Prevalence and factors associated with depression in people living with HIV in sub-Saharan Africa: A systematic review and meta-analysis

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Abstract

Depression, one of the most common psychiatric disorders, is two- to three-times more prevalent in people living with HIV (PLHIV) than in the general population in many settings as shown in western countries but remains neglected in sub-Saharan Africa (SSA). We aimed to summarize the available evidence on the prevalence of depression and associated factors according to the scales used and the treatment status in PLHIV in SSA. The pooled prevalence estimates of depression ranged between 9% and 32% in PLHIV on antiretroviral treatment (ART) and in untreated or mixed (treated/untreated) ones, with a substantial variability according to the measurement scale used and also for a given scale. Low socio-economic conditions in PLHIV on ART, female sex and immunosuppression in mixed/untreated PLHIV were frequently reported as associated factors but with no consensus. As depression could have deleterious consequences on the PLHIV life, it is critical to encourage its screening and management, integrating these dimensions in HIV care throughout SSA.

Introduction

With the improvement in antiretroviral therapy (ART) and the increasing access and use of HIV medical services over almost two decades, a dramatic positive change has been observed worldwide in the demographics of the people living with HIV (PLHIV) [1]. HIV infection can now be considered as a chronic disease in most settings including in sub-Saharan Africa (SSA) [2]. Among the non-communicable disorders observed in PLHIV on ART, insufficient attention has been paid to mental health issues, particularly in SSA where most PLHIV live and are in care.

Depression is one of the most common psychiatric disorders in PLHIV but is neglected in SSA [3]. A recent editorial in AIDS journal reported evidence on the disability associated with HIV-related depression and insisted on the need to act [3]. A meta-analysis conducted in western countries and including studies that used interviews to diagnose major depressive disorders have reported a prevalence of nearly two times higher in PLHIV than in HIV-uninfected

subjects [4]. In USA, with the short form of the Composite International Diagnostic Interview, it was also reported a prevalence of two- to three-times higher than in the general population [5] although direct comparisons are rare. The reasons for this higher risk of depression are numerous, including ART side effects, inflammatory processes [3], stigma/discrimination related to HIV/AIDS and fear of premature death [6].

Depression occurrence in PLHIV leads to alteration of economic productivity, decrease of working abilities, social isolation, physical decline and difficulties in solving problems, again more severely in PLHIV [3]. Depression has been shown to predict non-adherence to ART [7,8]. A recent study reported that non-adherent patients had a 3-fold higher risk of presenting moderate to severe depressive symptoms in comparison to adherent patients [9]. Studies in Africa revealed that in PLHIV, depression is also associated with poorer health status overall, including low weight gain, low CD4 progression [10], suicide [11] but also with faster progression to AIDS and increased mortality [3]. Depression could be clinically quite different from the depression among uninfected patients, as reported in one study, revealing that compared to depressed uninfected subjects, depressed PLHIV have a later onset of depressive illness, are more likely to take medications before the onset of depression and have more severe symptoms (ie more critical of themselves, poorer sleep, tired, loss of appetite. . .) [6]. In this context, depression could seriously compromise ART outcomes at individual and population levels.

As depression in PLHIV emerges as a public health issue, the risk of burden on the health care systems and human resources is significant, especially in SSA. Two reviews aimed to present the consequences of depression on ART adherence [12,13] and clinical outcomes [13]. They were not centered entirely on depression and combined all age groups including children. Another review focused on the reliability and the validity of the tools to screen for depression [14]. Two of these publications presented pooled prevalence estimates but with publications before 2012 for one of them [12] and without differentiating the scales used for the other one [14]. The aim of this new systematic review and meta-analysis is to summarize the most recent available evidence up to April 2016 in adult PLHIV living in SSA on: 1) the prevalence of Major Depressive Disorders (MDD), (ie patients meeting diagnosis criteria of depression according to the Diagnosis and Statistical Manual of Mental Disorders [DSM]) and depressive symptoms, (ie defined based on a screening instrument with a score higher than a specified threshold), and 2) the risk factors for depression. The strength of this updated review is to report the results according to the measurement scales used and the care and treatment characteristics (treated PLHIV vs untreated or mixed PLHIV, ie samples mixing treated and untreated patients). We combined a meta-analysis and a qualitative review to report thoroughly the data available on the topic. Pooled prevalence estimates were calculated when possible.

Methods

Eligibility criteria

The publications were searched on Medline, Scopus, specific neuropsychologic literature databases (PsycInfo, PsycArticles, Psychology and behavioral sciences collection) and specific African databases (African Index Medicus and African journal online) using the following terms (Mesh terms): "HIV Infections" AND ("Depressive Disorder" OR "Depression") AND ("Africa" OR "Africa South of the Sahara"). We also added filters on the date of publication (1996 to April 2016) and the age of the patients (≥18 years old) (S1 File). We included cross-sectional and longitudinal studies assessing the prevalence and the factors associated to major depression and depressive symptoms in adult PLHIV. Four papers were identified by complementary

researches and four others were recommended by an expert. No paper corresponding to our criteria was found in the grey literature (http://www.opengrey.eu).

After a first screening of titles or abstracts to remove duplicates and exclude papers out of the scope, 120 papers were identified (Fig 1). Among them, we excluded review papers (n = 2), qualitative papers (n = 2), papers neither focusing on PLHIV (n = 3), nor on African patients (n = 1) and those combining adults with patients under 18 years old (n = 2). We also excluded papers using inaccurate measurement scales or scales evaluating both anxiety and depression without giving specific information on depression (n = 7), papers with no full text and abstract with insufficient information (n = 11), papers with very specific populations (n = 4) or those focusing on depression consequences (n = 2). Among the 86 remaining papers, 19 papers were excluded when no information on patients' ART status was available (authors were contacted by email but no answer was obtained) and one with duplicate data reported.

Altogether, 66 papers were included in the review. Fifty-five full-text papers reported the prevalence of major depression and/or depressive symptoms (10 on MDD only, 40 on
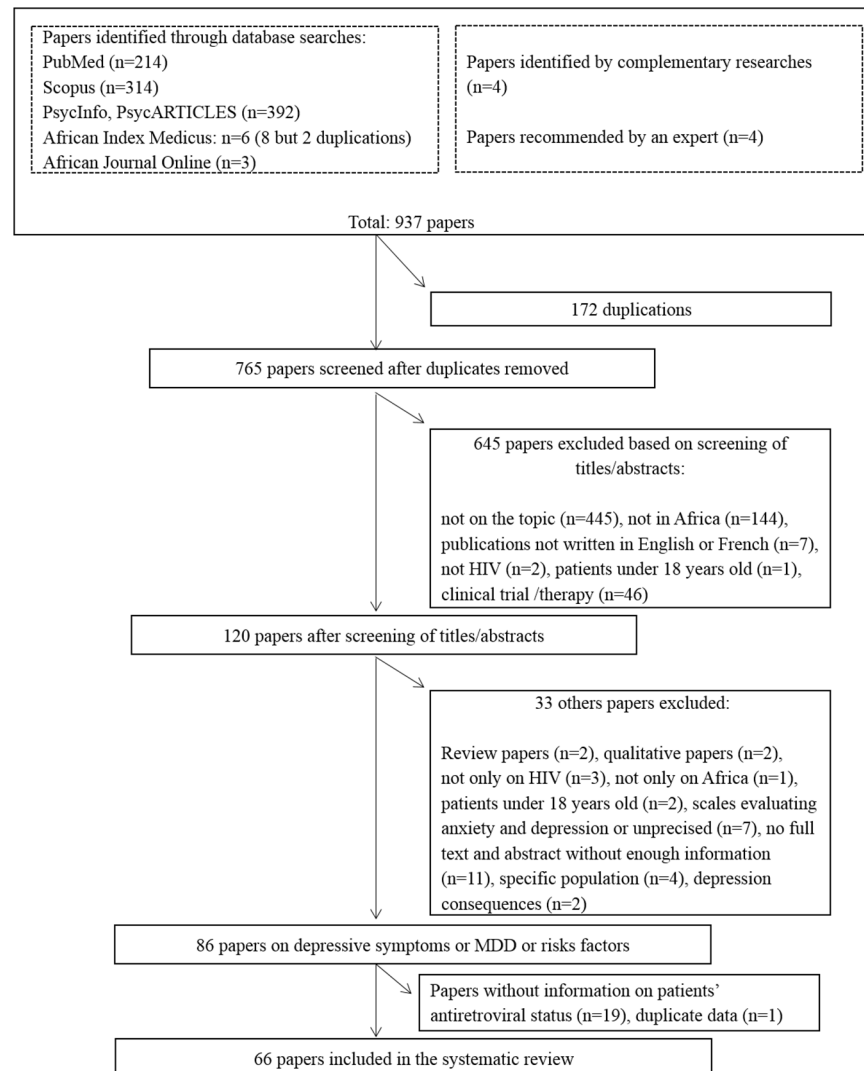
Fig 1. Flow diagram for systematic review process.

depressive symptoms only, and five on both) whereas 11 reported information only on factors associated with depression. Thirteen papers were published before 2010 and 53 (80.3%) between 2010 and April 2016. We reported pooled prevalence estimates for the studies using the scales with the same number of items and the same cut-off, e.g. for the Center for Epidemiologic Studies–Depression (CES-D) Scale [15] 20 items; we did not include the studies using CES-D with 11 or 10 items. Altogether, 25 papers were included to calculate the pooled prevalence of depressive symptoms (14 of them distinguished ART-treated PLHIV); nine papers allowed the computation of the pooled prevalence of MDD (3 of them distinguished ART-treated PLHIV).

Tools and validity

Among the 16 papers reporting MDD prevalence estimates, the Mini-International Neuropsychiatric Interview (MINI) [16], the usual gold standard, was used in nine of them. The MINI is a brief structured diagnostic interview across the major Axis I psychiatric disorders in the *DSM-III-R*, *DSM-IV*, and the *International Statistical Classification of Diseases and Related Health Problems* (*ICD-10).*

The majority of the studies selected used screening scales based on DSM-IV depression criteria to evaluate the severity of depressive symptoms. Among the 45 papers evaluating depressive symptoms, 14 (31.1%) used the CES-D scale. The CES-D is a 20-item self-rating scale that assesses symptoms experienced by the participant during the past week, such as depressed mood, feeling guilty, helplessness and somatic symptoms (loss of appetite, sleep disturbance). The total score ranges from 0 to 60 with scores ≥16 representing significant depressive symptoms. Eight reports (17.8%) used the Patient Health Questionnaire (PHQ-9) [17,18]. The PHQ-9 is a 9-item self-rating scale evaluating the key symptoms of depression during the past two weeks. The total score ranges from 0 to 27 with five categories of severity: minimal (0–4), mild (5–9), moderate (10–14), moderately severe (15–19) and severe (20–27). The 15-item depression sub-scale of the Hopkins Symptom Checklist (HSCL-D) [19] was also reported in eight (17.8%) papers, with a threshold >1.75 defining significant depressive symptoms. The Beck Depression Inventory (BDI) [20], a 21-item self-report measure, was reported in six (13.3%) papers.

In SSA studies, with this 16 score cut-off, the CES-D scale was reported having a good sensitivity but a limited specificity (79% to 91% and 44% to 81%, respectively) [21–23]. In a recent meta-analysis, pooled sensitivity and specificity for the CES-D, based on four African studies were high for the threshold ranges between 16 and 22 (sensitivity 82% [95% CI, 73–87], specificity 73% [95% CI, 63–80]).[14] For a PHQ-9 cut-off ≥10, three African studies reported a variable sensitivity but a high specificity (27% to 91.6% and 70.8% to 95.6% respectively) [21,24–26]. No validity study was available in Africa for the HSCL-D scale. There is no consensus on what cut-off to use for the BDI.

Statistical analyses

For the meta-analysis, forest plots were used to present pooled prevalence and 95% confidence interval (CI) of MDD and depressive symptoms based on the scales used and the care and treatment status (treated PLHIV vs untreated or mixed PLHIV). For each scale, we differentiated the results from the meta-analysis and from the qualitative review, by adding "Meta-analysis" or "Qualitative review" at the beginning of the paragraphs. The weight of each study was taken into account to estimate the pooled prevalence, as indicated on the forest plots. Between-study heterogeneity was assessed using I^2 statistics [27]. The analyses were performed with MetaXL version 5.1. Finally, the quality of the studies included in the

meta-analysis was assessed using the Grading of Recommendations Assessment, Development, and Evaluation—Guideline Development Tool (GRADEpro GDT). GRADEpro GDT (http://www.guidelinedevelopment.org/) is an easy and free tool, available online to facilitate the creation of evidence tables, allow to present clearly the criteria required for the quality assessment of the publications and facilitate the conclusion about the quality of the publications. For the tables, variety of formats are available: we have chosen the GRADE Evidence Profile.

The factors associated to MDD or depressive symptoms are reported based on the results of the meta-analysis.

This review was conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Table A in S2 File).

Results

Prevalence of MDD

Results of studies reporting the prevalence of MDD are shown in Tables 1 and 2 according to the tool used and the treatment status.

MINI. Results are presented in Table 1.

Meta-analysis

In untreated or mixed groups of PLHIV, the pooled prevalence of depressive symptoms was 19% [95% CI: 18–21] with a high between-group heterogeneity (I^2 = 99%) (Fig 2-right) [22,31–35]. In PLHIV on ART, the pooled prevalence of depressive symptoms was 12% [95% CI: 10–14] with a high between-group heterogeneity (I^2 = 89%) (Fig 2-left) [28–30].

Qualitative review

In untreated or mixed groups of PLHIV, in South Africa, a longitudinal study revealed that MDD was one on the most prevalent psychiatric disorders both at baseline (34.8%) and during follow-up (20%). Although more than half of the depressed PLHIV at baseline no longer met criteria for depression at follow-up times, new cases were diagnosed over time (8.1%) [31].

Other tools. Results are presented in Table 2.

Meta-analysis

No pooled prevalence was calculated due to the variety of scales used.

Qualitative review

In mixed groups of PLHIV, the prevalence of MDD ranged from 13% to 24% [39,40]. The prevalence of MDD was significantly higher in PLHIV aged 50 years old or above (30.1% vs 14.8%) in comparison with HIV-uninfected patients [41].

In PLHIV on ART, the prevalence of MDD ranged from 3% to 14.2% [36,37]. Only one study in Uganda where the diagnosis was made by a psychiatrist reported that 65% of the PLHIV had MDD. Among them, 61.5% were diagnosed after becoming HIV-positive and 38.4% after starting ART [38].

Prevalence of depressive symptoms

Results of studies reporting the prevalence of depressive symptoms severity are shown in Tables 3–7 according to the tool used and the treatment status.

CES-D. Results are presented in Table 3.

Meta-analysis

Based on the 20-item CES-D (cut-off≥16), the pooled prevalence of depressive symptoms among untreated or mixed groups of PLHIV was 31% [95% CI: 30–33] with a high between-group heterogeneity (I^2 = 98%) (Fi 3A-right) [22,23,45–47]. Among the PLHIV on ART and based on the 20-item CES-D (cut-off≥16), the pooled prevalence of depressive symptoms was

Table 1. Major depressive disorders in HIV-infected adults evaluated by the Mini International Neuropsychiatric Interview (MINI).

First Author, year by chronological order	Country	Study years	HIV + N	HIV- N	Demographic data			Clinical data			Tools	Main results or Prevalence (%) (95% CI)
					Age (years)	Men (%)	Education	CD4 cell count /mm³	CDC/ WHO stage (%)	ART (%)		
Adewuya et al, 2008 [28]	Nigeria	NA	87	NA	31–40 yo: 49.4% >40 yo 13.8%	43.7%	Secondary: 55.2% Tertiary: 9.2%	NA	NA	100%	MINI	28.7% (11.8% major / 15.1% minor)
Nakimuli-Mpungu et al, 2011 [29]	Uganda rural	2011	500	NA	40 (10.7)*	30.2%	Post-Secondary:17.4%	CD4<200: 26%	WHO3/4: 41.8%	100%	MINI	25% (9.5% both current and lifetime, 15.2% only lifetime)
Nakimuli-Mpungu et al, 2013 [30]	Uganda	2011	400	NA	>40 yo: 47%	34%	Post-Primary: 16%	NA	WHO 3/4: 41.7%	100%	MINI	• Current: 12.25% • ART adherence vs non-adherence • Lifetime: 19% vs 28.5% • Current: 8% vs16.5%
Olley et al, 2006 [31]	South Africa	2002–2003	149	NA	30 (7)*	29.5%	NA	346.32 (236.21)*	NA	1.3%	MINI	• At baseline: 34.8% • At follow-up: 20% (new cases 8.1%)
Myer et al, 2008 [22]	South Africa	2004–2005	465	NA	33 (29–38)**	25%	Post-Primary: 16%	234** CD4<200: 37%	NA	48%	MINI	14%
Akena, Musisi et al, 2012 [32]	Uganda	2011	368	NA	38.8 (9.81)*	28%	Secondary / post-secondary: 53.8%	329.7 (186.95)*	WHO 3 / 4: 25.8% / 11.1%	"a number of PLWHA were accessing ART"	MINI	17.4%
Nakku et al, 2013 [33]	Uganda	NA	618	NA	25–34 yo: 38.6% ≥45yo: 16.7%	27.3%	Secondary / post-secondary: 42.7%	CD4<250: 42.7%	NA	64.6%	MINI +	8%
Besa et al, 2015 [34]	Zambia	NA	185	NA	39*	28.1%	Secondary: 42.2%	CD4<350: 32.5%	NA	98.4%	MINI	7%
Spies et al, 2009 [35]	South Africa	2004–2005	429	NA	range 18–65 yo	24%	NA	NA	NA	treatment seeking	MINI	• Current MDD: 53.12% • Past MDD: 28.7%

Abbreviations: ART: Antiretroviral Therapy; CI: Confidence Interval; IQR: InterQuartile Range; NA: Not available; SD: Standard Deviation; yo: years old.

Longitudinal analyses are highlighted in grey.

*Mean (SD)

** Median (IQR)

NB: Articles are presented in function of ART status of included patients

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32% [95% CI: 28–35] with a high between-group heterogeneity (I^2 = 97%) (Fig 3A-left) [36,42–44]. In Poupard et al, different cut-off points were used for men (≥17) and women (≥23) [42].

Qualitative review

Among untreated or mixed groups of PLHIV, the CES-D scale without the somatic items, an approach limiting confounding of depression with HIV-related symptoms, was only used in one report with a prevalence of 30% [48]. Based on the 10-item CES-D, 40.9% PLHIV had higher-than-threshold levels of depressive symptoms [50]. Among the PLHIV on ART, it has been shown that after three and six months on ART, the prevalence decreased in one report and remained significantly higher in PLHIV initiating ART than among uninfected subjects at three months [43]. Based on the 10-item CES-D and among the PLHIV on ART, 8.7% of male and 13.1% of the women had higher-than-threshold levels of depressive symptoms [49].

Table 2. Major depressive disorders in HIV-infected adults evaluated by other scales than the MINI.

First Author, year by chronological order	Country	Study years	HIV + N	HIV-N	Demographic data			Clinical data			Tools	Main results or Prevalence (%) (95% CI)
					Age (years)	Men (%)	Education	CD4 cell count /mm³	CDC/ WHO stage (%)	ART (%)		
Olisah et al, 2010 [36]	Nigeria	2006	310	NA	35.5 (8.97)*	31.6%	Secondary: 37.4% Tertiary: 27.1%	NA	NA	100%	ICD-10	14.2%
Gaynes et al, 2012 [37]	Cameroon	2010	400	NA	41 (34–47)**	26%	Post-Primary (>6 years): 39%	NA	NA	100%	CIDI	7% in prior year, 5% in prior 6 months, 3% in past month; 21% during lifetime
Ngo et al, 2013 [38]	Uganda	2009	40	NA	<40 yo: 52.5%	32.5%	Secondary / post-secondary: 80%	204 (147)* CD4≤250: 69%	NA	100%	Semi-structured interview Diagnostic made in clinic psychiatric	65% (26/40 patients)
Lawler et al, 2011 [39]	Bostwana	2008	120	NA	37.5 (6.5)*	50%	Secondary: 48% Tertiary 15%	360.4 (181.4)* CD4<200: 20%	NA	97.5%	Mood Module (MM) of the Primary Care Evaluation of Mental Disorders (Prime-MD)	24%
Wagner et al, 2012 [40]	Uganda	2010–2011	602	NA	NA	NA	NA	NA	NA	49.8%	NA	13%
Nyirenda et al, 2013[41]	South Africa rural	2003–2007	422		≥50 yo	NA	NA	NA	NA	yes/ no	CIDI	Major: 14.8% (9.9–19.7%)HV + vs 30.1% (24.0–36.2%) HIV-affected

Abbreviations: ART: Antiretroviral Therapy; CI: Confidence Interval; CIDI: World Health Organization's Composite International Diagnostic Instrument; ICD-10: International Classification of Diseases; IQR: InterQuartile Range; NA: Not available; SD: Standard Deviation; yo: years old.

*Mean (SD)

** Median (IQR)

NB: Articles are presented in function of ART status of included patients

PHQ-9. Results are presented in Table 4.

Meta-analysis

Based on the PHQ-9 (cut-off ≥10), the pooled prevalence of depressive symptoms among untreated or mixed groups of PLHIV was 9% [95% CI: 8–11] with a high between-group heterogeneity (I^2 = 99%) (Fig 3B-right) [55–57]. Among the PLHIV on ART and based on the PHQ-9 (cut-off≥10), the pooled prevalence of depressive symptoms was 14% [95% CI: 12–16] with a high between-group heterogeneity (I^2 = 91%) (Fig 3B-left) [51–54,76].

BDI. Results are presented in Table 5.

Meta-analysis

In untreated or mixed groups of PLHIV, no pooled prevalence was calculated considering the limited number of studies available. Based on the BDI (21 items), the pooled prevalence of depressive symptoms among PLHIV on ART was 43% [95% CI: 38–49] with no between-
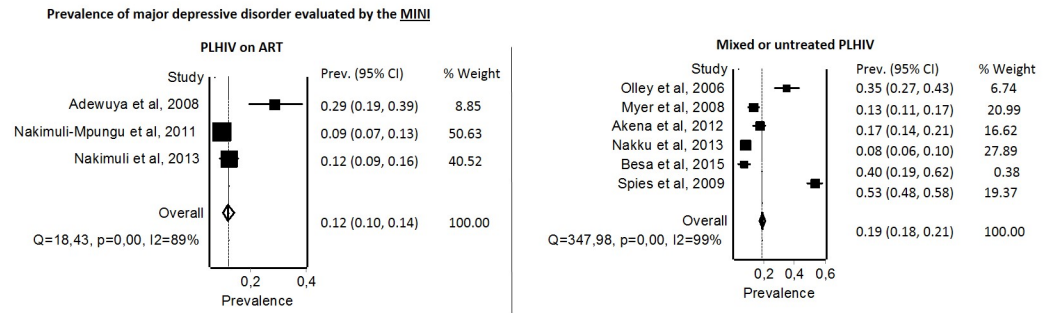
Fig 2. Forest plots presenting the prevalence of MDD according to the tool used and the treatment status. The between-study heterogeneity is reported using I^2 statistics and its associated p-value. Prev: Prevalence; CI: confidence interval.

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group heterogeneity ($I^2 = 0\%$) (Fig 3C-left) [9,59]. However, the cut-off scores were different from one study to another.

Qualitative review

In a series of PLHIV whose 97.5% were on ART, the prevalence figures of mild, moderate and severe depressive symptoms, based on fast screening BDI (7 items) were 59%, 27% and 14%, respectively [39]. In comparison to HIV-uninfected patients, ART-naïve PLHIV presented higher scores on BDI [77]. Using the 21-item BDI, prevalence figures of 24.7%, 20% and 17.6% of mild, moderate and severe depressive symptoms were respectively reported [60].

Among PLHIV on ART, in a longitudinal study using the BDI without somatic symptoms, the prevalence was relatively stable between baseline (55.8%) and after 3 months of follow-up (49.6%) [58].

HSCL. Results are presented in Table 6.

Meta-analysis

Based on the HSCL (cut-off>1.75 with 11–15 items) (Table 2D), the pooled prevalence of depressive symptoms among untreated or mixed groups of PLHIV was 24% [95% CI: 22–27] with a high between-group heterogeneity ($I^2 = 85\%$) (Fig 3D-right) [63–65]. Some studies specified that they used the scale without somatic symptoms [63,65]. Among the PLHIV on ART, the pooled prevalence of depressive symptoms was 13% [95% CI: 11–15] with a low between-group heterogeneity ($I^2 = 72\%$) (Fig 3D-left) [8,61,66].

Qualitative review

Among untreated or mixed groups of PLHIV, using 25 items and a cut-off of 44, one study reported a prevalence of 52.9% [60].

In PLHIV on ART living in Uganda, an unexpected lower prevalence (9.6%) was reported in comparison to uninfected subjects (21.1%) [66]. The authors explained this discrepancy by possible false negative observations in the general population (since the HIV prevalence in the study area was low) and by positive effects of counseling and ART in PLHIV. Using HSCL-25 items, one study reported a prevalence of 38% in treated PLHIV [62].

Other scales. Results are presented in Table 7.

Meta-analysis

No pooled prevalence was calculated due to the variety of scales used.

Qualitative review

Table 3. Severity of depressive disorders in HIV-infected adults evaluated by the Center for Epidemiologic Studies—Depression Scale (CES-D).

First Author, year by chronological order	Country	Study years	HIV+N	HIV-N	Demographic data			Clinical data			Tools	Main results or Prevalence (%) (95% CI)
					Age (years)	Men (%)	Education level (%)	CD4 cell count /mm^3	CDC/WHO stage (%)	ART (%)		
CES-D 20 items												
Poupard et al, 2007 [42]	Senegal	NA	200	NA	Women: 44 Men: 36**	36.5%	NA	341** range: 31–953; CD4<300: 54%	NA	100%	•Cut-off ≥17 for men •Cut-off ≥23 for women	•18% (12–23%) •(19% for PLHIV with protease inhibitor vs 17% for PLHIV with efavirenz)
Nakasujja et al, 2010 [43]	Uganda	2005–2007	102	25	34.2(6.23) vs 30.3(3.99)*	27% vs 60%	9.1 (4.3) vs 10.4 (4.2)*	130 (69.5)*	NA	initiating	Cut-off ≥16	•At baseline: 53.39% (44.1–63.6%) vs 28% (10.4–45.6%); OR 2.86 (1.03–7.95) adjusted on age and gender •At 3-month: 36% vs 13% •At 6-month: 30% vs 24%
Olisah et al, 2010 [36]	Nigeria	2006	310	NA	35.5 (8.97)*	31.6%	Secondary: 37.4% Tertiary: 27.1%	NA	NA	100%	Cut-off ≥16	21.3%
Kitshoff et al, 2012 [44]	South Africa	2010	146	NA	36 (31–42)**	27.4%	Primary: 51% Tertiary and post tertiary: 44%	312 (193–471)**	NA	100%	Cut-off ≥16	62%
Myer et al, 2008 [22]	South Africa	2004–2005	465	NA	33 (29–38)**	25%	Primary: 86%	234**; CD4<200: 37%	NA	48%	Cut-off NA	45%
Farley et al, 2010 [45]	Nigeria	2007	399	NA	≥18yo	31.8%	Post-secondary: 29.8%	CD4<200: 50.1%	NA	55.6%	Cut-off ≥16 or ≥21	•≥16: 13% •≥21: 6%
Seth et al, 2014 [46]	Kenya, Namibia, Tanzania	2009–2010	3538	NA	37.2 (8.4)*	41.9%	NA	348 (210–504)**; CD4<200: 23.7%	NA	64%	Mild: cut-off 16–26 Severe: cut-off >27	•28% (16% mild; 12% severe) •Women 32% (18% mild, 14% severe) •Men 22% (13% mild, 9% severe)
Kaharuza et al, 2006 [47]	Uganda	2003–2004	1017	NA	31-40yo: 44%; >50yo: 9%	23%	Post-primary: 21%	CD4<200: 45%	NA	naïve	•Cut-off ≥23 •Distress (scores 16–22)	47% / distress: 19%
Singh et al, 2008 [23]	South Africa	2007	20	NA	34 (30–39)**	40%	NA	35 (22–91)**	NA	naïve	Cut-off ≥16	40%
CES-D 11 items												
Simbayi et al, 2007 [48]	South Africa	NA	1063	NA	≥36yo: 28%	39.5%	NA	NA	NA	50%	Cut-off ≥16	30%
CES-D 10 items												
Alemu et al, 2012 [49]	Ethiopia	2010	1722	NA	37.93 (8.97)*	38.7%	NA	119** CD4<200: 28%	NA	100%	10 items	13.1% women / 8.7% for men
Klis et al, 2011 [50]	Gambia	2007	44	NA	32.3**	21.4%	≥1 year: 52.3%	CD4<200: 30%	NA	0%	•10 items •Cut-off ≥11	40.9%

Abbreviations: ART: Antiretroviral Therapy; CI: Confidence Interval; IQR: InterQuartile Range; NA: Not available; SD: Standard Deviation. **Longitudinal analyses are highlighted in grey.**

*Mean (SD)

** Median (IQR) NB: Articles are presented in function of ART status of included patients

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Table 4. Severity of depressive disorders in HIV-infected adults evaluated by the Patient Health Questionnaire (PHQ-9).

First Author, year by chronological order	Country	Study years	HIV + N	HIV- N	Demographic data			Clinical data			Tools	Main results or Prevalence (%) (95% CI)
					Age (years)	Men (%)	Education level (%)	CD4 cell count /mm³	CDC/WHO stage (%)	ART (%)		
Wagner et al, 2011 [51]	Uganda	NA	602	NA	36* Range: 20–62	32%	≤ primary: 54% Secondary: 37%	216*Range 1–846	45%	starting	≥10	13%
Asangbeh et al, 2015	Cameroon	2012	200	NA	43.4(11.5)*	34.7%	Only primary: 71.8%	40.1% CD4>500	NA	100%	≥10	28.7%
Belenky et al, 2014 [52]	Tanzania	2008–2009	403	NA	42 (36–48)**	31%	• Primary:74% • Secondary: 17.4%	304(191—443)**	NA	100%	• Mild/moderate/ severe ≥5 • Moderate or severe ≥10	• Mild, moderate or severe: 23% • Moderate or severe: 10%
Endeshaw et al, 2014 [53]	Ethiopia	NA	55	NA	34.68 * (IQR40-28)	36.4%	7th–12th grade: 41.8% ≥diploma: 10.9%	336.5*	NA	100%	NA	• Mild: 29.09% • Moderate: 20% • Moderately severe: 10.91%
Musisi et al, 2014 [54]	Uganda	2010–2011	386	NA	35.7(8.7)*	41.7%	Secondary: 16.5%	163(86) *	16.1%	starting	• Minor: 5–9 • Major: >9	• Minor: 19.2% • Major: 10.9%
L'akoa et al, 2013 [55]	Cameroon	2011	100	NA	40.4(10.4)*	48%	University level: 28%	234(129)*; 39% <200	NA	40%	• Moderate 10–14 • Moderately severe 15–19 • Severe ≥20	• 63% (53.2–71.8%) • Moderate: 46% (36.6–55.7%) • Moderately severe: 16% (10.1–24.4%) • Severe: 1% (0.2–5.4%)
Wagner, Ghosh-Dastidar et al, 2014 [56]	Uganda	2008–2011	750	NA	34.5 *	42%	Secondary / post-secondary 16%	222*	NA	67% starting	• Minor 5–9 • Major >9	• Minor : 28% • Major : 6%
Wagner, Ghosh-Dastidar et al, 2014 [57]	Uganda	2008–2011	1731	NA	35.6*	35%	Secondary / post-secondary 15%	209*	NA	69.5% starting	• Minor 5–9 • Major >9	• Minor : 28% • Major : 9%

Abbreviations: ART: Antiretroviral Therapy; CES-D: Center for Epidemiologic Studies—Depression Scale; CI: Confidence Interval; IQR: InterQuartile Range; NA: Not available; SD: Standard Deviation.

*Mean (SD)

** Median (IQR)

NB: Articles are presented in function of ART status of included patients

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Table 5. Severity of depressive disorders in HIV-infected adults evaluated by the Beck Depression Inventory (BDI).

First Author, year by chronological order	Country	Study years	HIV +N	HIV-N	Demographic data			Clinical data			Tools	Main results or Prevalence (%) (95% CI)
					Age (years)	Men (%)	Education level (%)	CD4 cell count /mm³	CDC/WHO stage (%)	ART (%)		
BDI 13 items												
Amberbir et al, 2008 [58]	Ethiopia	2006–2007	400	NA	•30** •Range 19–58	40.3%	Secondary 50.3%	CD4<200: 72.2%	•WHO 3/4: 66.3% / 24.8%	100%	Cut-off ≥10	•At baseline: 55.8% •At follow-up: 49.6%
BDI 21 items												
Kagee et al, 2013 [59]	South Africa	NA	200	NS	34.05 (7.6)*	21%	•Secondary: 65.3% •Tertiary: 7.1%	NA	NA	100%	•Moderate 17–30 •Severe ≥31	•Moderate 28.5% •Severe 16.2%
Nel et al, 2013 [9]	South Africa	NA	101	NA	35.04 (7.05)*	17.8%	NA	NA	NA	100%	•Mild 14–19 •Moderate 20–28 •Severe 29–63	•Mild 11.7% •Moderate 22.3% •Severe 18.1%
Kagee et al, 2010 [60]	South Africa	NA	85	NS	32.8 (7.6)*	24.7%	•Secondary: 10% •Tertiary: 90%	NA	NA	yes/no	•Mild 10–18 •Moderate 19–29 •Severe 30–63	•Mild 24.7% •Moderate 20% •Severe 17.6%
Lawler et al, 2011 [39]	Bostwana	2008	120	NA	37.5 (6.5)*	50%	•Secondary: 48% •Tertiary: 15%	360.4 (181.4)* CD4<200: 20%	NA	97.5%	•Fast screen 7 items •Cut-off ≥4	38% (mild: 59%; moderate: 27%; severe: 14%)

Abbreviations: ART: Antiretroviral Therapy; CI: Confidence Interval; IQR: InterQuartile Range; NA: Not available; SD: Standard Deviation.

*Mean (SD)

** Median (IQR)

NB: Articles are presented in function of ART status of included patients

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Table 6. Severity of depressive disorders in HIV-infected adults evaluated by the Hopkins Symptoms Checklist (HSCL).

First Author, year by chronological order	Country	Study years	HIV +N	HIV-N	Demographic data			Clinical data			Tools	Main results or Prevalence (%) (95% CI)
					Age (years)	Men (%)	Education level (%)	CD4 cell count/mm³	CDC/WHO stage (%)	ART (%)		
HSCL Cut-off>1.75												
Tsai et al, 2012 [61]	Uganda	since 2005	456	NA	Women: 34 (28–38.4) Men: 38.5 (33–44.9) **	29%	Secondary: Women: 22.2%; Men: 25.8%	• Women: 210.5 (138–304); • Men 177 • (107–265)**	NA	initiating	12 cognitive-affective items (without somatic symptoms)	At baseline: 20.4% for women vs 3.9% for men
Psaros et al, 2015 [62]	Uganda	2005–2010	453	NA	34.9(8.3)*	69.3	≥Secondary: 24.9%	150.2(104.3)*	NA	initiating	25 items	38%
Wroe et al, 2015 [8]	Rwanda	2008	292	NA	38.2 (11.8)*	37%	NA	at ART initiation: 187.5 (95–256.5)**	WHO 3/4: 44.4% / 3.8%	100%	15 items	11.2%
Martinez et al, 2008 [63]	Uganda	2005	421	NA	36 (31–42) **	36.8%	39.4% beyond primary education	218 (91–395) (n = 202)	WHO 3/4: 46.8% / 15.2%	57.1%	11 items; without somatic symptoms	18.8%
Hatcher et al, 2012 [64]	Uganda	2007	270	NA	34 (28–38)**	0%	Secondary : 23%	20 (136–308) **	WHO 4 : 30.4%	44.8%	15 items	23.7%
Chan et al, 2015 [65]	Uganda	2005–2012	534	NA	34.5 (8.9) *	29%	Post- primary: 26.4%	186.8(140.3)*	WHO 3/4: 28.7% / 4.6%	naïve	12 cognitive-affective items (without somatic symptoms)	• At baseline: 28.8% (34.5% for women ; 12.9% for men) • 3.1% of relative decline in the mean depression symptom severity score in each year of study recruitment after the first year
HSCL Cut-off>2												
Martin et al, 2014 [66]	Uganda	2011–2012	263	160	39.8 (9.76) vs 39.8 (15.22)*	32.7% vs 41.2%	Primary: 54.8% vs 58.1%	NA	NA	100%	15 items	9.6 vs 21.1%
HSCL Cut-off>44												
Kagee et al, 2010 [60]	South Africa	NA	85	NS	32.8 (7.6)*	24.7%	Secondary: 10%; Tertiary: 90%	NA	NA	yes/no	25 items	52.9% (distress)

Abbreviations: ART: Antiretroviral Therapy; CI: Confidence Interval; IQR: InterQuartile Range; NA: Not available; SD: Standard Deviation.

*Mean (SD)

** Median (IQR)

NB: Articles are presented in function of ART status of included patients

Table 7. Severity of depressive disorders in HIV-infected adults evaluated by others scales.
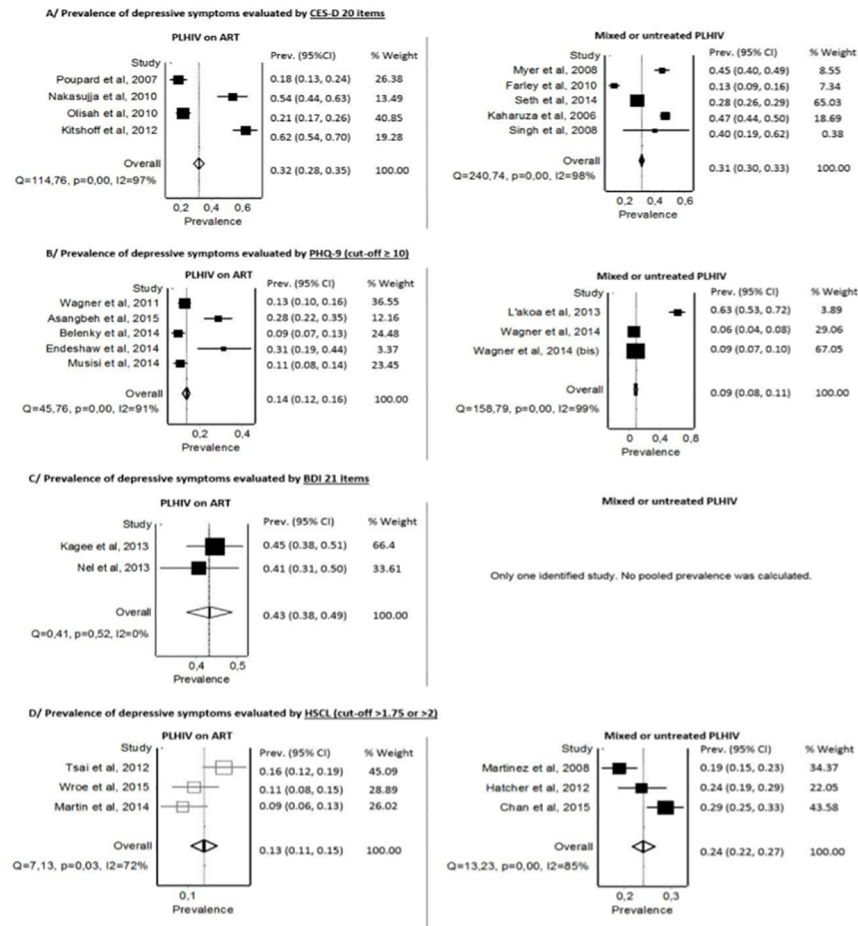
First Author, year by chronological order	Country	Study years	HIV +N	HIV-N	Demographic data			Clinical data			Tools	Main results or Prevalence (%) (95% CI)
					Age (years)	Men (%)	Education level (%)	CD4 cell count /mm^3	CDC/WHO stage (%)	ART (%)		
Hospital Anxiety and Depression Scale (HADS)												
Pappin et al, 2012 [67]	South Africa	2007–2008	716	NA	36 ** (30.8–42.8)	24.3%	• Primary: 31% • Secondary: 45.8%	NA	NA	100%	Information available on depression only	25.4%
Wouters et al, 2012 [68]	South Africa	2007–2008	716	NA	37.2 (8.9)*	24%	Secondary / post-secondary: 57.6%	NA	NA	100%	Information available on depression only	• Mild or subclinical 15.3% • Moderate 8.8% • Severe 1.3%
Others than HADS												
Do et al, 2010 [69]	Botswana	2005	300	NA	24-35yo 64%	23.7%	• Secondary: 55.7% • Tertiary: 17.7%	NA	NA	100%	Questions + European Quality of life (EQ-5D) + BDI	28.3%. Of them: 4.6% mild; 31.8% moderate; 21.2% severe
Gaynes et al, 2012 [37]	Cameroon	2010	400	NA	• 41 • (34–47) **	26%	Post-Primary (>6 years): 39%	NA	NA	100%	QIDS (n = 29)	• Moderate : 34.4% • Severe : 59% • Very severe : 7%
Berhe et al, 2013 [70]	Ethiopia	2011–2012	269	NA	• 35-44yo: 40.5%; • 45-54yo: 19%	48%	• Secondary/ 22.7% • Tertiary: 30.5%	NA	NA	100%	Hamilton Depression Rating Scale (HAM-D)	• Mild 35.69% • Moderate 8.18%
Bongongo et al, 2013 [71]	South Africa	NA	117	NA	• 36*; • 31-39yo: 41.9%	29.9%		NA	NA	100%	Zung self-rating depression scale	• Mild 69.2% • Moderate 1.7% • Severe 0.9%
Negash et al, 2013 [72]	Ethiopia	NA	355	NA	36.4*;	36.6%	NA	NA	WHO 3/4: 16.1% / 3.9%	100%	Interview with section dedicated to depression evaluation	5.4%
Yeji et al, 2014 [73]	South Africa	2007–2008	272	NA	37 (8.6)*,	21.3%	• Primary: 28.3% • Secondary: 38.9%	CD4 ≤200 : 30.9%	NA	100%	12-item General Health Questionnaire (GHQ12)	33 to 38% depending on the method used
Karambé et al, 2010 [74]	Mali	2004–2005	286	NA	36*; Range 18–65	47.59%	No schooling: 56.01%	CD4<200: 89.7%	NA	48.8%	NA	45.8% (most dominant among other psychological disorders)
Ramirez-Avila et al, 2012 [75]	South Africa	2006–2008	1,545	NA	34 (28–41)**	50%	• Some high school: 45.2%; • >high school: 30.5%	CD4<200: 59% (n =1,126)	NA	628 eligible. Among them: 40% started	5-item Mental Health Index (MHI-5)	55%
Wagner et al, 2012 [40]	Uganda	2010–2011	602	NA	NA	NA	NA	NA	NA	49.8%	NA	57%

Abbreviations: ART: Antiretroviral Therapy; CI: Confidence Interval; IQR: InterQuartile Range; NA: Not available; SD: Standard Deviation.

*Mean (SD)

** Median (IQR). NB: Articles are presented in function of ART status of included patients

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Fig 3. Forest plots presenting the prevalence of depressive symptoms according to the tool used and the treatment status. The between-study heterogeneity is reported using I² statistics and its associated p-value. Prev: Prevalence; CI: confidence interval.

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Based on depression screening scales which are infrequently used, the prevalence of depressive symptoms ranged between 45.8% and 57% [40,74,75] in mixed groups of PLHIV whereas in PLHIV on ART, the prevalence varied between 2.6% and 66% [37,67–73].

Associated factors

For MDD, we present the associated factors identified with the MINI only. For the severity of depressive symptoms, we present the associated factors identified with the two most used scales, i.e. CES-D 20 items and PHQ-9 and with the HSCL which presents the less heterogeneity. In each instance, the results are broken down according to the ART status.

Factors associated with MDD. In untreated or mixed groups of PLHIV, while one study reported no link between low CD4 count and depression [78], an association between low CD4 count and MDD was observed [31,32]. MDD was also associated with disability [31], being of younger age [32], being female [79], stigma [32], opportunistic infections [32], unemployment [6] and negative life events [31,79]. No association was reported with cognitive impairment [33], and educational level [32].

In PLHIV on ART, MDD was associated with WHO clinical stage 3 or 4 [29], poor health-related quality of life [28], additional comorbidities such as tuberculosis [29], prior history of MDD or other psychiatric disorders, such as past manic episode [29]. No association was reported with CD4 count, cognitive impairment, age and gender [29].

Factors associated with depressive symptoms. Among ART-naïve PLHIV, more severe depressive symptoms were observed in comparison to PLHIV on ART [45,56,57,66], except in one study using HSCL [63]. An improvement of the severity of depressive symptoms, based on HSCL, has also been observed over seven years of follow-up after initiating ART but only in women [65].

In untreated or mixed groups of PLHIV, even when the screening scale was restricted to somatic items, low CD4 count was the strongest predictor of severe depressive symptoms [47,55]. The severity of depression symptoms was also associated with poorer physical health [46,65], being female [46,47,65] (except in one report [55]) and being less educated [45,47]. The link between age and depression remained unclear [46,47]. Also, because of contradictory results, no consensus could be reached concerning substance abuse [46,55,63]. An association was reported with poor economic status [47], low social support [46] and negative life events [46] whereas no association was observed with an history of prior opportunistic infections [63]. These results were reported in only one publication each time.

In PLHIV on ART, the severity of depressive symptoms seemed unrelated to CD4 level [43,44], except in one [76]; whereas in another publication [52] a negative relationship was observed. Severity of depressive symptoms could be related to age [76] or low level of education [44] whereas no effect of gender was observed [42,53,76]. PLHIV with no more than primary school education seemed to have nearly a 2-fold risk of having more depressive symptoms [44]. Stigma [53], unemployment and lower income [44,76] seemed to be associated with severe depressive symptoms. Unemployed PLHIV could have a 3-fold risk to present severe depressive symptoms according to the same study [44]. No consensus could be reached concerning disease progression [43,76] whereas no association was observed for cognitive impairment [43].

Quality of evidence

Based on GRADEpro, the overall quality of the studies selected for the meta-analysis was low, since all of them were observational (Tables B and C in S2 File). For the studies evaluating MDD or the severity of depressive symptoms, the quality of the studies for the different outcomes had to be downgraded to very low due to high inconsistency in study results, variability in study population (sample size, clinical information on patients) and small number of studies to calculate the pooled prevalence.

Discussion

Since 2010, the number of published studies on depression in African PLHIV has substantially increased, highlighting the increasing concern on this emerging public health issue. Based on pooled prevalence estimates, the prevalence of MDD was 13% in PLHIV on ART and 24% in mixed/untreated groups of PLHIV. The prevalence of depressive symptoms varied between 14% and 32% in PLHIV on ART and between 9% and 31% in mixed/untreated groups of PLHIV according to the scale used. Overall, the pooled prevalence varied substantially according to the measurement scale used and also for a given scale even when the same cut-off or the same number of items was used in all studies. Few information on the procedures used to administer the scales (items' number, cut-off, inclusion of somatic symptoms or not, etc.) were available, explaining at least a part of the variability in the data.

In clinical practice, depression is still usually under-diagnosed in SSA [3,70]. Depression is often considered as a logical outcome in PLHIV and is difficult to diagnose due to its common symptoms with HIV disease such as fatigue, sleeping problems, loss of appetite and cognitive impairment [6,39]. PLHIV report also more easily somatic symptoms than emotional or affective ones [38]. The lack of time available in primary health care settings, the lack of knowledge of the clinicians on mental health and the poor integration of mental health services in SSA contribute to the difficulties to identify patients with depression [80]. The scarcity of resources for mental health in low-income countries constitute barriers to take care adequately of those health issues [81]. A WHO report also highlighted these aspects in details [82]. A recent editorial in AIDS insisted on the need to act and to manage depression based on mhGAP guidelines (WHO 2010) [3]. The lack of validated and culturally-sensitive scales in SSA is also a limitation [3,83]. Most of the current depression screening tools also required extensive staff training and time to be administered.

The impact of ART on MDD or depressive symptoms makes no consensus so far in SSA studies. In a previous meta-analysis analyzing data from seven SSA countries, HIV treatment status had a significant effect on the prevalence of depressive symptoms but not on MDD [14]. Due to the limited amount of data available on ART-naïve or untreated PLHIV, we had to group publications of untreated or mixed groups of PLHIV, which could influence pooled prevalence estimates. Indeed, most of the publications focused on the established ART period.

Concerning other associated factors with MDD, quality of life, additional comorbidities, prior history of MDD might be associated factors in PLHIV on ART [28,29], whereas disability, being a woman, stigma and unemployment could be associated factors in mixed or untreated groups of PLHIV [31,32,79]. Concerning depressive symptoms, poor social conditions seem to be the main factor associated with depressive symptoms in PLHIV on ART [44,76] whereas in untreated or mixed groups of PLHIV, it seems to be immunosuppression and being female [46,47,65]. However, it is important to appreciate that we focused on papers using the most used scales to present the associated factors, leading to a limited number of publications. Consensus was difficult to reach when contradictory results were reported or when, for a given factor, only one study reported an association. Further studies might be conducted to explore this further and depict more precisely the differences according to ART status and changes occurring over time in these chronically ART-treated patients. The identification of other predictors could also allow the identification of at-risk PLHIV who could benefit to specific prevention or early care measures.

The chronic aspect of the disease status could play an important role in PLHIV-related depression as a stressor. Indeed, PLHIV are aware of having a disease under control but not cured with a need to take care of their health status to avoid complications. A recent review on chronic diseases has reported that depression is more common in chronic diseases like heart disease, stroke and cancer than in the general population [84](Clarke et al, 2009). Even if HIV infection was not included in that review, this work highlighted the fact the chronic status is major risk factor to develop depression. Further studies are needed in the PLHIV living in Africa to further depict this issue.

Because of the deleterious consequences of depression on PLHIV [3,7–11] and since depression is a modifiable condition, the new WHO recommendations for ART use highlight the need to screen and manage depression over the continuum of HIV care [85]. Studies on feasibility and effectiveness of culturally-sensitive psychotherapeutic intervention [86] or group-based counseling intervention [87] using a task-shifting approach have been recently conducted in SSA, leading to promising results and encouraging the necessity of identifying as early as possible PLHIV suffering from depression.

Conclusion

The analysis of the available most recent literature confirmed that depression in PLHIV represents an increasing concern in SSA. The prevalence of depression is high even if the variability of the data does not allow to describe precisely the phenomenon and to identify strong predictors. Further studies are clearly needed to: 1) validate the most accurate tools according to the population of origin (language, education) as well as ART status; 2) provide practical guidelines for administration of the tests; and 3) evaluate MDD and/or depressive symptoms in most at-risk populations, including women, men having sex with men and older PLHIV. Depressed PLHIV are at increased risk of developing viral resistance and other poor outcomes because of low level of ART adherence, and more specifically older patients who have even a less efficient immune system. This may become a significant public health hazard, deserving preventive and corrective measures to assure PLHIV better quality of life and outcomes in SSA.

Supporting information

S1 File. Search strategy.
(DOCX)

S2 File. Supplementary tables.
(DOC)

Acknowledgments

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References

1. UNAIDS. World AIDS Day 2015. On the Fast-Track to end AIDS by 2030: Focus on Location and Population. 2015. 2015.

2. Deeks SG, Lewin SR, Havlir DV. The end of AIDS: HIV infection as a chronic disease. Lancet Lond Engl. 2013; 382: 1525–1533. https://doi.org/10.1016/S0140-6736(13)61809-7 PMID: 24152939

3. Abas M, Ali G-C, Nakimuli-Mpungu E, Chibanda D. Depression in people living with HIV in sub-Saharan Africa: time to act. Trop Med Int Health. 2014; 19: 1392–1396. https://doi.org/10.1111/tmi.12382 PMID: 25319189

4. Ciesla JA, Roberts JE. Meta-analysis of the relationship between HIV infection and risk for depressive disorders. Am J Psychiatry. 2001; 158: 725–730. https://doi.org/10.1176/appi.ajp.158.5.725 PMID: 11329393

5. Sherbourne CD, Hays RD, Fleishman JA, Vitiello B, Magruder KM, Bing EG, et al. Impact of psychiatric conditions on health-related quality of life in persons with HIV infection. Am J Psychiatry. 2000; 157: 248–254. https://doi.org/10.1176/appi.ajp.157.2.248 PMID: 10671395

6. Akena DH, Musisi S, Kinyanda E. A comparison of the clinical features of depression in HIV-positive and HIV-negative patients in Uganda. Afr J Psychiatry. 2010; 13: 43–51.

7. Memiah P, Shumba C, Etienne-Mesubi M, Agbor S, Hossain MB, Komba P, et al. The effect of depressive symptoms and CD4 count on adherence to highly active antiretroviral therapy in sub-Saharan Africa. J Int Assoc Provid AIDS Care. 2014; 13: 346–352. https://doi.org/10.1177/2325957413503368 PMID: 24114726

8. Wroe EB, Hedt-Gauthier BL, Franke MF, Nsanzimana S, Turinimana JB, Drobac P. Depression and patterns of self-reported adherence to antiretroviral therapy in Rwanda. Int J STD AIDS. 2015; 26: 257–261. https://doi.org/10.1177/0956462414535206 PMID: 24828554

9. Nel A, Kagee A. The relationship between depression, anxiety and medication adherence among patients receiving antiretroviral treatment in South Africa. AIDS Care. 2013; 25: 948–955. https://doi.org/10.1080/09540121.2012.748867 PMID: 23231527

10. Kingori C, Haile ZT, Ngatia P. Depression symptoms, social support and overall health among HIV-positive individuals in Kenya. Int J STD AIDS. 2015; 26: 165–172. https://doi.org/10.1177/0956462414531933 PMID: 24759561

11. Kinyanda E, Hoskins S, Nakku J, Nawaz S, Patel V. The prevalence and characteristics of suicidality in HIV/AIDS as seen in an African population in Entebbe district, Uganda. BMC Psychiatry. 2012; 12: 63. https://doi.org/10.1186/1471-244X-12-63 PMID: 22713589

12. Nakimuli-Mpungu E, Bass JK, Alexandre P, Mills EJ, Musisi S, Ram M, et al. Depression, Alcohol Use and Adherence to Antiretroviral Therapy in Sub-Saharan Africa: A Systematic Review. AIDS Behav. 2012; 16: 2101–2118. https://doi.org/10.1007/s10461-011-0087-8 PMID: 22116638

13. Mayston R, Kinyanda E, Chishinga N, Prince M, Patel V. Mental disorder and the outcome of HIV/AIDS in low-income and middle-income countries: a systematic review. AIDS Lond Engl. 2012; 26 Suppl 2: S117–135. https://doi.org/10.1097/QAD.0b013e32835bde0f PMID: 23303434

14. Tsai AC. Reliability and Validity of Depression Assessment Among Persons With HIV in Sub-Saharan Africa: Systematic Review and Meta-analysis. JAIDS J Acquir Immune Defic Syndr. 2014; 66: 503–511. https://doi.org/10.1097/QAI.0000000000000210 PMID: 24853307

15. Radloff L. The CES-D scale: a self-report depression scale for research in the general population. 1977; 1: 385–401.

16. Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, et al. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J Clin Psychiatry. 1998; 59 Suppl 20: 22-33-57.

17. Spitzer RL, Kroenke K, Williams JB. Validation and utility of a self-report version of PRIME-MD: the PHQ primary care study. Primary Care Evaluation of Mental Disorders. Patient Health Questionnaire. JAMA. 1999; 282: 1737–1744. PMID: 10568646

18. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med. 2001; 16: 606–613. https://doi.org/10.1046/j.1525-1497.2001.016009606.x PMID: 11556941

19. Derogatis LR, Lipman RS, Rickels K, Uhlenhuth EH, Covi L. The Hopkins Symptom Checklist (HSCL). A measure of primary symptom dimensions. Mod Probl Pharmacopsychiatry. 1974; 7: 79–110. PMID: 4607278

20. Beck A, Steer R, Garbin M. Psychometric properties of the Beck Depression Inventory: Twenty years of evaluation. Clin Psychol Rev. 1996; 8.

21. Akena D, Joska J, Obuku EA, Stein DJ. Sensitivity and specificity of clinician administered screening instruments in detecting depression among HIV-positive individuals in Uganda. AIDS Care. 2013; 25: 1245–1252. https://doi.org/10.1080/09540121.2013.764385 PMID: 23398282

22. Myer L, Smit J, Roux LL, Parker S, Stein DJ, Seedat S. Common Mental Disorders among HIV-Infected Individuals in South Africa: Prevalence, Predictors, and Validation of Brief Psychiatric Rating Scales. AIDS Patient Care STDs. 2008; 22: 147–158. https://doi.org/10.1089/apc.2007.0102 PMID: 18260806

23. Singh D, Sunpath H, John S, Eastham L, Gouden R. The utility of a rapid screening tool for depression and HIV dementia amongst patients with low CD4 counts- a preliminary report. Afr J Psychiatry. 2008; 11: 282–286.

24. Cholera R, Gaynes BN, Pence BW, Bassett J, Qangule N, Macphail C, et al. Validity of the patient health questionnaire-9 to screen for depression in a high-HIV burden primary healthcare clinic in Johannesburg, South Africa. J Affect Disord. 2014; 167: 160–166. https://doi.org/10.1016/j.jad.2014.06.003 PMID: 24972364

25. Bhana A, Rathod SD, Selohilwe O, Kathree T, Petersen I. The validity of the Patient Health Questionnaire for screening depression in chronic care patients in primary health care in South Africa. BMC Psychiatry. 2015; 15: 118. https://doi.org/10.1186/s12888-015-0503-0 PMID: 26001915

26. Pence BW, Gaynes BN, Atashili J, O'Donnell JK, Tayong G, Kats D, et al. Validity of an interviewer-administered patient health questionnaire-9 to screen for depression in HIV-infected patients in Cameroon. J Affect Disord. 2012; 143: 208–213. https://doi.org/10.1016/j.jad.2012.05.056 PMID: 22840467

27. Higgins JPT, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med. 2002; 21: 1539–1558. https://doi.org/10.1002/sim.1186 PMID: 12111919

28. Adewuya AO, Afolabi MO, Ola BA, Ogundele OA, Ajibare AO, Oladipo BF, et al. Relationship between depression and quality of life in persons with HIV infection in Nigeria. Int J Psychiatry Med. 2008; 38: 43–51. https://doi.org/10.2190/PM.38.1.d PMID: 18624016

29. Nakimuli-Mpungu E, Musisi S, Katabira E, Nachega J, Bass J. Prevalence and factors associated with depressive disorders in an HIV+ rural patient population in southern Uganda. J Affect Disord. 2011; 135: 160–167. https://doi.org/10.1016/j.jad.2011.07.009 PMID: 21851986

30. Nakimuli-Mpungu E, Mojtabai R, Alexandre PK, Musisi S, Katabira E, Nachega JB, et al. Lifetime depressive disorders and adherence to anti-retroviral therapy in HIV-infected Ugandan adults: A case-control study. J Affect Disord. 2013; 145: 221–226. https://doi.org/10.1016/j.jad.2012.08.002 PMID: 23017542

31. Olley BO, Seedat S, Stein DJ. Persistence of psychiatric disorders in a cohort of HIV/AIDS patients in South Africa: A 6-month follow-up study. J Psychosom Res. 2006; 61: 479–484. https://doi.org/10.1016/j.jpsychores.2006.03.010 PMID: 17011355

32. Akena D, Musisi S, Joska J, Stein DJ. The Association between Aids Related Stigma and Major Depressive Disorder among HIV-Positive Individuals in Uganda. Cameron DW, editor. PLoS ONE. 2012; 7: e48671. https://doi.org/10.1371/journal.pone.0048671 PMID: 23209556

33. Nakku J, Kinyanda E, Hoskins S. Prevalence and factors associated with probable HIV dementia in an African population: a cross-sectional study of an HIV/AIDS clinic population. BMC Psychiatry. 2013; 13: 126. https://doi.org/10.1186/1471-244X-13-126 PMID: 23641703

34. Besa N., Paul R, Hachaambwa L. Psychiatric symptoms among an HIV positive Urban Population in Lusaka, Zambia. 2015. 42: 84–89.

35. Spies G, Kader K, Kidd M, Smit J, Myer L, Stein DJ, et al. Validity of the K-10 in detecting DSM-IV-defined depression and anxiety disorders among HIV-infected individuals. AIDS Care. 2009; 21: 1163–1168. https://doi.org/10.1080/09540120902729965 PMID: 20024776

36. Olisah VO, Baiyewu O, Sheikh TL. Adherence to highly active antiretroviral therapy in depressed patients with HIV/AIDS attending a Nigerian university teaching hospital clinic. Afr J Psychiatry. 2010; 13: 275–279.

37. Gaynes BN, Pence BW, Atashili J, O'Donnell J, Kats D, Ndumbe PM. Prevalence and Predictors of Major Depression in HIV-Infected Patients on Antiretroviral Therapy in Bamenda, a Semi-Urban Center in Cameroon. Chêne G, editor. PLoS ONE. 2012; 7: e41699. https://doi.org/10.1371/journal.pone.0041699 PMID: 22860006

38. Ngo VK, Wagner GJ, Huynh A, Ryan G, Musisi S. A Qualitative Analysis of the Effects of Depression and Antidepressants on Physical and Work Functioning among Antiretroviral Therapy Clients in Uganda. J Int Assoc Provid AIDS Care JIAPAC. 2013; 12: 414–422. https://doi.org/10.1177/2325957412471992 PMID: 23442495

39. Lawler K, Mosepele M, Seloilwe E, Ratcliffe S, Steele K, Nthobatsang R, et al. Depression Among HIV-Positive Individuals in Botswana: A Behavioral Surveillance. AIDS Behav. 2011; 15: 204–208. https://doi.org/10.1007/s10461-009-9622-2 PMID: 19821023

40. Wagner GJ, Ghosh-Dastidar B, Garnett J, Kityo C, Mugyenyi P. Impact of HIV Antiretroviral Therapy on Depression and Mental Health Among Clients With HIV in Uganda: Psychosom Med. 2012; 74: 883–890. https://doi.org/10.1097/PSY.0b013e31826629db PMID: 22923701

41. Nyirenda M, Chatterji S, Rochat T, Mutevedzi P, Newell M- L. Prevalence and correlates of depression among HIV-infected and -affected older people in rural South Africa. J Affect Disord. 2013; 151: 31–38. https://doi.org/10.1016/j.jad.2013.05.005 PMID: 23726780

42. Poupard M, Ngom Gueye NF, Thiam D, Ndiaye B, Girard PM, Delaporte E, et al. Quality of life and depression among HIV-infected patients receiving efavirenz- or protease inhibitor-based therapy in Senegal. HIV Med. 2007; 8: 92–95. https://doi.org/10.1111/j.1468-1293.2007.00435.x PMID: 17352765

43. Nakasujja N, Skolasky RL, Musisi S, Allebeck P, Robertson K, Ronald A, et al. Depression symptoms and cognitive function among individuals with advanced HIV infection initiating HAART in Uganda. BMC Psychiatry. 2010; 10: 44. https://doi.org/10.1186/1471-244X-10-44 PMID: 20537129

44. Kitshoff C, Campbell L, Naidoo S. The association between depression and adherence to antiretroviral therapy in HIV-positive patients, KwaZulu-Natal, South Africa. Afr Fam Pr. 2012; 54: 145–150.

45. Farley J, Miller E, Zamani A, Tepper V, Morris C, Oyegunle M, et al. Screening for Hazardous Alcohol Use and Depressive Symptomatology Among HIV-Infected Patients in Nigeria: Prevalence, Predictors, and Association With Adherence. J Int Assoc Physicians AIDS Care JIAPAC. 2010; 9: 218–226. https://doi.org/10.1177/1545109710371133 PMID: 20798401

46. Seth P, Kidder D, Pals S, Parent J, Mbatia R, Chesang K, et al. Psychosocial Functioning and Depressive Symptoms Among HIV-Positive Persons Receiving Care and Treatment in Kenya, Namibia, and Tanzania. Prev Sci. 2014; 15: 318–328. https://doi.org/10.1007/s11121-013-0420-8 PMID: 23868419

47. Kaharuza FM, Bunnell R, Moss S, Purcell DW, Bikaako-Kajura W, Wamai N, et al. Depression and CD4 Cell Count Among Persons with HIV Infection in Uganda. AIDS Behav. 2006; 10: 105–111. https://doi.org/10.1007/s10461-006-9142-2

48. Simbayi LC, Kalichman S, Strebel A, Cloete A, Henda N, Mqeketo A. Internalized stigma, discrimination, and depression among men and women living with HIV/AIDS in Cape Town, South Africa. Soc Sci Med. 2007; 64: 1823–1831. https://doi.org/10.1016/j.socscimed.2007.01.006 PMID: 17337318

49. Alemu H, Haile Mariam D, Tsui A, Ahmed S, Shewamare A. Effect of depressive symptoms and social support on weight and CD4 count increase at HIV clinic in Ethiopia. AIDS Care. 2012; 24: 866–876. https://doi.org/10.1080/09540121.2011.648160 PMID: 22273149

50. Klis S, Velding K, Gidron Y, Peterson K. Posttraumatic stress and depressive symptoms among people living with HIV in the Gambia. AIDS Care. 2011; 23: 426–434. https://doi.org/10.1080/09540121.2010.507756 PMID: 21271395

51. Wagner GJ, Holloway I, Ghosh-Dastidar B, Kityo C, Mugyenyi P. Understanding the influence of depression on self-efficacy, work status and condom use among HIV clients in Uganda. J Psychosom Res. 2011; 70: 440–448. https://doi.org/10.1016/j.jpsychores.2010.10.003 PMID: 21511074

52. Belenky NM, Cole SR, Pence BW, Itemba D, Maro V, Whetten K. Depressive Symptoms, HIV Medication Adherence, and HIV Clinical Outcomes in Tanzania: A Prospective, Observational Study. Apetrei C, editor. PLoS ONE. 2014; 9: e95469. https://doi.org/10.1371/journal.pone.0095469 PMID: 24798428

53. Endeshaw M, Walson J, Rawlins S, Dessie A, Alemu S, Andrews N, et al. Stigma in Ethiopia: association with depressive symptoms in people with HIV. AIDS Care. 2014; 26: 935–939. https://doi.org/10.1080/09540121.2013.869537 PMID: 24382290

54. Musisi S, Wagner GJ, Ghosh-Dastidar B, Nakasujja N, Dickens A, Okello E. Depression and sexual risk behaviour among clients about to start HIV antiretroviral therapy in Uganda. Int J STD AIDS. 2014; 25: 130–137. https://doi.org/10.1177/0956462413495186 PMID: 23970636

55. L'akoa RM, Noubiap JJN, Fang Y, Ntone FE, Kuaban C. Prevalence and correlates of depressive symptoms in HIV-positive patients: a cross-sectional study among newly diagnosed patients in Yaoundé, Cameroon. BMC Psychiatry. 2013; 13: 228. https://doi.org/10.1186/1471-244X-13-228 PMID: 24053612

56. Wagner GJ, Ghosh-Dastidar B, Slaughter ME, Akena D, Nakasujja N, Musisi S. Changes in Condom Use During the First Year of HIV Treatment in Uganda and the Relationship to Depression. Ann Behav Med. 2014; 48: 175–183. https://doi.org/10.1007/s12160-013-9586-3 PMID: 24504978

57. Wagner GJ, Ghosh-Dastidar B, Slaughter M, Akena D, Nakasujja N, Okello E, et al. The Role of Depression in Work-Related Outcomes of HIV Treatment in Uganda. Int J Behav Med. 2014; 21: 946–955. https://doi.org/10.1007/s12529-013-9379-x PMID: 24402775

58. Amberbir A, Woldemichael K, Getachew S, Girma B, Deribe K. Predictors of adherence to antiretroviral therapy among HIV-infected persons: a prospective study in Southwest Ethiopia. BMC Public Health. 2008; 8: 265. https://doi.org/10.1186/1471-2458-8-265 PMID: 18667066

59. Kagee A, Nel A, Saal W. Factor structure of the Beck Depression Inventory-II among South Africans receiving antiretroviral therapy. AIDS Care. 2014; 26: 257–262. https://doi.org/10.1080/09540121.2013.802278 PMID: 23750786

60. Kagee A, Martin L. Symptoms of depression and anxiety among a sample of South African patients living with HIV. AIDS Care. 2010; 22: 159–165. https://doi.org/10.1080/09540120903111445 PMID: 20390494

61. Tsai AC, Bangsberg DR, Frongillo EA, Hunt PW, Muzoora C, Martin JN, et al. Food insecurity, depression and the modifying role of social support among people living with HIV/AIDS in rural Uganda. Soc Sci Med. 2012; 74: 2012–2019. https://doi.org/10.1016/j.socscimed.2012.02.033 PMID: 22513248

62. Psaros C, Haberer JE, Boum Y, Tsai AC, Martin JN, Hunt PW, et al. The factor structure and presentation of depression among HIV-positive adults in Uganda. AIDS Behav. 2015; 19: 27–33. https://doi.org/10.1007/s10461-014-0796-x PMID: 24854877

63. Martinez P, Andia I, Emenyonu N, Hahn JA, Hauff E, Pepper L, et al. Alcohol Use, Depressive Symptoms and the Receipt of Antiretroviral Therapy in Southwest Uganda. AIDS Behav. 2008; 12: 605–612. https://doi.org/10.1007/s10461-007-9312-x PMID: 17968651

64. Hatcher AM, Tsai AC, Kumbakumba E, Dworkin SL, Hunt PW, Martin JN, et al. Sexual Relationship Power and Depression among HIV-Infected Women in Rural Uganda. Braitstein P, editor. PLoS ONE. 2012; 7: e49821. https://doi.org/10.1371/journal.pone.0049821 PMID: 23300519

65. Chan BT, Weiser SD, Boum Y, Haberer JE, Kembabazi A, Hunt PW, et al. Declining Prevalence of Probable Depression Among Patients Presenting for Antiretroviral Therapy in Rural Uganda: The Role of Early Treatment Initiation. AIDS Behav. 2015; 19: 19–26. https://doi.org/10.1007/s10461-014-0785-0 PMID: 24788780

66. Martin F, Russell S, Seeley J. Higher Quality of Life and Lower Depression for People on ART in Uganda as Compared to a Community Control Group. Haberer JE, editor. PLoS ONE. 2014; 9: e105154. https://doi.org/10.1371/journal.pone.0105154 PMID: 25171340

67. Pappin M, Wouters E, Booysen FLR. Anxiety and depression amongst patients enrolled in a public sector antiretroviral treatment programme in South Africa: a cross-sectional study. BMC Public Health. 2012; 12: 244. https://doi.org/10.1186/1471-2458-12-244 PMID: 22452846

68. Wouters E, Booysen F le R, Ponnet K, Baron Van Loon F. Wording Effects and the Factor Structure of the Hospital Anxiety & Depression Scale in HIV/AIDS Patients on Antiretroviral Treatment in South Africa. Graham SM, editor. PLoS ONE. 2012; 7: e34881. https://doi.org/10.1371/journal.pone.0034881 PMID: 22536338

69. Do NT, Phiri K, Bussmann H, Gaolathe T, Marlink RG, Wester CW. Psychosocial factors affecting medication adherence among HIV-1 infected adults receiving combination antiretroviral therapy (cART) in Botswana. AIDS Res Hum Retroviruses. 2010; 26: 685–691. https://doi.org/10.1089/aid.2009.0222 PMID: 20518649

70. Berhe H, Bayray A. A: Prevalence of Depression and associated factors among people living with HIV/AIDS in Tigray, North Ethiopia: a Cross Sectional Hospital based study. Int J Pharm Sci Res. 2013; 4: 765–775.

71. Bongongo T, Tumbo J, Govender I. Depressive features among adult patients receiving antiretroviral therapy for HIV in Rustenburg district, SA. South Afr J Psychiatry. 2013; 19: 31. https://doi.org/10.7196/sajp.418

72. Negash T, Ehlers V. Personal factors influencing patients' adherence to ART in Addis Ababa, Ethiopia. J Assoc Nurses AIDS Care JANAC. 2013; 24: 530–538. https://doi.org/10.1016/j.jana.2012.11.004 PMID: 23465401

73. Yeji F, Klipstein-Grobusch K, Newell M-L, Hirschhorn LR, Hosegood V, Bärnighausen T. Are social support and HIV coping strategies associated with lower depression in adults on antiretroviral treatment? Evidence from rural KwaZulu-Natal, South Africa. AIDS Care. 2014; 26: 1482–1489. https://doi.org/10.1080/09540121.2014.931561 PMID: 24991994

74. Karambé M, Zoungrana J, Dembele JP, Fofana AS, Oumar AA, Sissoko M, et al. [The psychiatric manifestations of people living with HIV in Mali]. Mali Méd. 2010; 25: 32–35.

75. Ramirez-Avila L, Regan S, Giddy J, Chetty S, Ross D, Katz JN, et al. Depressive Symptoms and Their Impact on Health-seeking Behaviors in Newly-diagnosed HIV-infected Patients in Durban, South Africa. AIDS Behav. 2012; 16: 2226–2235. https://doi.org/10.1007/s10461-012-0160-y PMID: 22451351

76. Asangbeh SL, Sobngwi JL, Ekali GL, Eyoum C, Msellati P. Predictors of depression among patients on art in a rural health district in North West Cameroon. AIDS Care. 2016; 28: 205–208. https://doi.org/10.1080/09540121.2015.1074654 PMID: 26288104

77. Akolo C, Royal W, Cherner M, Okwuasaba K, Eyzaguirre L, Adebiyi R, et al. Neurocognitive impairment associated with predominantly early stage HIV infection in Abuja, Nigeria. J Neurovirol. 2014; 20: 380–387. https://doi.org/10.1007/s13365-014-0254-6 PMID: 24927825

78. Kinyanda E, Hoskins S, Nakku J, Nawaz S, Patel V. Prevalence and risk factors of major depressive disorder in HIV/AIDS as seen in semi-urban Entebbe district, Uganda. BMC Psychiatry. 2011; 11: 205. https://doi.org/10.1186/1471-244X-11-205 PMID: 22208452

79. Olley BO, Seedat S, Nei DG, Stein DJ. Predictors of major depression in recently diagnosed patients with HIV/AIDS in South Africa. AIDS Patient Care STDs. 2004; 18: 481–487. https://doi.org/10.1089/1087291041703700 PMID: 15321019

80. Akena D, Stein DJ, Joska J. Does Screening HIV-Positive Individuals in Uganda for Major Depressive Disorder Improve Case Detection Rates and Antidepressant Prescription? AIDS Behav. 2013; 17: 2802–2807. https://doi.org/10.1007/s10461-012-0383-y PMID: 23247361

81. Saxena S, Thornicroft G, Knapp M, Whiteford H. Resources for mental health: scarcity, inequity, and inefficiency. Lancet Lond Engl. 2007; 370: 878–889. https://doi.org/10.1016/S0140-6736(07)61239-2

82. WHO. mhGAP Mental Health Gap Action Programme: Scaling up Care for Mental, Neurological and Substance use Disorders. World Health Organisation, Geneva. 2010.

83. Brandt R. The mental health of people living with HIV/AIDS in Africa: a systematic review. Afr J AIDS Res AJAR. 2009; 8: 123–133. https://doi.org/10.2989/AJAR.2009.8.2.1.853 PMID: 25875564

84. Clarke DM, Currie KC. Depression, anxiety and their relationship with chronic diseases: a review of the epidemiology, risk and treatment evidence. Med J Aust. 2009; 190: S54–60. PMID: 19351294

85. Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection: Recommendations for a Public Health Approach. 2nd edition. Geneva: World Health Organization; 2016. 5, CLINICAL GUIDELINES: MANAGING COMMON COINFECTIONS AND COMORBIDITIES. Available from: http://www.ncbi.nlm.nih.gov/books/NBK374304/. 2016.

86. Nakimuli-Mpungu E, Wamala K, Okello J, Alderman S, Odokonyero R, Mojtabai R, et al. Group support psychotherapy for depression treatment in people with HIV/AIDS in northern Uganda: a single-centre randomised controlled trial. Lancet HIV. 2015; 2: e190–199. https://doi.org/10.1016/S2352-3018(15)00041-7 PMID: 26423001

87. Petersen I, Hanass Hancock J, Bhana A, Govender K. A group-based counselling intervention for depression comorbid with HIV/AIDS using a task shifting approach in South Africa: a randomized controlled pilot study. J Affect Disord. 2014; 158: 78–84. https://doi.org/10.1016/j.jad.2014.02.013 PMID: 24655769