Symptom Checklist-15 $\geq$1.75, Hospital Anxiety and Depression Scale $\geq$11, Hamilton Depression Rating Scale $\geq$8, Centre for Epidemiological Studies Depression Scale $\geq$16, EQ-5D $\geq$1, Clinical Interview Schedule-Revised $\geq$12, Beck Depression Inventory-21 $\geq$11. PMDD were defined with the following minimal score for each tool used: Zung Self-Rating Depression $\geq$15, Patient Health Questionnaire $\geq$9, Mood Module $\geq$5, Mini-International Neuropsychiatric Interview $\geq$5, Kessler Depression Scale $\geq$30, Hamilton Depression Rating Scale $\geq$19, Composite International Diagnostic Interview $\geq$5, Clinical Interview Schedule-Revised $\geq$18, and Beck Depression Inventory-21 $\geq$31. The United Nations Statistics Division (UNSD) of Africa region was assigned to each study according to the country of recruitment [15]. Disagreements were reconciled through discussion and consensus between review authors, or arbitration by another review author (JJB). When relevant data were not available, we contacted directly the corresponding author of the study to request the information, at least on two different attempts.

2.4. Data synthesis and analysis

Data were analyzed using the packages ‘*meta*’ and ‘*metafor*’ of R (version 3.5.1). We calculated the unadjusted prevalence on the basis of crude numerators and denominators provided by individual studies. To keep the effect of studies with extremely small or extremely large prevalence estimates on the overall estimate to a minimum, we stabilized the variance of the study-specific prevalence using the Freeman-Tukey double arc-sine transformation before pooling data with a random-effects meta-analysis model [16]. Following the crude overall prevalence, we conducted a sensitivity analysis to assess the robustness of our findings including only studies with low risk of bias. Pooled estimates were reported with their 95% confidence interval (CI) and 95% prediction interval. Heterogeneity across included studies was assessed using the χ^2 test, and quantified using the H and I^2 statistics [17]. When substantial heterogeneity was detected ($p < 0.05$) [18], we did subgroup and meta-regression analyses to investigate the possible sources of heterogeneity. We reported the explained heterogeneity (R^2) of variables that explained the residual heterogeneity of the overall (probable major) depressive disorders prevalence. Multivariate meta-regression models used manual stepwise backward selection excluding variables if p value > 0.20. A p value < 0.05 was considered statistically significant. The symmetry of funnel plots and the Egger test served to assess presence of publication and selective reporting bias [19]. Inter-rater agreements between investigators for study inclusion and

methodological quality assessment were assessed using Cohen's κ [20].

This systematic review is registered in the PROSPERO International Prospective Register of systematic reviews, registration number CRD42017058118 and its protocol was published in a peer-reviewed journal [13]. The Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines served as the template for reporting the present review [21].

3. Results

3.1. Review process

Initially, 1367 records were identified, of which 1034 remained after elimination of duplicates. Titles and abstracts were screened and 803 records were found irrelevant; hence, they were excluded. Agreement between investigators on abstract selection was κ = 0.79. Full-texts, of the remaining 231 papers were scrutinized for eligibility, among which 113 were excluded with reasons (Supplementary Fig. 1). Overall, 118 full texts were included in the meta-analysis [22–134] (Supplementary Fig. 1). The inter-rater agreement for study inclusion and data extraction between investigators varied between κ = 0.73–0.93 and 0.83–0.92, respectively.

3.2. Characteristics of included studies

Sixty-four (54.2%), 49 (41.5%), and five (4.2%) studies had low, moderate, and high risk of bias, respectively. Supplementary Table 1 summarizes studies characteristics. Studies were published between 2002 and 2018 and recruited patients between 1995 and 2016. Most studies used the Centre for Epidemiology Studies Depression Scale to screen the presence of depressive symptoms (Table 1). For the screening tool considered, multiple languages were used within and across studies. Thirty forty studies did not describe the language of the screening tool used (Supplemental Table 2). The mean/median age varied from 25 to 47 years (118 studies). The mean/median lymphocytes T CD4 count ranged between 35 and 1043 cells/mm^3 (39 studies). Mean/median time since HIV diagnosis was between 0 and 7.2 years (22 studies). Proportion of males varied from 0 to 62.5% (115 studies). Proportion of people on ART varied from 0 to 100% (84 studies). Majority of studies were cross-sectional, prospective, used consecutive sampling, were conducted in the Eastern region of Africa, in urban settings, and were hospital-based. In most studies, the administration of the tool to identify depressive symptoms was done by another person than the patient (Supplementary Table 1). Individual characteristics of included studies are depicted in Supplementary Table 2.

3.3. Prevalence of (major) depressive disorders in people living with HIV in Africa

In total, 60,476 people living with HIV were included from 19 countries. Tables 1 and 2 summarize statistics from meta-analysis. The overall prevalence of depressive disorders and PMDD was 36.6% (95% CI 32.3–41.0) (Fig. 1) and 14.9% (95%CI 12.1–17.9) (Fig. 2), with substantial heterogeneity and no publication bias (no effect of small studies with high prevalence estimate) (Supplementary Figs. 2 and 3). The prevalence including only studies with low risk of bias was close to that of the crude prevalence (Tables 1 and 2). There was a wide variation of prevalence of (major) depressive disorders depending on the tool used with statistical difference ($p < 0.0001$) (Tables 1 and 2). The prevalence varied widely from 4.0% to 67.7% for depressive disorders (Table 1) and from 2.7% to 21.6% for PMDD (Table 2).

In subgroup comparisons (Tables 1 and 2), the prevalence was higher in the Northern region of Africa compared to other regions for (probable major) depressive disorders (Figs. 1 & 2; p values < 0.05). The prevalence was higher in studies after 2010 compared with those conducted before with statistical difference for PMDD. There was no difference for study setting, site of study, and the way of administration of the tool to identify depressive symptoms (Tables 1 and 2). In meta-regression analysis, the residual heterogeneity (I^2 = 98.7%) of overall prevalence of depressive disorders was significantly explained by the screening tool used (R^2 = 22.5%, p = 0.0094) and distribution in sub-regions (R^2 = 1.9%, p = 0.0037). The prevalence of depressive disorders was higher in Eastern, Northern and Southern Africa after adjustment on tool used (Supplemental Table 3). The residual heterogeneity (I^2 = 97.7%) of overall prevalence of PMDD was significantly explained by tool used to identify depressive symptoms (R^2 = 5.6%, p = 0.024) (Supplemental Table 4). The prevalence of PMDD was higher in Northern and Southern Africa after adjustment on tool used.

4. Discussion

This first systematic review and meta-analysis summarizes available evidence on the prevalence of (major) depressive disorders in people living with HIV in Africa. The overall prevalence was 36.4% and 15.6% for depressive and major depressive disorders, respectively. The prevalence of (major) depressive disorders in people living with HIV was higher in Northern, Eastern, and Southern Africa and in studies conducted after 2010, and varied widely according to the screening tool used. CD4 cell counts, proportion of males, proportion of people with undetectable viral load, and way of administration of the tool to identify depressive symptoms were not sources of heterogeneity for the prevalence of (major) depressive disorders among people living with HIV in Africa. Another key finding of this study, like in previous meta-analyses [6–8], is the very high heterogeneity highlighting the absence of homogeneity in the distribution of the burden of depressive disorders among HIV patients in the entire continent.

The prevalence of (major) depressive disorders found in this review are close to the prevalence of 29.5% (95%CI 20.5–39.4) and 13.9% (95%CI 9.7–18.6) reported in a systematic review and meta-analysis including 13 studies (5373 participants) from 7 sub-Saharan Africa countries [6]. Our findings on depressive disorders with different tools used were also in the range of that found by in a systematic review and meta-analysis in sub-Saharan Africa (9% to 32%) [8]. Another review published in 2012 for sub-Saharan Africa region reported a pooled prevalence of 31.2% (95% CI 25.5–38.2%; 23 studies) and 18% (95% CI 12.3–25.8%; 6 studies) for depressive and major depressive symptoms [7]. Our review included more studies, more participants, more countries, more recent data, and data from the entire African continent. Similar elevated estimations of the burden of (major) depressive disorders among HIV-infected people have also been reported from outside Africa [5,12,135], but some other reports including for instance a meta-analysis of 10 studies conducted outside Africa reported a lower prevalence estimate, around 9.4% [135]. This difference can be explained by the fact that people living with HIV in Africa seem to face higher frequency of well-known risk factors for depression including stigma and advanced stage of HIV infection than others [12,136].

We found a higher prevalence of (probable major) depressive disorders in Northern, Western and Eastern Africa compared to other sub-regions of the continent. The high prevalence in Northern Africa should be interpreted with caution since few studies were from this region. Although we found no clear explanation to support this observation, it could be hypothesized that the burden of major drivers of depressive disorders in HIV such as stigma, occupational disability, body image changes, isolation and debilitation [12], may be higher in these regions than in other parts of the continent. Further well-designed studies are warranted to elucidate this issue. We also found a higher prevalence in recent studies highlighting the need for specific attention to depression in people living HIV in Africa.

On the other hand, we identified no relation between the variation in prevalence estimates of (major) depressive disorders and CD4 cell counts, HIV viral load and sex. Although we conducted a meta-regression analysis to investigate these associations, we lacked enough power

Table 1
Summary statistics of meta-analysis of prevalence of depressive disorders in people living with HIV in Africa.

	Prevalence, %	95% Confidence Interval	95% Prediction Interval	N Studies	N participants	I^2 (95%CI)	H (95%CI)	P heterogeneity	P Egger	P difference
Overall	36.5	32.3–41.0	3.5–80.1	101	47,537	98.7 (98.6–98.8)	9.9 (9.5–10.2)	< 0.0001	0.994	–
Low risk of bias studies	37.5	31.6–43.5	3.1–82.3	58	32,935	99.1 (99.0–99.2)	10.5 (10.1–11.0)	< 0.0001	0.956	–
By diagnostic tool										
AIDS relief adherence survey	56.6	52.9–60.1	NA	1	732	NA	NA	NA	NA	< 0.0001
Hamilton depression rating scale	55.3	32.2–77.3	NA	2	343	92.5 (74.4–97.8)	3.4	0.0003	NA	
Mental health index-5	54.8	52.3–57.2	NA	1	1545	NA	NA	NA	NA	
Beck depression inventory	52.5	43.0–61.9	16.8–86.8	13	5023	98.9 (98.7–99.1)	9.6 (8.7–10.6)	< 0.0001	0.056	
Patient health questionnaire – 9	47.8	38.4–57.4	13.6–83.3	12	6116	98.4 (98.2–98.7)	8.0 (7.4–8.7)	< 0.0001	0.371	
Hospital anxiety and depression scale	44.9	21.5–69.5	0.0–100.0	6	1911	99.3 (99.1–99.5)	12.0 (10.5–13.6)	< 0.0001	0.852	
Zung Self-reported questionnaire-20	47.9	30.6–65.5	0.3–99.0	5	1009	86.4 (60.6–95.3)	2.7 (1.6–4.6)	0.0007	0.992	
Hopkins symptom checklist	34.3	25.2–44.0	3.2–76.9	16	7601	98.4 (98.0–98.8)	8.0 (7.2–9.0)	< 0.0001	0.150	
Center for epidemiological studies depression scale	31.7	23.7–40.2	2.0–75.1	22	13,697	99.1 (98.9–99.2)	10.4 (9.7–11.2)	< 0.0001	0.618	
Kessler	27.0	12.8–44.1	0.0–97.9	4	1713	98.1 (96.9–98.9)	7.3 (5.7–9.4)	< 0.0001	0.998	
Composite international diagnostic interview	24.2	8.7–44.4	0.0–100	3	2009	98.8 (98.4–99.2)	12.5	< 0.0001	0.835	
Montgomery-Åsberg depression rating scale	22.9	15.3–31.4	NA	1	105	NA	NA	NA	NA	
Mini-international neuropsychiatric interview	21.8	12.6–44.1	0.0–67.9	11	4953	98.1 (97.7–98.5)	7.4 (6.6–8.2)	< 0.0001	0.183	
Schedule for clinical assessment in neuropsychiatry	21.1	8.3–37.6	NA	2	460	92.9 (76.2–97.9)	3.7	0.0002	NA	
Clinical interview schedule-revised	15.5	11.0–20.6	NA	1	220	NA	NA	NA	NA	
ED-5D	4.0	0.9–8.9	NA	1	100	NA	NA	NA	NA	
By region										
Northern	81.6	53.1–98.4	NA	2	436	95.9 (88.3–98.6)	4.9	< 0.0001	NA	0.0006
Southern	43.7	36.4–51.0	10.4–80.6	26	8342	97.7 (97.2–98.1)	6.5 (5.9–7.2)	< 0.0001	0.812	
Eastern	34.8	28.6–41.3	2.1–80.4	49	26,772	99.1 (99.0–99.2)	19.5 (10.1–11.0)	< 0.0001	0.762	
Western	28.8	21.0–37.2	1.9–69.8	19	5236	97.9 (97.4–98.3)	6.8 (6.2–7.6)	< 0.0001	0.956	
Central	21.1	6.6–40.7	2.7–54.1	3	869	97.5 (95.1–98.7)	6.3 (4.5–8.8)	< 0.0001	0.360	
By setting										
Rural	33.0	24.7–41.9	4.3–72.0	15	6375	98.4 (98.1–98.7)	7.9 (7.2–8.7)	< 0.0001	0.757	0.104
Urban	43.2	34.7–51.8	3.7–89.3	33	10,636	98.7 (98.5–98.9)	8.8 (8.3–9.4)	< 0.0001	0.101	
By site										
Hospital-based	37.1	32.4–41.9	3.8–80.2	85	39,784	98.9 (98.9–99.0)	9.7 (9.3–10.0)	< 0.0001	0.275	0.456
Population-based	30.0	13.9–48.9	0.0–92.9	7	4814	99.7 (99.6–99.7)	12.2 (10.8–13.9)	< 0.0001	0.085	
By the way of administration										
Self-administered	40.6	32.3–49.2	14.1–70.4	8	1841	91.5 (85.7–95.0)	3.4 (2.6–4.5)	< 0.0001	0.003	0.152
Heterogeneous	33.5	28.5–38.6	2.0–78.5	76	37,471	99.2 (99.1–99.2)	10.9 (10.5–11.2)	< 0.0001	0.781	
By period										
Before 2010	33.9	28.5–39.6	2.1–78.8	61	31,385	99.1 (99.0–99.2)	10.4 (10.0–10.9)	< 0.0001	0.548	0.141
2011 or after	40.7	33.8–47.7	5.0–83.8	40	16,152	98.8 (98.6–98.9)	9.0 (8.4–9.5)	< 0.0001	0.468	

CI: confidence interval.

Table 2
Summary statistics of meta-analysis of prevalence of probable major depressive disorders in people living with HIV in Africa.

	Prevalence, %	95% Confidence interval	95% Prediction interval	N Studies	N participants	I^2 (95%CI)	H (95%CI)	P heterogeneity	P Egger	P difference
Overall	14.9	12.1–17.9	0.7–41.5	55	27,496	97.7 (97.4–98.0)	6.6 (6.2–7.1)	< 0.0001	0.158	–
Low risk of bias	13.4	9.7–17.5	0.2–40.5	28	13,859	97.7 (97.3–98.1)	6.6 (6.1–7.3)	< 0.0001	0.361	–
By diagnostic tool										
Mood module	25.8	19.6–32.4	NA	2	182	0.0	1.0	0.470	NA	< 0.0001
Mini-international neuropsychiatric interview	21.6	13.0–31.7	0.3–61.6	6	3933	97.3 (95.8–98.3)	6.1 (4.9–7.6)	< 0.0001	0.935	
Patient health questionnaire – 9	20.1	15.2–25.4	1.7–51.0	24	10,755	97.7 (97.2–98.1)	6.6 (6.0–7.3)	< 0.0001	0.079	
AIDS relief adherence survey	13.9	11.5–16.5	NA	1	732	NA	NA	NA	NA	
Hamilton depression rating scale	11.1	0.0–67.9	NA	2	343	98.9 (97.9–99.5)	9.7	< 0.0001	NA	
Beck depression inventory	10.0	6.5–14.0	0.9–26.2	9	4233	90.6 (84.5–94.3)	3.3 (2.5–4.2)	< 0.0001	0.317	
Composite international diagnostic interview	8.2	3.2–15.2	0.0–41.1	6	6258	97.9 (96.8–98.6)	6.9 (5.6–8.4)	< 0.0001	0.444	
Zung self-reported questionnaire-20	4.5	1.6–8.7		3						
Clinical interview schedule-revised	2.7	0.9–5.4	NA	1	220	NA	NA	NA	NA	
Schedule for clinical assessment in neuropsychiatry	2.7	0.6–7.0	NA	1		NA	NA	NA	NA	
By region										
Northern	37.8	27.1–49.2	NA	1	74	NA	NA	< 0.0001	NA	< 0.0001
Southern	18.1	11.1–26.4	0.0–59.5	16	8127	98.3 (97.9–98.6)	7.7 (6.9–8.6)	< 0.0001	0.078	
Eastern	15.0	11.0–19.6	1.0–40.8	21	12,655	97.7 (97.2–98.2)	6.7 (6.0–7.4)	< 0.0001	0.876	
Western	10.1	5.8–15.4	0.0–33.9	10	2520	93.6 (90.3–95.8)	4.0 (3.2–4.9)	< 0.0001	0.761	
Central	12.3	2.7–27.2	0.0–76.5	6	1776	98.4 (97.8–98.9)	8.0 (6.7–9.6)	< 0.0001	0.006	
By setting										
Rural	16.6	8.8–26.3	0.0–56.9	6	4013	97.6 (96.4–98.4)	6.5 (5.2–8.0)	< 0.0001	0.429	0.632
Urban	13.9	8.4–20.5	0.0–45.4	13	3042	95.6 (93.8–96.8)	4.7 (4.0–5.6)	< 0.0001	0.414	
By site										
Hospital-based	15.8	12.6–19.2	0.6–44.3	48	19,257	97.6 (97.2–97.9)	6.5 (6.0–7.0)	< 0.0001	0.740	0.198
Population-based	10.7	4.9–18.3	0.0–57.6	4	7584	98.6 (97.8–99.1)	8.4 (6.7–10.6)	< 0.0001	0.494	
By the way of administration										
Self-administered	11.0	6.8–15.9	0.6–30.4	5	878	73.4 (33.6–89.3)	1.9 (1.2–3.1)	0.005	0.655	0.273
Heterogeneous	14.5	11.1–18.2	0.4–42.7	38	23,102	98.4 (98.1–98.6)	7.9 (7.3–8.5)	< 0.0001	0.326	
By period										
Before 2010	10.3	8.0–12.8	1.3–26.0	27	16,728	95.7 (94.6–96.5)	4.8 (4.3–5.4)	< 0.0001	0.259	0.0005
2011 or after	20.0	14.9–25.5	0.7–54.6	28	10,768	97.8 (97.4–98.2)	6.8 (6.2–7.4)	< 0.0001	0.935	

CI: confidence interval.

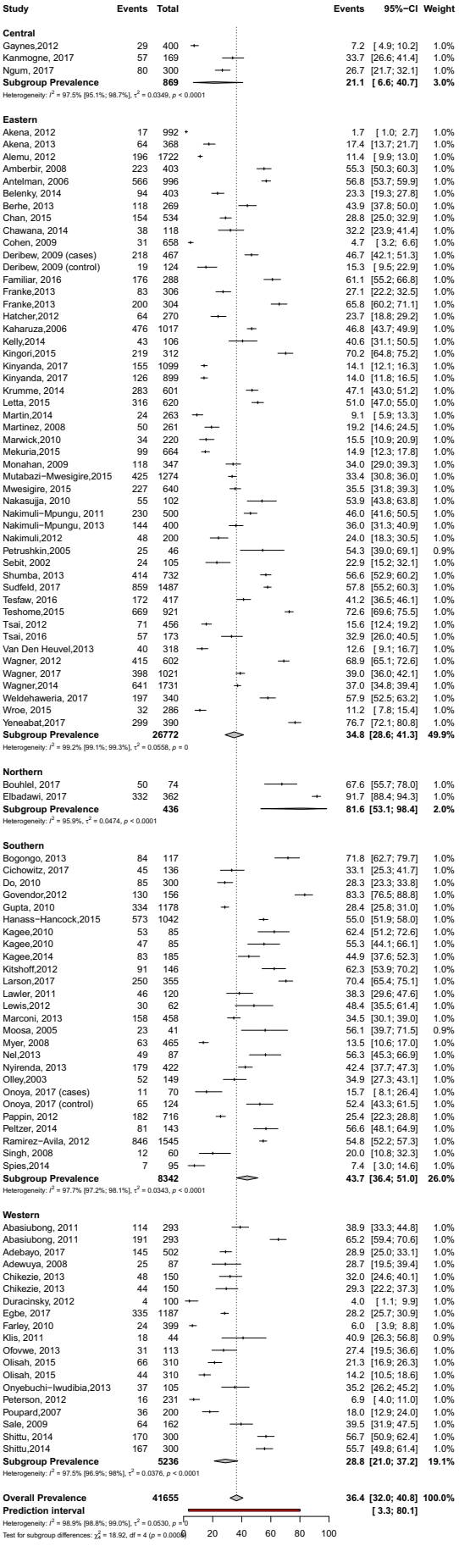

Fig. 1. Forest plot of meta-analysis prevalence of depressive disorders among people living with HIV in Africa.

to detect any significant association with CD4 cell counts and HIV viral load since there were very few studies reporting data on these variables. It is well described that people living with HIV and depression have higher risk for negative clinical outcomes such as reduction in adherence to ART, poor quality of life and treatment outcomes [5]. Depression in people living with HIV leads to alteration in the function of lymphocytes and decreased natural killer cells activity, contributing thereby to the increased mortality in these patients [5,12]. Additionally, the high variability of tools to identify depressive disorders across studies included in this review may have hidden any association between depressive disorders and investigated factors. We surprisingly found no association between (probable major) depressive disorders with female sex as in previous studies [8]. This finding should be interpreted with caution since there was low number of studies included for meta-regression to identifying factors associated with depressive disorders and PMDD.

The prevalence of major depressive disorders is two times higher in people living with HIV compared to those HIV-negative as reported in a meta-analysis from USA [135]. The mechanism of occurrence of depressive disorders in people living with HIV is well described. Indeed, the pathophysiological pathways include psychosocial factors like stigma, biological factors (HIV viral proteins, thyroid dysfunction, and alteration of white matter), history of psychiatric disease and the perinatal period [5,12].

Our findings have important policy implications for the management of HIV disease. With > 25 million of people living with HIV in Africa [1], close to 10 million might have depressive disorders among whom half with can be major. Policy makers should be aware of this to better prepare and strengthen health systems for proper management of the condition in this vulnerable population considering that depressive disorders can negatively impact the course of HIV disease. If nothing was done, it would be difficult to achieve the third 90 of the 90–90-90 ambitious treatment target to help end the AIDS epidemic.

Our findings also have important implications for clinical practice. For instance, depression still underdiagnosed in Africa and action needed [137]. This may be explained by the weakness of health system in Africa due to high workload in primary health care settings, lack of knowledge of the clinicians on mental health, the poor integration of mental health services, and scarcity of financial resources and quantitative health personal for mental health [138,139]. The high burden of depressive disorders in HIV found in this review deserve more attention for HIV healthcare providers. Systematic screening for depressive disorders in HIV patients can be integrated on patient follow-up. However, this can be limited by scarcity of resources [138,139]. Evidence on the cost-effectiveness of adding systematic screening for depressive disorders in HIV patients on the already stretched health system and HIV program in African countries are highly needed to inform health policies. Task shifting to non-physician healthcare workers and community-based organization can be explored for first screening and identifying probable cases of depressive disorders [140–142]. This is supported by the potential benefit of addressing depressive disorders and improving morbidity and mortality of HIV patients in Africa, the epicentre of HIV epidemic.

This review should be interpreted in consideration of certain limitations. First and common to most reviews of this type, we found a high heterogeneity between studies, which could not be explained by the study setting, site, CD4 cell counts, proportion of males, and proportion of people with undetectable viral load. There may still be other factors likely explaining the heterogeneity found in this review such as the political stability prevailing in the country when the study was conducted, the prevalence of HIV-stigma, and the social context. This high heterogeneity can limit generalizability of the finding to the entire

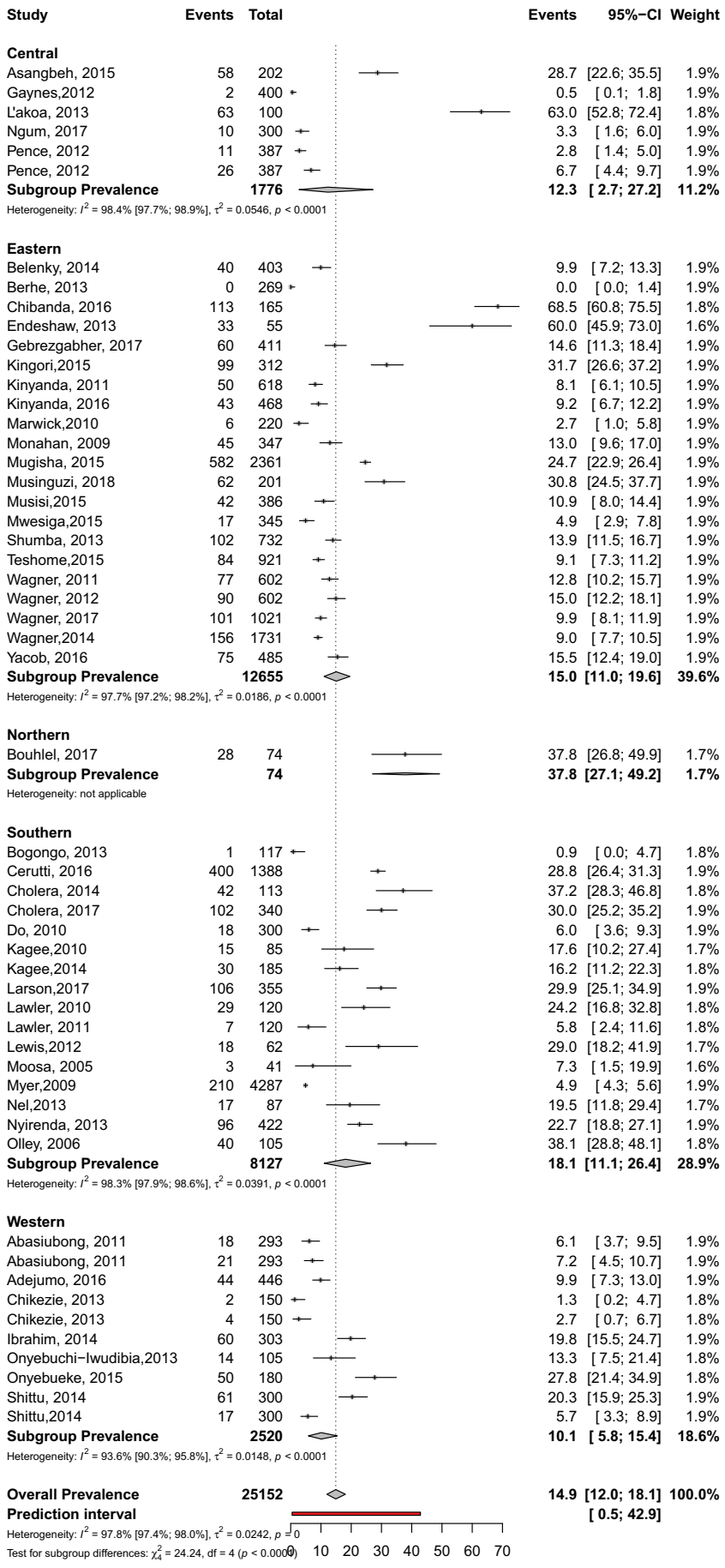

Fig. 2. Forest plot of meta-analysis prevalence of probable major depressive disorders among people living with HIV in Africa.

continent. However, we were unable to assess these factors because they were not fully reported in primary data. Second, the various UNSD sub-regions in Africa were not proportionally represented in the review, which may hinder the translatability of our findings to the entire continent. Third, although there is a multiculturalism and a socio-economic context specific to Africa, the tools used to measure the presence of depressive disorders in people living with HIV in this continent are not all validated in this population. We need further studies to harmonize and validate tools for depressive disorders in HIV-infected patients living in Africa. This review included studies over a long period (since 1994), so the estimates found in this review may be distorted by the current reality, however most of the data are recent.

Nonetheless and to the best of our knowledge, this is the first systematic review and meta-analysis which has given a clear and accurate estimate of the burden of depressive disorders in people living with HIV from all regions in Africa. We also extensively investigated sources of heterogeneity with data from 19 countries. We searched the biggest electronic databases and used rigorous methodological and statistical procedures to generate our prevalence estimates. More than half of studies were assessed as having a low risk of bias in their methodological quality, suggesting that we can be confident in the quality of these estimates. In addition, the sensitivity analysis including only studies with a low risk of bias yielded a very close prevalence to that estimated in the crude analysis.

This study shows a high prevalence of depressive disorders among people living with HIV in Africa. As such, depressive disorders should deserve more attention from HIV healthcare providers, researchers, policy makers, and stakeholders for improved detection, overall proper management, and efficient control in people living with HIV in Africa. Depressive disorders should be routinely screened, identified, and treated by HIV healthcare providers to avoid their negative impact on the progression of HIV disease. Moreover, further studies are warranted to better investigate all factors impacting depression in people living with HIV in Africa, and to develop, standardize or validate related tools for the African continent.

Conflicts of interest

We declare no competing interests.

Source of funding

None.

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None to declare.

Data Availability

All data generated or analyzed during this study are included in this published article and its supplementary information files.

Contributors

Conception of the review: JJB and JRN. Design of the protocol: JJB, LNU, SLA, ATS, ADK, and JRN. Literature search conception: JJB. Studies selection: JJB, AMK, and JRN. Searching of full texts: AMK, AJF, DNT, LNU, MSN, TD, and JJB. Data extraction: DNT, AJF, LNU, SLA, TD, MSN, and JJB. Data synthesis and analysis: JJB and JRN. Data interpretation: JJB and JRN. Manuscript drafting: DNT, JJB, and JRN. Manuscript revision: JJB, LNU, SLA, ATS, ADK, AMK, DNT, MSN, TD, AJF, and JRN. Guarantor of the review: JJB. Manuscript approval: All authors.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.genhosppsych.2018.10.005.

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