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Complete List of Authors:	Endomba Angong, Francky Teddy; University of Yaoundé I, Department of Internal Medicine, Faculty of Medicine and Biomedical Sciences; University of Bourgogne, Psychiatry Internship Program Mazou, Temgoua Ngou ; University of Yaounde I, Department of Internal Medicine, Faculty of Medicine and Biomedical Sciences Bigna, Jean Joel; Centre Pasteur of Cameroon, Department of Epidemiology and Public Health
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Epidemiology of depressive disorders in people living with hypertension in Africa: a systematic review and meta-analysis

Francky Teddy **Endomba**,[1, 2] Mazou N. **Temgoua**,[1] Jean Joel **Bigna**[3*]

1. Department of Internal Medicine, Faculty of Medicine and Biomedical Sciences, University of Yaoundé I, Yaoundé, Cameroon
2. Psychiatry Internship Program, University of Bourgogne, 21000 Dijon, France.
3. Department of Epidemiology and Public Health, Centre Pasteur of Cameroon, Yaoundé, Cameroon

E-mail addresses: FTE (franckyteddyea@gmail.com); MNT (neurotemgoua@yahoo.fr); JJB (bignarimjj@yahoo.fr)

*Corresponding author

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Abstract

Objectives: Better knowledge of epidemiology of depressive disorders in people living with hypertension can help to implement pertinent strategies to address its burden. The objective was to estimate the prevalence of depressive disorders and symptoms in people living with hypertension in Africa.

Design: Systematic review and meta-analysis.

Population: People living with hypertension in Africa.

Data sources and synthesis: PubMed, EMBASE, African Index Medicus, Africa Journal Online were searched up to January 31st, 2020; regardless of language of publication. Two independent investigators selected studies, extracted data, and assessed the methodological quality of included studies. Multivariate random-effects meta-analysis served to pool data taking in account the variability between diagnostic tools for identifying patients with depressive disorders or symptoms.

Results: We included 11 studies with 5,299 participants with hypertension. The mean age varied between 50.3 and 59.6 years. The proportion of males varied between 28% and 54%. Data were collected between 2002 and 2017.Four studies were conducted in South Africa, three studies in Nigeria, one in Ghana, one in both Ghana and Nigeria, one in Ethiopia, and one in Burkina-Faso. The adjusted prevalence of depressive disorders taking in account the variance between diagnostic tools was 17.9% (95% confidence interval [CI]: 13.0-23.4). The prevalence of depressive symptoms and major depressive symptoms was 33.3% (95%CI: 9.9-61.6) and 7.8% (95%CI: 3.0-14.5). There was heterogeneity attributable to the diagnostic tools for depressive disorders and symptoms. There was no publication bias.

Limitation: All regions of Africa were not represented weakening the generalizability of findings to the entire region.

Conclusion: Depressive disorders and symptoms are prevalent in people living with hypertension in Africa, indicating that strategies from clinicians, researchers, and public health makers are needed to reduce its burden in the region.

Keywords

Depression; Depressive symptoms; Depressive disorders; Hypertension; Africa

Strengths and Limitations of this study

- Not all sub-regions of Africa were represented in this review
- This is the first review performed among people living with hypertension Africa to investigate the epidemiology of depressive disorders and symptoms.
- We found a huge heterogeneity between studies explained by the difference between diagnostic tools for depressive disorders.
- We were not able to explore all sources of heterogeneity due to scarcity of epidemiological data.

Introduction

Cardiovascular diseases (CVDs) are the leading killers worldwide with approximately 18 million deaths per year,[1] and hypertension is involved in approximately 50% of CVDs.[2–4] According to the World Health Organization (WHO), the number of people living with hypertension worldwide is estimated at 1.13 billion, and the African region has the highest prevalence of hypertensive patients (27%).[4] Hypertension deleterious effects are linked to direct human consequences with increased morbidity and mortality but also harmful economic outcomes pertaining to its management and its invalidating complications.[5–7] Detrimental human outcomes related to chronic high blood pressure encompass target organ damage involving cerebrovascular, heart, and kidney diseases;[4,5] but also mental health repercussions notably anxiety, stress and depression.[8–10]

Depressive disorder is recognized to be the most common mental health illness and the second cause of disability worldwide,[11,12] after cardiovascular diseases. It accounts for 3% of global disability adjusted life years (DALYs).[12] According to the WHO, depressive disorder affects more than 300 million people (4.4% of the world population), and its prevalence in the African region is estimated at 9% (29.9 million of cases).[13] Some subpopulations have been identified as depression risk groups, including patients with chronic cardiometabolic conditions such as hypertension.[9,14] A wide range of previously published works have interested on the interaction between hypertension and depression.[8,10,15,16] Comprehensively, the majority of these studies concluded to the fact that hypertensive disease and depressive disorder share bidirectional interplay with patients with hypertension more likely to develop depression and inversely.[8,17] As examples of evidence, a meta-analysis of 41 studies (including 31 studies from China and three from Africa) which included 30,796 patients with hypertension found that 26.8% have depression,[10] and another one which included 22,367 participants found that depression significantly increase the risk of hypertension incidence

with an adjusted relative risk of 1.42.[15] Additionally, it has been reported that hypertensive patients with comorbid depression are more exposed to poor medication adherence with uncontrolled blood pressure as well as chronic vascular complications and cardiovascular disease related mortality.[8,10,15,16,18] The burden of the depression-hypertension co-occurrence is worsened by the fact that approximately one hypertensive patients on ten have untreated depression.[10,19]

Considering up-to-date scientific literature, depression is frequent and harmful in hypertensive patients in occidental settings,[10,20]hypertension and depression are commonly encountered amongst African populations,[2,4,13] but data summarizing and focusing on the burden of depression among hypertensive Africans are not yet available. Hence, we conducted this systematic review and meta-analysis with the aim to determine the prevalence of depressive disorders/symptoms in people living with hypertension in Africa.

Methods

Design

This systematic review and meta-analysis was conducted according to the Joanna Briggs Institute guidelines.[21] This study was reported according to the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines.[22] The protocol of this review was registered in PROSPERO.

Eligibility criteria

Condition

We considered studies reporting the prevalence (or enough data to compute this estimate) of depressive disorders and symptoms.

Context

We considered studies conducted in people living in Africa. Studies conducted in Africans living outside Africa were not considered.

Population

We considered studies conducted in people with diagnosed hypertension.

Study design

Cross-sectional, case-control, and cohort studies.

Data sources

We searched PubMed, Excerpta Medica Database (EMBASE), Africa Index Medicus, and Africa Journal Online to identify all relevant records published up to January 31st, 2020; with any language restriction. The search strategy in EMBASE is available in the Appendix (Supplementary Table 1). To supplement the bibliographic database searches and identify potential additional data sources, we scrutinized the reference list of all relevant original and review papers.

Study selection

Titles and abstracts of articles retrieved from literature search were independently screened by two investigators (FTE and JJB), and the full-texts of those potentially eligible were obtained and further assessed for final inclusion. Disagreements were resolved through consensus.

Data collection and management

A preconceived and standardized data extraction form was used to collect information on first author's name, study country, year of publication, period of participants' recruitment, study design, setting, sampling method, timing of data collection, response rate, mean or median age of the population, age range, proportion of males, number of participants with hypertension, the number of participants with depressive disorders. In case of multinational studies, data were separated to show the estimate within individual countries. Two

investigators (FTE and JJB) independently extracted the data from individual studies, with disagreements being resolved through consensus.

Two investigators (FTE and JJB) independently assessed study methodological quality of included studies with tool developed by Joanna Briggs Institute,[21] with disagreements being resolved through discussion and consensus.

Data synthesis and analysis

Meta-analyses were performed with the *meta, metafor, and dmetar* packages of the statistical software *R* (version 3.6.2). Prevalence estimates were reported with 95% confidence interval (95%CI). Prevalence pooling was done with Freeman-Tukey double arcsine transformation using random-effects meta-analysis model.[23] We adjusted the prevalence in a multivariate meta-analysis to take in account the variance between tools used to identify patients with depressive disorders/symptoms. Egger's test served for detecting the presence of publication bias.[24] A p-value < 0.10 on Egger test was considered indicative of statistically significant publication bias. Heterogeneity was evaluated by the χ^2 test on Cochran's Q statistic,[25] which was quantified byI^2 values. The I^2 statistic estimates the percentage of total variation across studies due to true between-study differences rather than chance. In general, I^2 values greater than 60-70% indicate the presence of substantial heterogeneity.[26]Inter-rater agreements between investigators for study inclusion and methodological quality assessment were assessed using Kappa Cohen's coefficient.[27]

Patient and public involvement

Patients or the public were not involved in the design, conduct, reporting, or dissemination of our research.

Results

The review process and study characteristics

We initially identified 890 records and finally retained 11 full texts (13 prevalence data) in the meta-analysis (Supplementary Figure 1).[28–38] Agreement between investigators on selection based on title and abstract was κ = 0.88 and κ = 1.0 for final inclusion.

Of the 11 included studies, eight studies used probabilistic sampling while three used non-probabilistic sampling. All studies prospectively collected and analysed data and used the same method to identify patients with depressive disorders. Sample size was adequate in nine studies and response rate in two studies (Supplementary Table 2).

The characteristics of included studies are presented in the Table 1. All studies were cross-sectional (Table 1). Patient Health Questionnaire-9 was the most used tool, n = 4. The mean age varied between 50.3 and 59.6 years. The proportion of males varied between 28% and 54%. Data on depressive disorders/symptoms were collected between 2002 and 2017.Four studies were conducted in South Africa, three studies in Nigeria, one study in Ghana, one study in both Ghana and Nigeria, one study in Ethiopia, and one study in Burkina-Faso. None of the study was conducted in Central Africa and North Africa.

Prevalence of depressive disorders/symptoms in people with hypertension in Africa

In total, 5,299 participants with hypertension were included. There was substantial heterogeneity for all analyses, all $I^2 > 75\%$ (Figure 1). The prevalence of depressive disorders was 18.6% (95%CI: 13.8-23.9; 5 studies) (Figure 1). The adjusted prevalence taking in account the variance between diagnostic tools was 17.9% (95%CI: 13.0-23.4) with 52.7% of variance due to difference between tools. There was no publication bias (p = 0.789). There was no data on major depressive disorders.

The prevalence of depressive symptoms was 37.3% (95%CI: 19.3-57.3; 6 studies). The adjusted prevalence taking in account the variance between diagnostic tools was 33.3% (95%CI: 9.9-61.6) with 74.1% of variance due to difference between tools. There was no publication bias (p = 0.115).

The prevalence of major depressive symptoms was 7.9% (95%CI: 1.7-17.9; 2 studies). The adjusted prevalence taking in account the variance between diagnostic tools was 7.8% (95%CI: 3.0-14.5) with 43.3% of variance due to difference between tools. The p value on Egger test was 0.789.

Discussion

This meta-analysis of data from 5,299 people with hypertension living in five countries in Africa revealed that depressive disorders and symptoms are prevalent in this population with substantial heterogeneity according to the diagnostic tools. The present systematic review suggests that approximately one on five and one-third of patients with hypertension have respectively depression and depressive symptoms.

Globally, there are dissimilarities between our findings and the one of previous studies on depression among hypertensive patients. For instance, compared to our findings, a meta-analysis on the prevalence of depression in patients with hypertension and which included 41 studies (most of them from China) found higher rates of depression with a summarized prevalence of 26.9% (95%CI: 21.7% - 32.3%).[10] The same meta-analysis found that 28.5% (95% CI: 22.2% - 35.3%) of Chinese patients with hypertension had depression.[10] Our review revealed more cases of depression among patients with hypertension compared to occidental studies. For example, considering data of United States Multi-Disciplinary Group Practice Observational Study which included 4,362 adult patients with hypertension (13% of anxiety and/or depression), our study's prevalence of depressive disorder is higher.[39] Also, a cross-sectional study done in Spain among 5,954 hypertensive patients with high cardiovascular risk profile found that 15.6% had depression, of which 61.4% were untreated.[19] This variability in results can be explained by the changeability pertaining to the criteria and/or diagnostic tools used to screen depressive disorder across studies' populations.[40,41] Noteworthy, Li and

colleagues who studied depressive disorder among hypertension in a meta-analysis of 41 studies suggested that self-assessed screening tools of depression or depressive symptoms might overestimate the prevalence of depression.[10] Indeed they found a 30% depression prevalence using self-administrated diagnostic scales versus a 21% prevalence using clinical-interviewed tools.[10] This could be link to patients' confusion about depression and hypertension symptoms such as poor appetite, fatigue and sleep disturbances.[10]In our review the most used diagnostic tool was the PHQ-9 and another fact to highpoint is that differences in prevalence can also be explained by the cut-off-point used for a same tool to define a positive screening for depression.[29,42,43] Mahmood and colleagues while assessing depression among 411 hypertensive outpatients in a Pakistan hospital by using PHQ-9 with a score of 10 or above as cut-off point found a prevalence of 40.1%,[44] more than two folds ours. In our study we had a substantial heterogeneity for all analyses which can also be related to the variance between diagnostic tools used for depression assessment. The previously cited meta-analysis of Li and colleagues also showed evidence of high-level heterogeneity.[10]

This meta-analysis highlights the fact that depressive disorder is frequently encountered among hypertensive patients. This review might substantiate the relevancy to conduct further studies with the aim to investigate on the better diagnosis tool for depression among hypertensive patients in order to reduce heterogeneity of results. Moreover, our review could justify carrying out epidemiological studies on the depression-hypertension comorbidity in other African regions in order to have more representative regional picture of the evidence. All this might help to establish adapted policies pertaining to the management of hypertensive patients with depression, notably for a tailored pharmacological treatment.[18,45,46] Nevertheless, our analysis could already draw clinician's awareness on the necessity to assess depression symptoms among hypertensive patients, especially since previously published works found that comorbid depression contribute to more deleterious cardiovascular outcomes.[8,10,15,16,18]

This study should however be interpreted considering some limitations. First and most common to meta-analyses of prevalence studies,[47] we found a huge heterogeneity between studies for which we undertook adjusted analysis to take account the variance due to diagnostic tools. However, some characteristics that may further explain heterogeneity were not reported or there was no enough study to conduct such analysis including sex, sub-regions, and age groups. Second, the various geographic regions and countries were variably represented and some countries were represented. This may weaken the generalizability of our findings and call for more epidemiological studies in this region.

Despite these limitations, this first systematic review and meta-analysis on depressive disorders/symptoms in people living with hypertension in Africa provided a clear summary of the existing knowledge. A protocol had been registered before, and we used rigorous methodological and statistical procedures to obtain and pool data. Furthermore, we have taken in account the variability due to diagnostic tools. There was no publication bias.

Conclusions

Overall, our review found that depression is prevalent among patients with hypertension. This may have significant implications for routine clinical practice while treating and following hypertensive patients. However, since our analysis has limitations pertaining to diagnostic tools consistency within studies and also to the unrepresentative geographic distribution, further studies would be relevant in order to reinforce our findings. All this could be a support for a personalized management of patients with hypertension and depression.

Author Contributors

Conception: JJB, FTE. Designing of the protocol: FTE, JJB. Literature search: JJB. Studies selection: FTE, JJB. Data extraction: FTE, JJB. Data management: JJB. Data synthesis and

analysis: JJB. Writing of the first draft: JJB, FTE. Critical revision: FTE, MNT, JJB. Approved the final version: FTE, MNT, JJB. Guarantor of the review: JJB.

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Competing interests

We declare no competing interests.

Patient consent

Not applicable.

Data sharing statement

All data generated for this study are in the manuscript and its supporting files.

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Figures legend

Figure 1. Crude prevalence of depressive disorders/symptoms in people living with hypertension in Africa

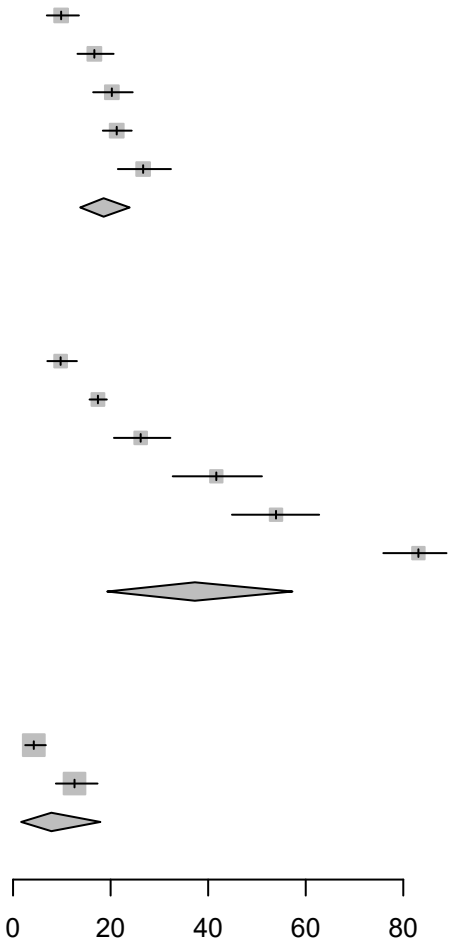
413 **Table 1. Characteristics of included studies**

Author	Year	Setting	Diagnosis of conditions	Inclusion criteria	Population	Period of inclusion	Country	Sample
Ademola	2019	Hospital	Patient Health Questionnaire 9 (PHQ-9)	Age ≥ 18 y, diagnosis of hypertension, treatment with an antihypertensive medication for at least 12 months	%Males: 41.7; Mean age: 57	2013	Ghana, Nigeria	357
Bhana	2015	Population	Depression module of the Structured Clinical Interview for DSM-IV (SCID)	Age ≥ 18 y, clinic attendance for routine chronic disease services (e.g., HIV, hypertension, diabetes) and ability to comprehend and complete study components in Tswana or English.	NR	2014	South Africa	345
Geldsetzer	2019	Population	Center for Epidemiological Studies—Depression (CES-D) screening tool	Age ≥ 40 y and continuously living in the area during the 12 months prior to study enrollment	%Males: 37.4	2014-2015	South Africa	1822
Grimsrud	2009	Population	Composite International Diagnostic Interview Version 3.0 (CIDI-3.0)	South Africans ≥ 18 years who lived in households and hostels during the field period of the study	%Males: 28; Mean age: 50.3	2002-2004	South Africa	767
Hamer	2012	Population	Patient Health Questionnaire 9 (PHQ-9)	Age: 25-60 y with hypertension	NR	2008-2009	South Africa	254
Igwe	2013	Hospital	Mini International Neuro-psychiatric Interview (MINI)	Age: 18 - 64 years. Hypertension for at least 1 year and stable without need for hospital admission for 3 months prior to assessment	%Males: 53.7; Mean year: 50.4	2010-2011	Nigeria	270
Iloh	2018	Hospital	Patient Health Questionnaire 9 (PHQ-9)	Age ≥18 years with hypertension	%Males: 40.7	2017	Nigeria	142
Kretchy	2014	Hospital	Depression Anxiety Stress Scale (DASS) – 21	Age ≥ 18 y, a diagnosis of hypertension, reporting prescription of at least one antihypertensive medication for a minimum of two months	%Males: 37.25	2012	Ghana	400
Okunrinboye	2019	Hospital	Mini International Neuro-psychiatric Interview (MINI)	Age: 18 and 64 y who were diagnosed by a consultant physician at the Centre as suffering from hypertension and have been on anti-hypertensive medication for at least 6 months, spoke Yoruba or English language fluently	%Males: 38; Mean age: 59.6	2012	Nigeria	400
Umer	2019	Hospital	Patient Health Questionnaire 9 (PHQ-9)	Age ≥ 18 y, follow-up for hypertension	%Males: 52.8	2014	Ethiopia	128

Yaméogo	2015	Hospital	Hospital Anxiety and Depression Scale (HADS)	Hypertensive consenting adult outpatients	%Males: 40.1; Mean age: 54.6	2010-2011	Burkina-Faso	414

414 NR: not reported.

Author, Year	Cases	Total	Prevalence, %	[95% C.I.]	Weight
A. Depressive disorders					
Bhana, 2015	34	345	9.9	[6.9; 13.5]	19.9%
Yaméogo, 2015	69	414	16.7	[13.2; 20.6]	20.0%
Okunrinboye, 2019	81	400	20.2	[16.4; 24.5]	20.0%
Grimsrud, 2009	163	767	21.3	[18.4; 24.3]	20.2%
Igwe, 2013	72	270	26.7	[21.5; 32.4]	19.8%
Subgroup prevalence		**2196**	**18.6**	**[13.8; 23.9]**	**100.0%**
Heterogeneity: I^2 = 89.2%, p < 0.0001					
B. Depressive symptoms					
Kretchy, 2014	39	400	9.8	[7.0; 13.1]	17.0%
Geldsetzer, 2019	317	1822	17.4	[15.7; 19.2]	17.3%
Ademola, 2019	62	237	26.2	[20.7; 32.2]	16.8%
Ademola, 2019	50	120	41.7	[32.7; 51.0]	16.2%
Umer, 2019	69	128	53.9	[44.9; 62.8]	16.3%
Iloh, 2018	118	142	83.1	[75.9; 88.9]	16.4%
Subgroup prevalence		**2849**	**37.3**	**[19.3; 57.3]**	**100.0%**
Heterogeneity: I^2 = 98.7%, p < 0.0001					
C. Major depressive symptoms					
Kretchy, 2014	17	400	4.2	[2.5; 6.7]	50.3%
Hamer, 2012	32	254	12.6	[8.8; 17.3]	49.7%
Subgroup prevalence		**654**	**7.9**	**[1.7; 17.9]**	**100.0%**
Heterogeneity: I^2 = 93.3%, p = 0.0001					



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

Francky Teddy **Endomba**, Mazou N. **Temgoua**, Jean Joel **Bigna**

APPENDIX

Supplementary Table 1. Search strategy

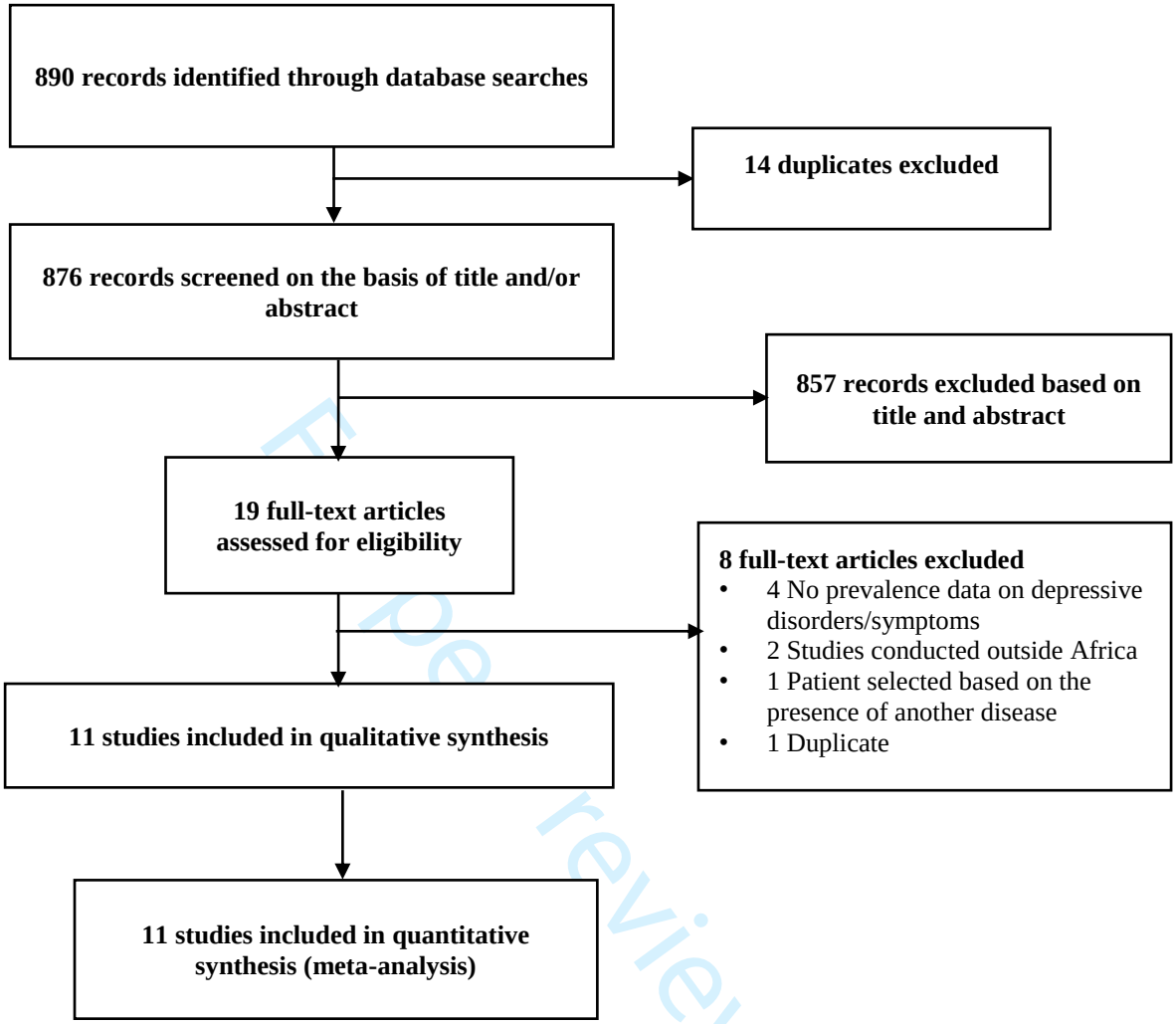
Search	Search terms
#1	'africa'/exp OR africa OR 'algeria'/exp OR algeria OR 'angola'/exp OR angola OR 'benin'/exp OR benin OR 'botswana'/exp OR botswana OR 'burkina faso'/exp OR 'burkina faso' OR 'burundi'/exp OR burundi OR 'cameroon'/exp OR cameroon OR 'canary islands'/exp OR 'canary islands' OR 'cape verde'/exp OR 'cape verde' OR 'central african republic'/exp OR 'central african republic' OR 'chad'/exp OR chad OR 'comoros'/exp OR comoros OR 'congo'/exp OR congo OR 'democratic republic of congo' OR 'djibouti'/exp OR djibouti OR 'egypt'/exp OR egypt OR 'equatorial guinea'/exp OR 'equatorial guinea' OR 'eritrea'/exp OR eritrea OR 'ethiopia'/exp OR ethiopia OR 'gabon'/exp OR gabon OR 'gambia'/exp OR gambia OR 'ghana'/exp OR ghana OR 'guinea'/exp OR guinea OR 'guinea bissau'/exp OR 'guinea bissau' OR 'ivory coast'/exp OR 'ivory coast' OR 'cote ivoire' OR jamahiriya OR 'kenya'/exp OR kenya OR 'lesotho'/exp OR lesotho OR 'liberia'/exp OR liberia OR 'libya'/exp OR libya OR 'madagascar'/exp OR madagascar OR 'malawi'/exp OR malawi OR 'mali'/exp OR mali OR 'mauritania'/exp OR mauritania OR 'mauritius'/exp OR mauritius OR 'mayotte'/exp OR mayotte OR 'morocco'/exp OR morocco OR 'mozambique'/exp OR mozambique OR 'namibia'/exp OR namibia OR 'niger'/exp OR niger OR 'nigeria'/exp OR nigeria OR principe OR 'reunion'/exp OR reunion OR 'rwanda'/exp OR rwanda OR 'sao tome' OR 'senegal'/exp OR senegal OR 'seychelles'/exp OR seychelles OR 'sierra leone'/exp OR 'sierra leone' OR 'somalia'/exp OR somalia OR 'south africa'/exp OR 'south africa' OR 'st helena'/exp OR 'st helena' OR 'sudan'/exp OR sudan OR 'swaziland'/exp OR swaziland OR 'tanzania'/exp OR tanzania OR 'togo'/exp OR togo OR 'tunisia'/exp OR tunisia OR 'uganda'/exp OR uganda OR 'western sahara'/exp OR 'western sahara' OR 'zaire'/exp OR zaire OR 'zambia'/exp OR zambia OR 'zimbabwe'/exp OR zimbabwe OR 'central africa'/exp OR 'central africa' OR 'central african'/exp OR 'central african' OR 'west africa'/exp OR 'west africa' OR 'west african'/exp OR 'west african' OR 'western africa'/exp OR 'western africa' OR 'western african'/exp OR 'western african' OR 'east africa'/exp OR 'east africa' OR 'east african'/exp OR 'east african' OR 'eastern africa'/exp OR 'eastern africa' OR 'eastern african'/exp OR 'eastern african' OR 'north africa'/exp OR 'north africa' OR 'north african'/exp OR 'north african' OR 'northern africa'/exp OR 'northern africa' OR 'northern african'/exp OR 'northern african' OR 'south african'/exp OR 'south african' OR 'southern africa'/exp OR 'southern africa' OR 'southern african'/exp OR 'southern african' OR 'sub saharan africa'/exp OR 'sub saharan africa' OR 'sub saharan african'/exp OR 'sub saharan african' OR 'subsaharan africa'/exp OR 'subsaharan africa' OR 'subsaharan african'
#2	'depression'/exp OR depression OR 'depressive disorder'/exp OR 'depressive disorder' OR 'depressive symptom'/exp OR 'depressive symptom' OR 'depressive neuros*' OR 'depressive syndrome*'

#3	'hypertension'/exp OR hypertension OR 'high blood pressure'/exp OR 'high blood pressure' OR (high AND ('blood'/exp OR blood) AND ('pressure'/exp OR pressure))
#4	#1 AND #2 AND #3

Supplementary Table 2. Methodological quality of included studies

Author, Year	Sampling method	Timing of data collection	Sample size adequate	Response rate	Same method of data collection for all participants
Ademola, 2019	Convenience	Prospectively	No	Not described	Yes
Bhana, 2015	Convenience	Prospectively	Yes	Not described	Yes
Geldsetzer, 2019	Stratified Random	Prospectively	Yes	Adequate	Yes
Grimsrud, 2009	Stratified Multistage	Prospectively	Yes	Not described	Yes
Hamer, 2012	Convenience	Prospectively	Yes	Not described	Yes
Igwe, 2013	Convenience	Prospectively	Yes	Not described	Yes
Iloh, 2018	Convenience	Prospectively	Yes	Not described	Yes
Kretchy, 2014	Time-Location	Prospectively	Yes	Not described	Yes
Okunrinboye, 2019	Systematic Random	Prospectively	Yes	Not described	Yes
Umer, 2019	Convenience	Prospectively	No	Adequate	Yes
Yaméogo, 2015	Convenience	Prospectively	Yes	Not described	Yes

Supplementary Figure 1. PRISMA flow diagram



PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5-6
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	6
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6-7
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	7
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	7, Appendix
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	7
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	7-8
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	7-8
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	8
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	8
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	8

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	8
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	8
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	9
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	9
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	9, Appendix
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	9, Table 1
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	9-10
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	9-10
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	9-10
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	10
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	12
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	12
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	13

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

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Primary Subject Heading:	Mental health
Secondary Subject Heading:	Cardiovascular medicine
Keywords:	Depression & mood disorders < PSYCHIATRY, Hypertension < CARDIOLOGY, EPIDEMIOLOGY

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

Francky Teddy **Endomba**,[1, 2] Mazou N. **Temgoua**,[1] Jean Joel **Bigna**[3*]

1. Health Economics and Policy Research and Evaluation for Development Results Group, Yaoundé, Cameroon
2. Psychiatry Internship Program, University of Bourgogne, 21000 Dijon, France.
3. Department of Epidemiology and Public Health, Centre Pasteur du Cameroon, Yaoundé, Cameroon

E-mail addresses: FTE (franckyteddyea@gmail.com); MNT (neurotemgoua@yahoo.fr); JJB (bignarimjj@yahoo.fr)

*Corresponding author

Word count: 2,692; Abstract: 318 words

Abstract

Objectives: Better knowledge of epidemiology of depressive disorders in people living with hypertension can help to implement pertinent strategies to address its burden. The objective was to estimate the prevalence of depressive disorders and symptoms in people living with hypertension in Africa.

Design: Systematic review and meta-analysis.

Data sources: PubMed, EMBASE, African Index Medicus, Africa Journal Online were searched up to January 31, 2020; regardless of the language of publication.

Eligibility criteria: We included studies conducted among adults (≥ 18 years) living in Africa, and reporting the prevalence of depressive disorders and symptoms.

Data extraction and synthesis: Two independent investigators selected studies, extracted data, and assessed the methodological quality of included studies by using the tool developed by Joanna Briggs Institute. Multivariate random-effects meta-analysis served to pool data by considering the variability between diagnostic tools for identifying patients with depressive disorders or symptoms.

Results: We included 11 studies with 5,299 adults with hypertension. The mean age varied between 50.3 and 59.6 years. The proportion of males varied between 28% and 54%. Data were collected between 2002 and 2017. Data were from South Africa, Nigeria, Ghana, Ethiopia, and Burkina-Faso. The adjusted prevalence of depressive disorders taking in account the variance between diagnostic tools was 17.9% (95% confidence interval [CI]: 13.0-23.4). The prevalence of depressive symptoms and major depressive symptoms was 33.3% (95%CI: 9.9-61.6) and 7.8% (95%CI: 3.0-14.5). There was heterogeneity attributable to the diagnostic tools for depressive disorders and symptoms. There was no publication bias.

Limitation: All regions of Africa were not represented weakening the generalizability of findings to the entire region.

Conclusion: Depressive disorders and symptoms are prevalent in people living with hypertension in Africa, indicating that strategies from clinicians, researchers, and public health makers are needed to reduce its burden in the region.

Keywords

Depression; Depressive symptoms; Depressive disorders; Hypertension; Africa

Strengths and Limitations of this study

- Not all sub-regions of Africa were represented in this review.
- This is the first review performed among people living with hypertension Africa to investigate the epidemiology of depressive disorders and symptoms.
- We found a huge heterogeneity between studies explained by the difference between diagnostic tools for depressive disorders.
- We were not able to explore all sources of heterogeneity due to scarcity of epidemiological data.

Introduction

Cardiovascular diseases (CVDs) are the leading killers worldwide with approximately 18 million deaths per year,[1] and hypertension is involved in approximately 50% of CVDs.[2–4] According to the World Health Organization (WHO), the number of people living with hypertension worldwide is estimated at 1.13 billion, and the African continent has the highest prevalence of hypertensive patients (27%).[4] The deleterious effect of hypertension are linked to direct human consequences with increased morbidity and mortality but also harmful economic outcomes pertaining to its management and the repercussions of its complications.[5–7] Detrimental human outcomes related to chronic high blood pressure encompass target organ damage involving cerebrovascular, heart, and kidney diseases;[4,5] but also mental health repercussions notably anxiety, stress and depression.[8–10]

Depressive disorder is recognized to be the most common mental health illness and the second cause of disability worldwide,[11,12] after cardiovascular diseases. It accounts for 3% of global disability adjusted life years (DALYs).[12] According to the WHO, depressive disorder affects more than 300 million people (4.4% of the world population), and its prevalence in the African continent is estimated at 9% (29.9 million of cases).[13] Some subpopulations have been identified as depression risk groups, including patients with chronic cardiometabolic conditions such as hypertension.[9,14] A wide range of previously published works addressed an interest on the interaction between hypertension and depression.[8,10,15,16] Comprehensively, the majority of these studies concluded that hypertensive disease and depressive disorder share bidirectional interplay with patients with hypertension more likely to develop depression and conversely.[8,17] As examples of evidence, a meta-analysis of 41 studies (including 31 studies from China and three from Africa) which included 30,796 patients with hypertension found that 26.8% have depression,[10] and another one which included 22,367 participants found that depression significantly increase the risk of hypertension incidence with an adjusted relative

risk of 1.42.[15] Additionally, it has been reported that hypertensive patients with comorbid depression are more exposed to poor medication adherence with uncontrolled blood pressure as well as chronic vascular complications and cardiovascular disease related mortality.[8,10,15,16,18] The burden of the depression-hypertension co-occurrence is worsened by the fact that approximately one hypertensive patient in ten has untreated depression.[10,19]

Considering up-to-date scientific literature, depression in hypertensive patients is common in western contexts,[10,20] hypertension and depression are commonly encountered amongst African populations,[2,4,13] but data summarizing and focusing on the burden of depression among hypertensive Africans are not yet available. Hence, we conducted this systematic review and meta-analysis with the aim to explore the prevalence of depressive disorders/symptoms, and major depression in individuals living with hypertension in Africa.

Methods

Design

This systematic review and meta-analysis was conducted according to the Joanna Briggs Institute guidelines.[21] This study was reported according to the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines.[22] The protocol of this review was registered in PROSPERO, with the following registration number CRD42020168979.

Eligibility criteria

Condition

We considered studies reporting the prevalence (or enough data to compute this estimate) of depressive disorders and symptoms. We considered depressive disorders (and major depressive disorders) diagnosed according to the Diagnostic and Statistical Manual of Mental Health Disorders IV or V [23,24], or International Statistical Classification of Diseases and Related

Health Problems-10 [25]. In studies were depressive disorders were not defined using the aforementioned criteria, we considered the definition used by authors, including especially diagnostic scores such as the Patient Health Questionnaire-9. Major depressive symptoms notably included depressive mood and anhedonia.

Context

We considered studies conducted in people living in Africa. Studies conducted in Africans living outside Africa were not considered.

Population

We considered studies conducted in adults (≥ 18 years) living with hypertension, independently of the diagnosis criteria used, of the therapeutic regimen and the control status for the hypertensive disease.

Study design

Cross-sectional, case-control, and cohort studies.

Data sources

We searched PubMed, Excerpta Medica Database (EMBASE), Africa Index Medicus, and Africa Journal Online to identify all relevant records published up to January 31st, 2020;-without any language restriction. The search strategy in EMBASE is available in the Appendix (Supplementary Table 1). To supplement the bibliographic database searches and identify potential additional data sources, we scrutinized the reference list of all relevant original and review papers.

Study selection

Titles and abstracts of articles retrieved from literature search were independently screened by two investigators (FTE and JJB), and the full-texts of those potentially eligible were obtained and further assessed for final inclusion. Disagreements were resolved through consensus.

Data collection and management

A preconceived and standardized data extraction form was used to collect information on first author's name, study country, year of publication, period of participants' recruitment, study design, setting, sampling method, timing of data collection, response rate, mean or median age of the population, age range, proportion of males, number of participants with hypertension, the number of participants with depressive disorders. In case of multinational studies, data were separated to show the estimate within individual countries. Two investigators (FTE and JJB) independently extracted the data from individual studies, with disagreements being resolved through consensus.

Two investigators (FTE and JJB) independently assessed study methodological quality of included studies with tool developed by Joanna Briggs Institute [21], with disagreements being resolved through discussion and consensus. Risk of bias was considered low for each criterion if studies used probabilistic sampling, prospectively collected data, had adequate sample size (required sample size attained), response rate > 80%, and same method of data collection for participants. Studies with low risk of bias had to have four or more criteria, two or three for moderate risk of bias, and no or one for low risk of bias.

Data synthesis and analysis

Meta-analyses were performed with the '*meta', 'metafor', and 'dmetar'* packages of the statistical software *R* (version 3.6.2). Prevalence estimates were reported with 95% confidence interval (95%CI). Prevalence pooling was done with Freeman-Tukey double arcsine transformation using random-effects meta-analysis model.[26] We adjusted the prevalence in a multivariate meta-analysis to take in account the variance between tools used to identify patients with depressive disorders/symptoms. Egger's test served for detecting the presence of publication bias.[27] A p-value < 0.10 on Egger test was considered indicative of statistically significant publication bias. Heterogeneity was evaluated by the χ^2 test on Cochran's Q statistic,[28] which was quantified by I^2 values. The I^2 statistic estimates the percentage of total

variation across studies due to true between-study differences rather than chance. In general, I^2 values greater than 60-70% indicate the presence of substantial heterogeneity.[29] Inter-rater agreements between investigators for study inclusion and methodological quality assessment were assessed using Kappa Cohen's coefficient.[30]

Patient and public involvement

Patients or the public were not involved in the design, conduct, reporting, or dissemination of our research.

Results

The review process and study characteristics

We initially identified 890 records and finally retained 11 full texts (13 prevalence data) in the meta-analysis (Supplementary Figure 1).[31–41] Agreement between investigators on selection based on title and abstract was $\kappa = 0.88$ and $\kappa = 1.0$ for final inclusion.

Of the 11 included studies, eight studies used non-probabilistic sampling while three used probabilistic sampling. All studies prospectively collected and analysed data and used the same method to identify patients with depressive disorders. Sample size was adequate in nine studies and response rate in two studies (Supplementary Table 2). Three studies had low risk of bias and eight moderate risk. None of the studies had high risk of bias.

The characteristics of included studies are presented in the Table 1. All studies were cross-sectional. Patient Health Questionnaire-9 was the most used tool, n = 4. The mean age varied between 50.3 and 59.6 years. The proportion of males varied between 28% and 54%. Data on depressive disorders/symptoms were collected between 2002 and 2017.Four studies were conducted in South Africa, three studies in Nigeria, one study in Ghana, one study in both Ghana and Nigeria, one study in Ethiopia, and one study in Burkina-Faso. None of the study was conducted in Central Africa and North Africa. Talking about the language of the tool used

to assess depressive status, four studies indicated that they use native/local languages back translated in English for reporting.[32,33,35,36]

Prevalence of depressive disorders/symptoms in people with hypertension in Africa

In total, 5,299 participants with hypertension were included. There was substantial heterogeneity for all analyses, all $I^2 > 75\%$ (Figure 1). The prevalence of depressive disorders was 18.6% (95%CI: 13.8-23.9; 5 studies) (Figure 1). The adjusted prevalence taking in account the variance between diagnostic tools was 17.9% (95%CI: 13.0-23.4) with 52.7% of variance due to difference between tools. There was no publication bias (p = 0.789). There was no data on major depressive disorders.

The prevalence of depressive symptoms was 37.3% (95%CI: 19.3-57.3; 6 studies). The adjusted prevalence taking in account the variance between diagnostic tools was 33.3% (95%CI: 9.9-61.6) with 74.1% of variance due to difference between tools. There was no publication bias (p = 0.115).

The prevalence of major depressive symptoms was 7.9% (95%CI: 1.7-17.9; 2 studies). The adjusted prevalence taking in account the variance between diagnostic tools was 7.8% (95%CI: 3.0-14.5) with 43.3% of variance due to difference between tools. The *p* value on Egger test was 0.789.

In subgroup analysis, there was no difference between population-based and hospital-based for all outcomes except for major depressive disorders where the prevalence was higher in population-based study (12.6%; 95%CI: 8.8-17.0; 1 study) compared to hospital-based study (4.2%; 95%CI: 2.5-6.5; 1 study), p = 0.0001 (Supplementary Figures 2, 3, and 4). However, there was low number of studies in compared groups. The prevalence of depressive disorders was higher among women (23.8%; 95%CI: 18.7-29.3; 1 study) compared to men (14.5%; 95%CI: 9.3-20.6; 1 study), p = 0.0227) (Supplementary Figure 5). There was no difference for depressive symptoms (Supplementary Figure 6).

Discussion

This meta-analysis of data from 5,299 adults with hypertension living in five countries in Africa revealed that depressive disorders and symptoms are prevalent in this population with substantial heterogeneity according to the diagnostic tools. This systematic review suggests that approximately one on five and one-third of patients with hypertension have respectively depression and depressive symptoms.

Globally, there are dissimilarities between our findings and previous studies on depression among adults with hypertension. For instance, in China, compared to our findings, a meta-analysis of 41 studies on the prevalence of depression in patients with hypertension found higher rates of depression with a pooled prevalence of 26.9% (95%CI: 21.7% - 32.3%) [10]. Our review revealed a higher prevalence of depression among patients with hypertension compared to occidental studies. For instance, considering data of United States Multi-Disciplinary Group Practice Observational Study which included 4,362 adult patients with hypertension (13% of anxiety and/or depression).[42] A cross-sectional study done in Spain among 5,954 hypertensive patients with high cardiovascular risk profile found that 15.6% had depression.[19] These differences across regions can be explained by the changeability pertaining to the criteria and/or diagnostic tools used to screen depressive disorder across studies.[43,44] Noteworthy, Li and colleagues who studied depressive disorder among hypertension in a meta-analysis of 41 studies suggested that self-assessed screening tools of depression or depressive symptoms might overestimate the prevalence of depression.[10] Indeed they found a 30% depression prevalence using self-administrated diagnostic scales versus a 21% prevalence using clinical-interviewed tools.[10] This could be linked to patients' confusion about depression and hypertension symptoms such as poor appetite, fatigue and sleep disturbances.[10] In our review the most used diagnostic tool was the PHQ-9 and another fact

to highpoint is that differences in prevalence can also be explained by the cut-off-point used for a same tool to define a positive screening for depression.[32,45,46] Mahmood and colleagues while assessing depression among 411 hypertensive outpatients in a Pakistan hospital by using PHQ-9 with a score of 10 or above as cut-off point found a prevalence of 40.1%,[47] more than two folds ours. In our study, we had a substantial heterogeneity for all analyses which can also be related to the variance between diagnostic tools used for depression assessment. The previously cited meta-analysis of Li and colleagues also showed evidence of high-level heterogeneity.[10]

In our sub-group analysis, we found that there was no difference between population-based and hospital-based for all outcomes except for major depressive disorders which prevalence was higher in population-based study. This result has to be cautiously interpreted regarding the amount of studies in each group (only one study per group measured with depression investigated with different tools). We also found that the prevalence of depressive disorders was higher for women when compared to men. This finding is in accordance with what is known concerning gender differences in depression. [48–50] This can be linked to hormonal differences between the two genders, and the fact that women experience periods of physiological changes such as menstruation, pregnancy and perimenopause. [49,51,52] There are growing evidence on the potential positive role of hormone replacement therapy on postmenopausal depression.[51,52] Previous studies on twins revealed that women are more sensitive to interpersonal relationship.[51,53] This could be more pronounced in sub-Saharan African cultures considering the role of ale gender in families, with as consequence a lesser capacity to express their psychological distress.[53–55]

This meta-analysis highlights the fact that depressive disorder is frequently encountered among hypertensive patients. This review might substantiate the relevancy to conduct further studies with the aim to investigate on the better diagnosis tool for depression among hypertensive

patients in order to reduce heterogeneity of results. Moreover, our review could justify carrying out epidemiological studies on the depression-hypertension comorbidity in other African regions in order to have more representative regional picture of the evidence. Since we were able to identify only 11 studies in the last 20 years our study calls for more primary research on the relationship between hypertension and mental health in the continent, by using homogenous diagnostic tools. Researchers, clinicians, and public health policy makers can also explore implementing registries to better measure the burden of mental health disorders in the continent.[56–58] All this might help to establish adapted policies pertaining to the management of hypertensive patients with depression, notably for a tailored pharmacological treatment.[18,59,60] Nevertheless, our analysis could already draw clinician's awareness on the necessity to screen depression symptoms among hypertensive patients, especially since previously published works found that comorbid depression contribute to more deleterious cardiovascular outcomes.[8,10,15,16,18]

This study should however be interpreted considering some limitations. First and most common to meta-analyses of prevalence studies [61], we found a huge heterogeneity between studies for which we undertook subgroup analysis to investigate sources of heterogeneity and adjusted analysis to take account the variance due to diagnostic tools. However, some characteristics that may further explain heterogeneity were not reported or there were not enough studies to conduct such analysis including sub-regions and age groups. Second, there was a substantial variability regarding the representativeness of regions and countries, with some ones less or not represented. This may weaken the generalizability of our findings and call for more epidemiological studies in this region. Not all studies had low risk of bias, especially, most of studies used non-probabilistic sampling. However, due to low number of studies included in this meta-analysis, we were not able to perform sensitivity analysis to assess the robustness of our findings based on methodological quality.

Despite these limitations, this first systematic review and meta-analysis on depressive disorders/symptoms in people living with hypertension in Africa provided a clear summary of the existing knowledge. This systematic review is a starting point for understanding the epidemiology and relationship between mental health and hypertension in African countries where it is challenging to have such data. A protocol had been registered before, and we used rigorous methodological and statistical procedures to obtain and pool data. Furthermore, we have taken in account the variability due to diagnostic tools. There was no publication bias.

Conclusions

Overall, our review found that depressive disorders and symptoms are prevalent in people living with hypertension in select African countries. Including an assessment of mental health in patients with hypertension seems prudent, with the potential for intervention. However, since our analysis has limitations pertaining to diagnostic tools consistency within studies and also to the unrepresentative geographic distribution, further studies would be relevant in order to reinforce our findings. All this could be a support for a personalized management of patients with hypertension and depression.

Author Contributors

Conception: JJB, FTE. Designing of the protocol: FTE, JJB. Literature search: JJB. Studies selection: FTE, JJB. Data extraction: FTE, JJB. Data management: JJB. Data synthesis and analysis: JJB. Writing of the first draft: JJB, FTE. Critical revision: FTE, MNT, JJB. Approved the final version: FTE, MNT, JJB. Guarantor of the review: JJB.

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Competing interests

We declare no competing interests.

Patient consent

Not applicable.

Data sharing statement

All data generated for this study are in the manuscript and its supporting files.

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Figures legend

Figure 1. Crude prevalence of depressive disorders/symptoms in people living with hypertension in Africa

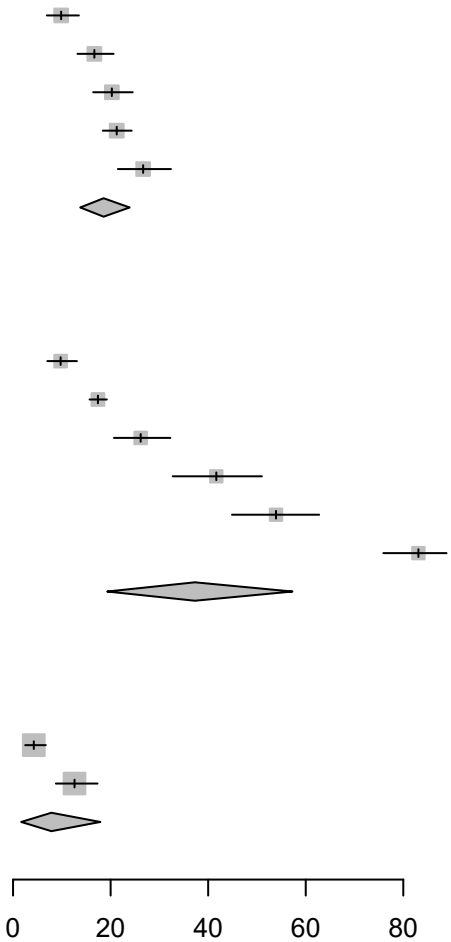
491 **Table 1. Characteristics of included studies**

Author	Year	Design, Setting	Diagnosis of conditions	Validity of the tool used	Language of the tool used	Inclusion criteria	Population	Period of inclusion	Country	Sample
Ademola	2019	Cross-sectional, Hospital	Patient Health Questionnaire 9 (PHQ-9)	Validated	NR	Age ≥ 18 y, diagnosis of hypertension, treatment with an antihypertensive medication for at least 12 months	%Males: 41.7; Mean age: 57	2013	Ghana, Nigeria	357
Bhana	2015	Cross-sectional, Population	Depression module of the Structured Clinical Interview for DSM-IV (SCID)	NR	English, seTsawa	Age ≥ 18 y, clinic attendance for routine chronic disease services (e.g., HIV, hypertension, diabetes) and ability to comprehend and complete study components in Tswana or English.	NR	2014	South Africa	345
Geldsetzer	2019	Cross-sectional, Population	Center for Epidemiological Studies—Depression (CES-D) screening tool	NR	English, Shangaan	Age ≥ 40 y and continuously living in the area during the 12 months prior to study enrolment	%Males: 37.4 Mean age : NR	2014-2015	South Africa	1822
Grimsrud	2009	Cross-sectional, Population	Composite International Diagnostic Interview Version 3.0 (CIDI-3.0)	NR	NR	South Africans ≥ 18 y who lived in households and hostels during the field period of the study	%Males: 28.0; Mean age: 50.3	2002-2004	South Africa	767
Hamer	2012	Cross-sectional, Population	Patient Health Questionnaire 9 (PHQ-9)	Validated	English and local language	Age: 25-60 y with hypertension	NR	2008-2009	South Africa	254
Igwe	2013	Cross-sectional, Hospital	Mini International Neuro-psychiatric Interview (MINI)	NR	NR	Age: 18 - 64 y. Hypertension for at least 1 year and stable without need for hospital admission for 3 months prior to assessment	%Males: 53.7; Mean age: 50.4	2010-2011	Nigeria	270
Iloh	2018	Cross-sectional, Hospital	Patient Health Questionnaire 9 (PHQ-9)	Validated	NR	Age ≥18 y with hypertension	%Males: 40.7; Mean age : NR	2017	Nigeria	142

Kretchy	2014	Cross-sectional, Hospital	Depression Anxiety Stress Scale (DASS) – 21	NR	NR	Age ≥ 18 y, a diagnosis of hypertension, reporting prescription of at least one antihypertensive medication for a minimum of two months	%Males: 37.3; Mean age : NR	2012	Ghana	400
Okunrinboye	2019	Cross-sectional, Hospital	Mini International Neuro-psychiatric Interview (MINI)	NR	Yoruba, English	Age: 18 and 64 y who were diagnosed by a consultant physician at the Centre as suffering from hypertension and have been on anti-hypertensive medication for at least 6 months, spoke Yoruba or English language fluently	%Males: 38.0; Mean age: 59.6y	2012	Nigeria	400
Umer	2019	Cross-sectional, Hospital	Patient Health Questionnaire 9 (PHQ-9)	Validated	English, Afan Oromo, Amharic	Age ≥ 18 y, follow-up for hypertension	%Males: 52.8; Mean age : NR	2014	Ethiopia	128
Yaméogo	2015	Cross-sectional, Hospital	Hospital Anxiety and Depression Scale (HADS)	NR	NR	Hypertensive consenting adult outpatients	%Males: 40.1; Mean age: 54.6y	2010-2011	Burkina-Faso	414

NR: not reported.

Author, Year	Cases	Total	Prevalence, %	[95% C.I.]	Weight
A. Depressive disorders					
Bhana, 2015	34	345	9.9	[6.9; 13.5]	19.9%
Yaméogo, 2015	69	414	16.7	[13.2; 20.6]	20.0%
Okunrinboye, 2019	81	400	20.2	[16.4; 24.5]	20.0%
Grimsrud, 2009	163	767	21.3	[18.4; 24.3]	20.2%
Igwe, 2013	72	270	26.7	[21.5; 32.4]	19.8%
Subgroup prevalence		**2196**	**18.6**	**[13.8; 23.9]**	**100.0%**
Heterogeneity: I^2 = 89.2%, p < 0.0001					
B. Depressive symptoms					
Kretchy, 2014	39	400	9.8	[7.0; 13.1]	17.0%
Geldsetzer, 2019	317	1822	17.4	[15.7; 19.2]	17.3%
Ademola, 2019	62	237	26.2	[20.7; 32.2]	16.8%
Ademola, 2019	50	120	41.7	[32.7; 51.0]	16.2%
Umer, 2019	69	128	53.9	[44.9; 62.8]	16.3%
Iloh, 2018	118	142	83.1	[75.9; 88.9]	16.4%
Subgroup prevalence		**2849**	**37.3**	**[19.3; 57.3]**	**100.0%**
Heterogeneity: I^2 = 98.7%, p < 0.0001					
C. Major depressive symptoms					
Kretchy, 2014	17	400	4.2	[2.5; 6.7]	50.3%
Hamer, 2012	32	254	12.6	[8.8; 17.3]	49.7%
Subgroup prevalence		**654**	**7.9**	**[1.7; 17.9]**	**100.0%**
Heterogeneity: I^2 = 93.3%, p = 0.0001					



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

Francky Teddy **Endomba**, Mazou N. **Temgoua**, Jean Joel **Bigna**

APPENDIX

Supplementary Table 1. Search strategy

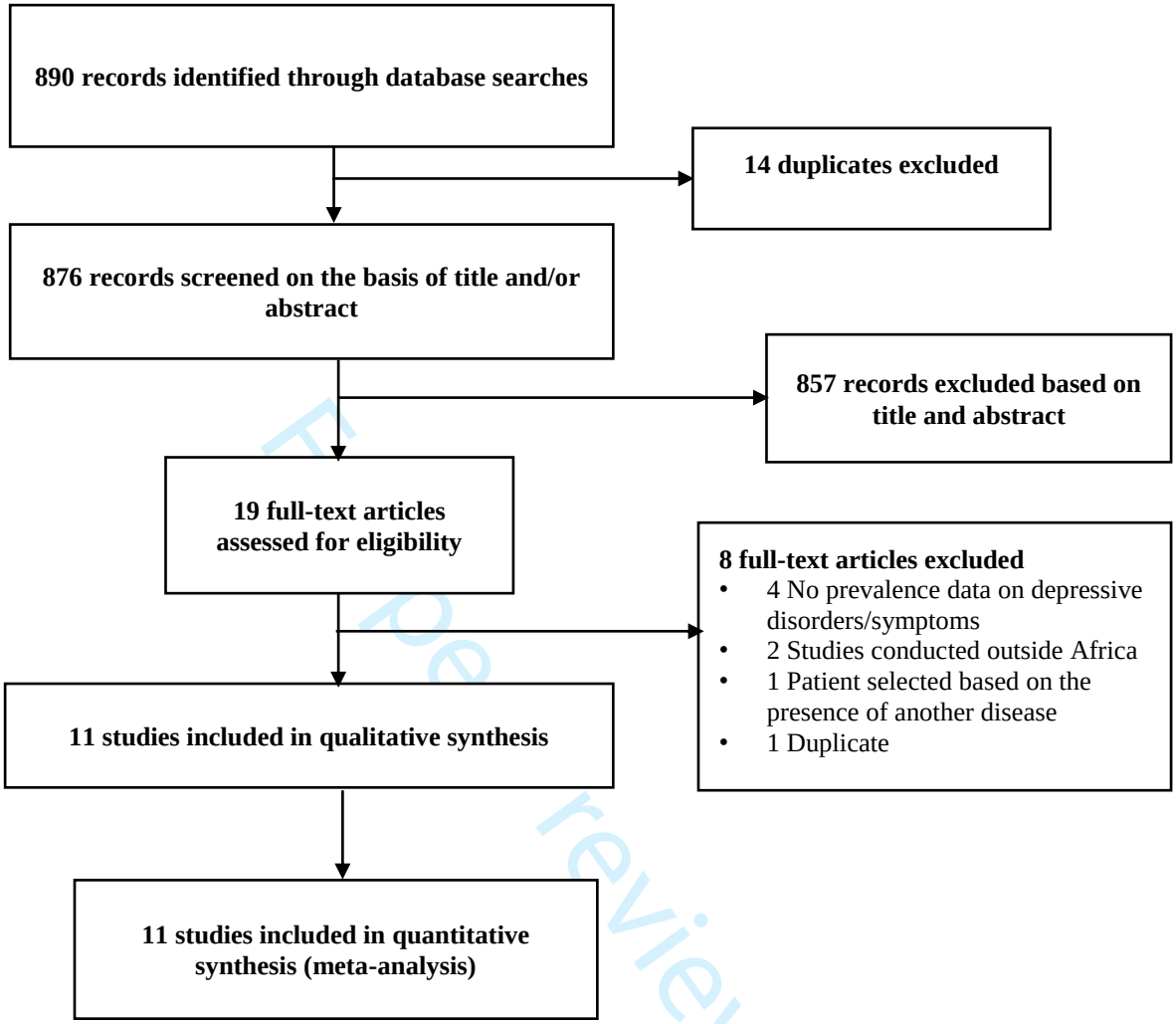
Search	Search terms
#1	'africa'/exp OR africa OR 'algeria'/exp OR algeria OR 'angola'/exp OR angola OR 'benin'/exp OR benin OR 'botswana'/exp OR botswana OR 'burkina faso'/exp OR 'burkina faso' OR 'burundi'/exp OR burundi OR 'cameroon'/exp OR cameroon OR 'canary islands'/exp OR 'canary islands' OR 'cape verde'/exp OR 'cape verde' OR 'central african republic'/exp OR 'central african republic' OR 'chad'/exp OR chad OR 'comoros'/exp OR comoros OR 'congo'/exp OR congo OR 'democratic republic of congo' OR 'djibouti'/exp OR djibouti OR 'egypt'/exp OR egypt OR 'equatorial guinea'/exp OR 'equatorial guinea' OR 'eritrea'/exp OR eritrea OR 'ethiopia'/exp OR ethiopia OR 'gabon'/exp OR gabon OR 'gambia'/exp OR gambia OR 'ghana'/exp OR ghana OR 'guinea'/exp OR guinea OR 'guinea bissau'/exp OR 'guinea bissau' OR 'ivory coast'/exp OR 'ivory coast' OR 'cote ivoire' OR jamahiriya OR 'kenya'/exp OR kenya OR 'lesotho'/exp OR lesotho OR 'liberia'/exp OR liberia OR 'libya'/exp OR libya OR 'madagascar'/exp OR madagascar OR 'malawi'/exp OR malawi OR 'mali'/exp OR mali OR 'mauritania'/exp OR mauritania OR 'mauritius'/exp OR mauritius OR 'mayotte'/exp OR mayotte OR 'morocco'/exp OR morocco OR 'mozambique'/exp OR mozambique OR 'namibia'/exp OR namibia OR 'niger'/exp OR niger OR 'nigeria'/exp OR nigeria OR principe OR 'reunion'/exp OR reunion OR 'rwanda'/exp OR rwanda OR 'sao tome' OR 'senegal'/exp OR senegal OR 'seychelles'/exp OR seychelles OR 'sierra leone'/exp OR 'sierra leone' OR 'somalia'/exp OR somalia OR 'south africa'/exp OR 'south africa' OR 'st helena'/exp OR 'st helena' OR 'sudan'/exp OR sudan OR 'swaziland'/exp OR swaziland OR 'tanzania'/exp OR tanzania OR 'togo'/exp OR togo OR 'tunisia'/exp OR tunisia OR 'uganda'/exp OR uganda OR 'western sahara'/exp OR 'western sahara' OR 'zaire'/exp OR zaire OR 'zambia'/exp OR zambia OR 'zimbabwe'/exp OR zimbabwe OR 'central africa'/exp OR 'central africa' OR 'central african'/exp OR 'central african' OR 'west africa'/exp OR 'west africa' OR 'west african'/exp OR 'west african' OR 'western africa'/exp OR 'western africa' OR 'western african'/exp OR 'western african' OR 'east africa'/exp OR 'east africa' OR 'east african'/exp OR 'east african' OR 'eastern africa'/exp OR 'eastern africa' OR 'eastern african'/exp OR 'eastern african' OR 'north africa'/exp OR 'north africa' OR 'north african'/exp OR 'north african' OR 'northern africa'/exp OR 'northern africa' OR 'northern african'/exp OR 'northern african' OR 'south african'/exp OR 'south african' OR 'southern africa'/exp OR 'southern africa' OR 'southern african'/exp OR 'southern african' OR 'sub saharan africa'/exp OR 'sub saharan africa' OR 'sub saharan african'/exp OR 'sub saharan african' OR 'subsaharan africa'/exp OR 'subsaharan africa' OR 'subsaharan african'
#2	'depression'/exp OR depression OR 'depressive disorder'/exp OR 'depressive disorder' OR 'depressive symptom'/exp OR 'depressive symptom' OR 'depressive neuros*' OR 'depressive syndrome*'

#3	'hypertension'/exp OR hypertension OR 'high blood pressure'/exp OR 'high blood pressure' OR (high AND ('blood'/exp OR blood) AND ('pressure'/exp OR pressure))
#4	#1 AND #2 AND #3

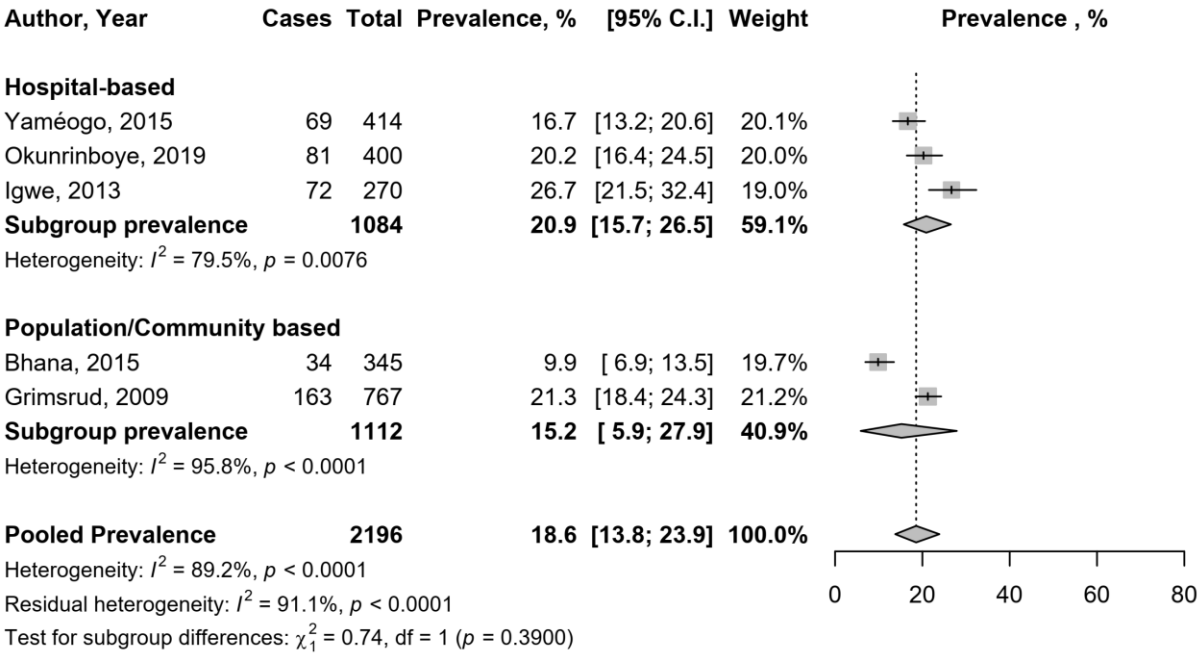
Supplementary Table 2. Methodological quality of included studies

Author, Year	Sampling method	Timing of data collection	Sample size adequate	Response rate	Same method of data collection for all participants	SUMMARY (Risk of bias)
Ademola, 2019	Convenience	Prospectively	No	Not described	Yes	Moderate
Bhana, 2015	Convenience	Prospectively	Yes	Not described	Yes	Moderate
Geldsetzer, 2019	Stratified Random	Prospectively	Yes	Adequate	Yes	Low
Grimsrud, 2009	Stratified Multistage	Prospectively	Yes	Not described	Yes	Low
Hamer, 2012	Convenience	Prospectively	Yes	Not described	Yes	Moderate
Igwe, 2013	Convenience	Prospectively	Yes	Not described	Yes	Moderate
Iloh, 2018	Convenience	Prospectively	Yes	Not described	Yes	Moderate
Kretchy, 2014	Time-Location	Prospectively	Yes	Not described	Yes	Moderate
Okunrinboye, 2019	Systematic Random	Prospectively	Yes	Not described	Yes	Low
Umer, 2019	Convenience	Prospectively	No	Adequate	Yes	Moderate
Yaméogo, 2015	Convenience	Prospectively	Yes	Not described	Yes	Moderate

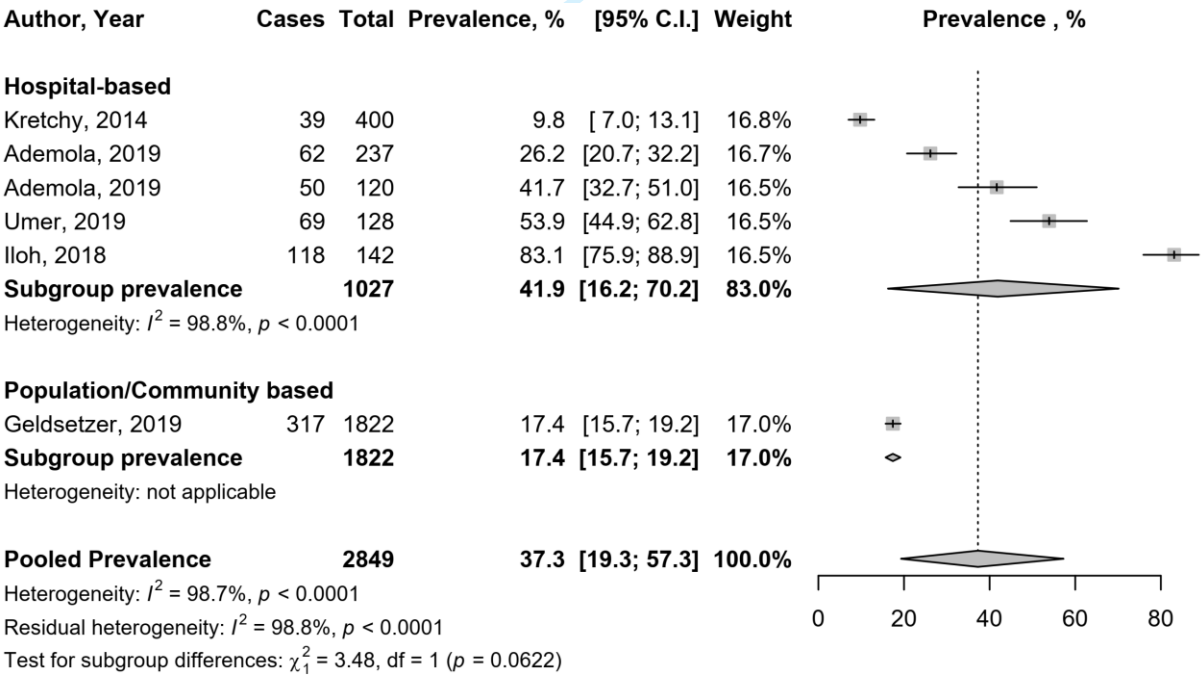
Supplementary Figure 1. PRISMA flow diagram



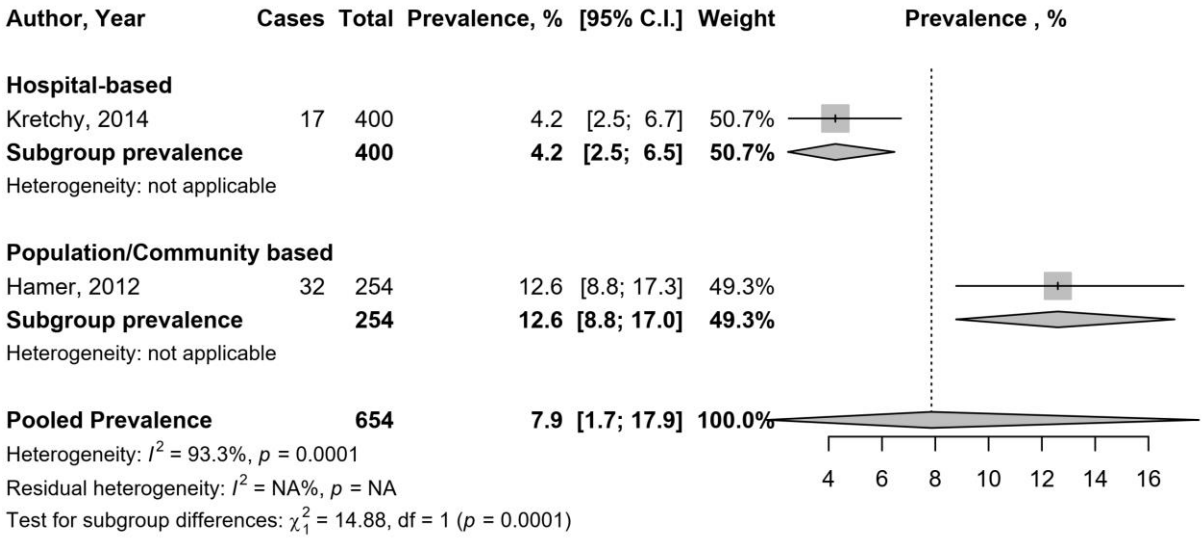
Supplementary Figure 2. Meta-analysis prevalence of depressive disorders by setting



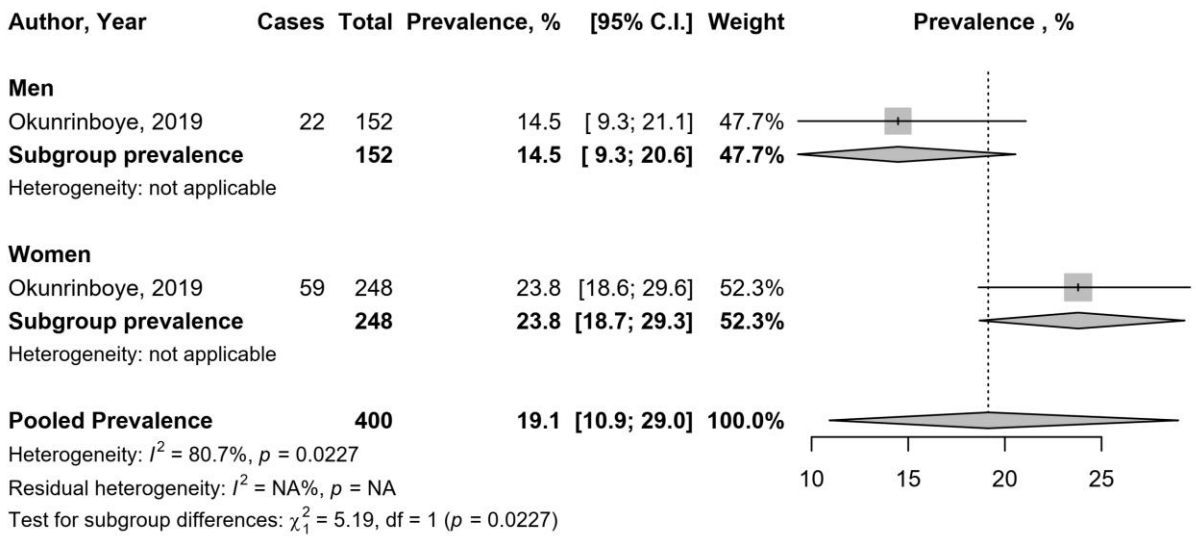
Supplementary Figure 3. Meta-analysis prevalence of depressive symptoms by setting



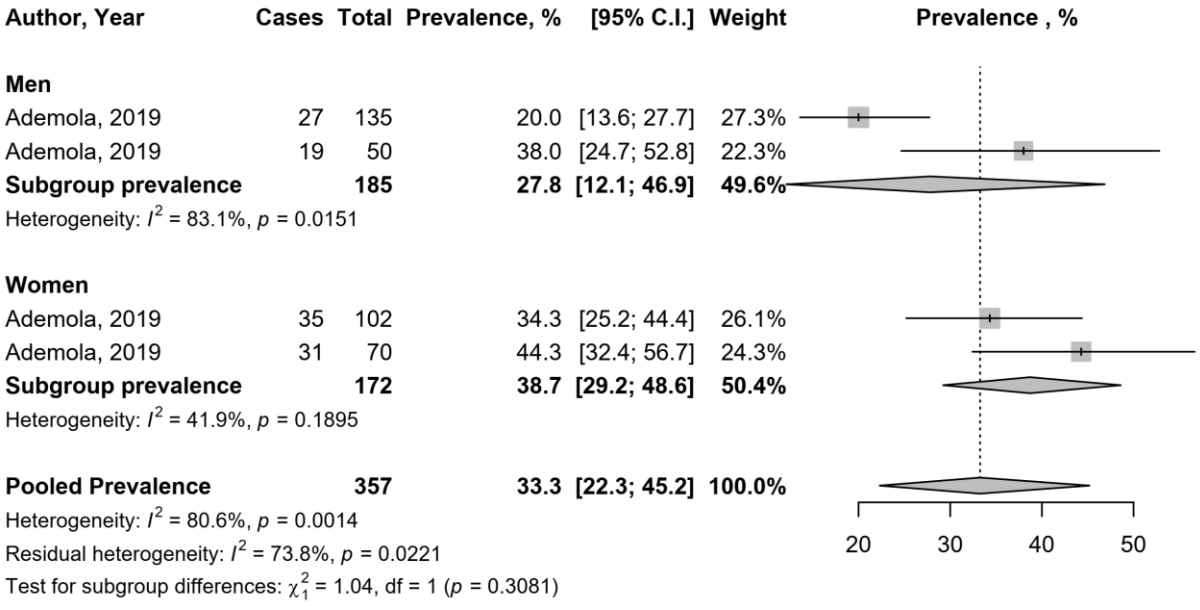
Supplementary Figure 4. Meta-analysis prevalence of major depressive disorders by setting



Supplementary Figure 5. Meta-analysis prevalence of depressive disorders by sex



Supplementary Figure 6. Meta-analysis prevalence of depressive symptoms by sex



PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5-6
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	6
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6-7
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	7
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	7, Appendix
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	7
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	7-8
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	7-8
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	8
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	8
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	8

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	8
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	8
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	9
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	9
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	9, Appendix
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	9, Table 1
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	9-10
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	9-10
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	9-10
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	10
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	12
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	12
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	13

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

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Primary Subject Heading:	Mental health
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Epidemiology of depressive disorders in people living with hypertension in Africa: a systematic review and meta-analysis

Francky Teddy **Endomba**,[1, 2] Mazou N. **Temgoua**,[1] Jean Joel **Bigna**[3*]

1. Health Economics and Policy Research and Evaluation for Development Results Group, Yaoundé, Cameroon
2. Psychiatry Internship Program, University of Bourgogne, 21000 Dijon, France.
3. Department of Epidemiology and Public Health, Centre Pasteur du Cameroon, Yaoundé, Cameroon

E-mail addresses: FTE (franckyteddyea@gmail.com); MNT (neurotemgoua@yahoo.fr); JJB (bignarimjj@yahoo.fr)

*Corresponding author

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Abstract

Objectives: Better knowledge of epidemiology of depressive disorders in people living with hypertension can help to implement pertinent strategies to address its burden. The objective was to estimate the prevalence of depressive disorders and symptoms in people living with hypertension in Africa.

Design: Systematic review and meta-analysis.

Data sources: PubMed, EMBASE, African Index Medicus, Africa Journal Online were searched up to January 31, 2020; regardless of the language of publication.

Eligibility criteria: We included studies conducted among hypertensive adult patients (≥ 18 years) living in Africa and reporting the prevalence of depressive disorders and symptoms.

Data extraction and synthesis: Two independent investigators selected studies, extracted data, and assessed the methodological quality of included studies by using the tool developed by Joanna Briggs Institute. Multivariate random-effects meta-analysis served to pool data by considering the variability between diagnostic tools used to identify patients with depressive disorders or symptoms.

Results: We included 11 studies with 5,299 adults with hypertension. Data were collected between 2002 and 2017, from South Africa, Nigeria, Ghana, Ethiopia, and Burkina-Faso. The mean age varied between 50.3 and 59.6 years. The proportion of males ranged from 28% to 54%. The adjusted prevalence of depressive disorders taking into account the variance between diagnostic tools was 17.9% (95% confidence interval [CI]: 13.0-23.4). The prevalence of depressive symptoms and major depressive symptoms was 33.3% (95%CI: 9.9-61.6) and 7.8% (95%CI: 3.0-14.5). There was heterogeneity attributable to the diagnostic tools for depressive disorders and symptoms. There was no publication bias.

Conclusion: Notwithstanding the representativeness lack of some (sub) regions of Africa, weakening the generalizability of findings to the entire region; depressive disorders and symptoms are prevalent in people living with hypertension in Africa, indicating that strategies from clinicians, researchers, and public health makers are needed to reduce its burden in the region.

Keywords

Depression; Depressive symptoms; Depressive disorders; Hypertension; Africa

Strengths and Limitations of this study

- Not all sub-regions of Africa were represented in this review.
- This is the first review performed among people living with hypertension Africa to investigate the epidemiology of depressive disorders and symptoms.
- We found a huge heterogeneity between studies explained by the difference between diagnostic tools for depressive disorders.
- We were not able to explore all sources of heterogeneity due to scarcity of epidemiological data.

Introduction

Cardiovascular diseases (CVDs) are the leading cause of deaths worldwide with approximately 18 million deaths per year [1]. Hypertension is involved in approximately 50% of CVDs [2–4]. According to the World Health Organization (WHO), the number of people living with hypertension worldwide is estimated at 1.13 billion, and Africa has the highest prevalence of people with hypertension (27%) [4]. In addition to high morbidity and mortality, hypertension is also associated with high socio-economic burden related to its management and complications [5–7]. Detrimental outcomes related to chronic high blood pressure encompass target organ damage involving cerebrovascular, heart, and kidney diseases [4,5]; but also, mental health repercussions including anxiety, stress and depression [8–10].

Depressive disorder is the most common mental health disease and the second cause of disability worldwide after cardiovascular diseases [11,12]. It accounts for 3% of the global disability adjusted life years (DALYs) [12]. According to the WHO, depressive disorder affects more than 300 million people (4.4% of the global population), and its prevalence in the African continent is estimated at 9% (29.9 million of cases) in the general population [13]. Some subpopulations have been identified as higher risk of depression, including patients with chronic CVDs such as hypertension [9,14]. A wide range of previously published studies addressed the interaction between hypertension and depression [8,10,15,16]. Most of these studies concluded that hypertension and depressive disorder share bidirectional interplay where patients with hypertension were more likely to develop depression and conversely [8,17]. As examples of evidence, a meta-analysis of 41 studies (including 31 studies from China and three from Africa) which included 30,796 patients with hypertension found that 26.8% have depression, and another one which included 22,367 participants found that depression significantly increases the risk of hypertension incidence [10,15] Additionally, it has been reported that patients living with hypertension with comorbid depression are at higher risk of

suboptimal medication adherence with uncontrolled blood pressure, complicated by chronic vascular complications and cardiovascular disease related mortality [8,10,15,16,18]. The burden of the depression-hypertension co-occurrence is worsened by the fact that approximately one hypertensive patient in ten has untreated depression [10,19].

Considering up-to-date scientific literature, depression in hypertensive patients is common in western contexts [10,20], hypertension and depression are commonly encountered amongst African populations [2,4,13], but data summarizing and focusing on the burden of depression among hypertensive Africans are not yet available. Hence, we conducted this systematic review and meta-analysis with the aim to explore the prevalence of depressive disorders/symptoms, and major depression in people living with hypertension in Africa.

Methods

Design

This systematic review and meta-analysis was conducted according to the Joanna Briggs Institute guidelines [21]. This study was reported according to the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines [22]. The protocol of this review was registered in PROSPERO with the following registration number: CRD42020168979.

Eligibility criteria

Condition

We considered studies reporting the prevalence (or enough data to compute this estimate) of depressive disorders and symptoms. We considered depressive disorders (and major depressive disorders) diagnosed according to the Diagnostic and Statistical Manual of Mental Health Disorders IV or V [23,24], or International Statistical Classification of Diseases and Related Health Problems-10 [25]. In the studies were depressive disorders were not defined using the aforementioned criteria, we considered the definition used by authors, including especially

diagnostic scores such as the Patient Health Questionnaire-9. Major depressive symptoms notably included depressive mood and anhedonia.

Context

We considered studies conducted in people living in Africa. Studies conducted in Africans living outside Africa were not considered.

Population

We considered studies conducted in adults (≥ 18 years) living with hypertension regardless of the diagnosis criteria used, of the therapeutic regimen and the control status for the hypertensive disease.

Study design

Cross-sectional, case-control, and cohort studies.

Data sources

We searched PubMed, Excerpta Medica Database (EMBASE), Africa Index Medicus, and Africa Journal Online to identify all relevant records published up to January 31st, 2020;-without any language restriction. The search strategy in EMBASE is available in the Appendix (Supplementary Table 1). To supplement the bibliographic database searches and identify potential additional data sources, we scrutinized the reference list of all relevant original and review papers.

Study selection

Titles and abstracts of articles retrieved from literature search were independently screened by two investigators (FTE and JJB), and the full-texts of those potentially eligible were obtained and further assessed for final inclusion. Disagreements were resolved through consensus.

Data collection and management

A preconceived and standardized data extraction form was used to collect information on first author's name, study country, year of publication, period of participants' recruitment, study

design, setting, sampling method, timing of data collection, response rate, mean or median age of the population, age range, proportion of males, number of participants with hypertension, the number of participants with depressive disorders. In case of multinational studies, data were separated to show the estimate within individual countries. Two investigators (FTE and JJB) independently extracted the data from individual studies, with disagreements being resolved through consensus.

Two investigators (FTE and JJB) independently assessed study methodological quality of included studies with tool developed by Joanna Briggs Institute [21], with disagreements being resolved through discussion and consensus. Risk of bias was considered low for each criterion if studies used probabilistic sampling, prospectively collected data, had adequate sample size (required sample size attained), response rate > 80%, and same method of data collection for participants. Studies with low risk of bias had to have four or more criteria, two or three for moderate risk of bias, and no or one for low risk of bias.

Data synthesis and analysis

Meta-analyses were performed with the *'meta', 'metafor', and 'dmetar'* packages of the statistical software *R* (version 3.6.2). Prevalence estimates were reported with 95% confidence interval (95%CI). Prevalence pooling was done with Freeman-Tukey double arcsine transformation using random-effects meta-analysis model [26]. We adjusted the prevalence in a multivariate meta-analysis to take in account the variance between tools used to identify patients with depressive disorders/symptoms. Egger's test served for detecting the presence of publication bias [27]. A p-value < 0.10 on Egger test was considered indicative of statistically significant publication bias. Heterogeneity was evaluated by the χ^2 test on Cochran's Q statistic [28], which was quantified by I^2 values. The I^2 statistic estimates the percentage of total variation across studies due to true between-study differences rather than chance. In general, I^2 values greater than 60-70% indicate the presence of substantial heterogeneity [29]. Inter-rater

agreements between investigators for study inclusion and methodological quality assessment were assessed using Kappa Cohen's coefficient [30].

Patient and public involvement

Patients or the public were not involved in the design, conduct, reporting, or dissemination of our research.

Results

The review process and study characteristics

We initially identified 890 records and finally retained 11 full texts (13 prevalence data) in the meta-analysis (Supplementary Figure 1) [31–41]. Agreement between investigators on selection based on title and abstract was $\kappa = 0.88$ and $\kappa = 1.0$ for final inclusion.

Of the 11 included studies, eight studies used non-probabilistic sampling while three used probabilistic sampling. All studies prospectively collected and analysed data and used the same method to identify patients with depressive disorders. Sample size was adequate in nine studies and response rate in two studies (Supplementary Table 2). Three studies had low risk of bias and eight moderate risk. None of the studies had high risk of bias.

The characteristics of included studies are presented in the Table 1. All studies were cross-sectional. Patient Health Questionnaire-9 was the most used tool, n = 4. The mean age varied between 50.3 and 59.6 years. The proportion of males varied between 28% and 54%. Data on depressive disorders/symptoms were collected between 2002 and 2017. Four studies were conducted in South Africa, three studies in Nigeria, one study in Ghana, one study in both Ghana and Nigeria, one study in Ethiopia, and one study in Burkina-Faso. None of the study was conducted in Central Africa and North Africa. Talking about the language of the tool used to assess depressive status, four studies indicated that they use native/local languages back translated in English for reporting [32,33,35,36].

Prevalence of depressive disorders/symptoms in people with hypertension in Africa

In total, 5,299 participants with hypertension were included. There was substantial heterogeneity for all analyses, all $I^2 > 75\%$ (Figure 1). The prevalence of depressive disorders was 18.6% (95%CI: 13.8-23.9; 5 studies) (Figure 1). The adjusted prevalence taking into account the variance between diagnostic tools was 17.9% (95%CI: 13.0-23.4) with 52.7% of variance due to difference between tools. There was no publication bias (p = 0.789). There was no data on major depressive disorders.

The prevalence of depressive symptoms was 37.3% (95%CI: 19.3-57.3; 6 studies). The adjusted prevalence taking into account the variance between diagnostic tools was 33.3% (95%CI: 9.9-61.6) with 74.1% of variance due to difference between tools. There was no publication bias (p = 0.115).

The prevalence of major depressive symptoms was 7.9% (95%CI: 1.7-17.9; 2 studies). The adjusted prevalence taking into account the variance between diagnostic tools was 7.8% (95%CI: 3.0-14.5) with 43.3% of variance due to difference between tools. The *p* value on Egger test was 0.789.

In subgroup analysis, there was no difference between population-based and hospital-based for all outcomes except for major depressive disorders where the prevalence was higher in population-based study (12.6%; 95%CI: 8.8-17.0; 1 study) compared to hospital-based study (4.2%; 95%CI: 2.5-6.5; 1 study), p = 0.0001 (Supplementary Figures 2, 3, and 4). However, there was low number of studies in compared groups. The prevalence of depressive disorders was higher among women (23.8%; 95%CI: 18.7-29.3; 1 study) compared to men (14.5%; 95%CI: 9.3-20.6; 1 study), p = 0.0227) (Supplementary Figure 5). There was no difference for depressive symptoms (Supplementary Figure 6).

Discussion

This meta-analysis of data from 5,299 adults with hypertension living in five countries in Africa revealed that depressive disorders and symptoms are prevalent in this population with substantial heterogeneity according to the diagnostic tools. This systematic review suggests that approximately one on five and one-third of patients with hypertension have respectively depression and depressive symptoms.

Globally, there are dissimilarities between our findings and previous studies on depression among adults with hypertension. For instance, in China, a meta-analysis of 41 studies on the prevalence of depression in patients with hypertension found higher rate of depression with a pooled prevalence of 26.9% (95%CI: 21.7% - 32.3%) [10]. Our review revealed a higher prevalence of depression among patients with hypertension compared to occidental studies. For instance, considering data of United States Multi-Disciplinary Group Practice Observational Study which included 4,362 adult patients with hypertension, 13% had anxiety and/or depression [42]. A cross-sectional study done in Spain among 5,954 hypertensive patients with high cardiovascular risk factors found that 15.6% of them had depression [19]. These differences across regions can be explained by the changeability pertaining to the criteria and/or diagnostic tools used to screen depressive disorder [43,44]. Noteworthy, Li and colleagues who studied depressive disorder among patients with hypertension in a meta-analysis of 41 studies suggested that self-assessed screening tools of depression or depressive symptoms might overestimate the prevalence of depression [10]. Indeed, they found a 30% depression prevalence using self-administrated diagnostic scales versus a 21% prevalence using clinical-interviewed tools [10]. This could be linked to patients' confusion about symptoms possibly encountered in both depression and hypertension such as poor appetite, fatigue and sleep disturbances [10]. In our review, the most used diagnostic tool was the PHQ-9 and another fact to highpoint is that differences in prevalence can also be explained by the cut-off-points used for a same tool to define a positive screening for depression [32,45,46]. Mahmood and

colleagues while assessing depression among 411 hypertensive outpatients in a Pakistan hospital by using PHQ-9 with a score of 10 or above as cut-off point found a prevalence of 40.1% [47], more than two folds compared to our findings. In our study, we had a substantial heterogeneity for all analyses which can also be related to the variance between diagnostic tools used for depression assessment. The previously cited meta-analysis of Li and colleagues also showed evidence of high-level heterogeneity due to diagnostic tools considered in original studies [10].

In our sub-group analysis, we found that there was no difference between population-based and hospital-based for all outcomes except for major depressive disorders which prevalence was higher in population-based study. This result has to be cautiously interpreted regarding the amount of studies in each group (only one study per group measured with depression investigated with different tools). We also found that the prevalence of depressive disorders was higher among women compared to men. This finding is in accordance with what is known concerning gender differences in depression [48–50]. This can be linked to hormonal differences between the two genders, and the fact that women experience periods of physiological changes such as menstruation, pregnancy and perimenopause [49,51,52]. There are growing evidence on the potential positive role of hormone replacement therapy on postmenopausal depression [51,52]. This could be more pronounced in sub-Saharan African cultures considering the role of male gender in families, with as consequence a lesser capacity to express their psychological distress [53–55].

This meta-analysis highlights the fact that depressive disorder is frequently encountered among hypertensive patients compared to the general population. This review might substantiate the relevancy to conduct further studies with the aim to investigate on the better diagnosis tool for depression among hypertensive patients in order to reduce heterogeneity of results. Moreover, our review could justify carrying out epidemiological studies on the depression-hypertension

comorbidity in other African regions in order to have more representative regional picture of the evidence. Since we were able to identify only 11 studies in the last 20 years our study calls for more primary research on the relationship between hypertension and mental health in the continent, by using homogenous diagnostic tools. Researchers, clinicians, and public health policy makers can also explore implementing registries to better measure the burden of mental health disorders in the continent [56–58]. All this might help to establish adapted policies pertaining to the management of hypertensive patients with depression, notably for a tailored pharmacological treatment [18,59,60]. Nevertheless, our analysis could already draw clinician's awareness on the necessity to screen depression symptoms among hypertensive patients, especially since previously published works found that comorbid depression contribute to more deleterious cardiovascular outcomes [8,10,15,16,18]. A meta-analysis of prospective cohort studies suggested that people with depressive disorders had higher risk of hypertension [61]. Therefore, implementing strategies to reduce the burden of depressive disorders could help to reduce the prevalence of hypertension. Although pharmacological interventions can help to reduce the burden of depressive disorders [62], cost-effective non-pharmacological interventions should be explored first in a context of resources limited setting like most of countries in Africa [63, 64].

This study should however be interpreted considering some limitations. First and most common to meta-analyses of prevalence studies [65], we found a huge heterogeneity between studies for which we undertook subgroup analysis to investigate sources of heterogeneity and adjusted analysis to take account the variance due to diagnostic tools. However, some characteristics that may further explain heterogeneity were not reported or there were not enough studies to conduct such analysis including sub-regions and age groups. Second, there was a substantial variability regarding the representativeness of regions and countries, with some ones less or not represented. This may weaken the generalizability of our findings and call for more

epidemiological studies in this region. Not all studies had low risk of bias, especially, most of studies used non-probabilistic sampling. However, due to low number of studies included in this meta-analysis, we were not able to perform sensitivity analysis to assess the robustness of our findings based on methodological quality.

Despite these limitations, this first systematic review and meta-analysis on depressive disorders/symptoms in people living with hypertension in Africa provided a clear summary of the existing knowledge. This systematic review is a starting point for understanding the epidemiology and relationship between mental health and hypertension in African countries where it is challenging to have such data. A protocol had been registered before, and we used rigorous methodological and statistical procedures to obtain and pool data. Furthermore, we have taken in account the variability due to diagnostic tools. There was no publication bias.

Conclusions

Overall, our review found that depressive disorders and symptoms are prevalent in people living with hypertension in select African countries. Including an assessment of mental health in patients with hypertension seems prudent, with the potential for intervention. However, since our analysis has limitations pertaining to diagnostic tools consistency within studies and also to the unrepresentative geographic distribution, further studies would be relevant in order to reinforce our findings. All this could be a support for a personalized management of patients with hypertension and depression.

Author Contributors

Conception: JJB, FTE. Design of the protocol: FTE, JJB. Literature search: JJB. Studies' selection: FTE, JJB. Data extraction: FTE, JJB. Data management: JJB. Data synthesis and

analysis: JJB. Writing of the first draft: JJB, FTE. Critical revision: FTE, MNT, JJB. Approved the final version: FTE, MNT, JJB. Guarantor of the review: JJB.

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Competing interests

We declare no competing interests.

Patient consent

Not applicable.

Data sharing statement

All data generated for this study are in the manuscript and its supporting files.

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Figures legend

Figure 1. Crude prevalence of depressive disorders/symptoms in people living with hypertension in Africa

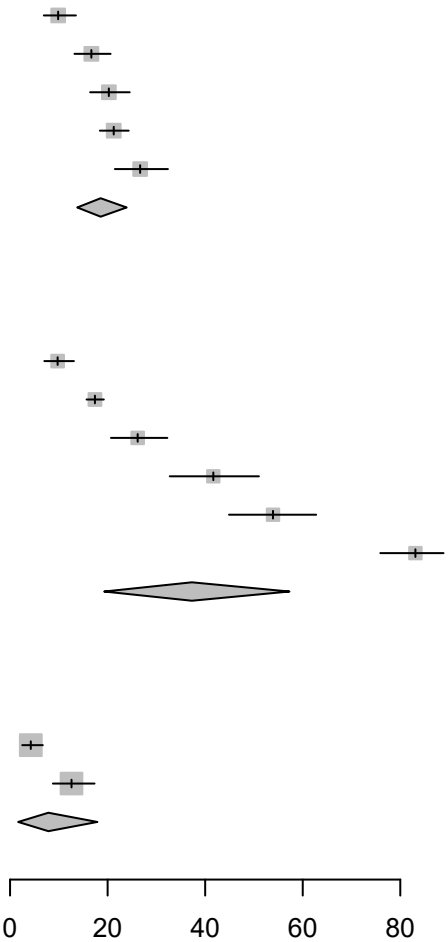
507 **Table 1. Characteristics of included studies**

Author	Year	Design, Setting	Diagnosis of conditions	Validity of the tool used	Language of the tool used	Inclusion criteria	Population	Period of inclusion	Country	Sample
Ademola	2019	Cross-sectional, Hospital	Patient Health Questionnaire 9 (PHQ-9)	Validated	NR	Age ≥ 18 y, diagnosis of hypertension, treatment with an antihypertensive medication for at least 12 months	%Males: 41.7; Mean age: 57	2013	Ghana, Nigeria	357
Bhana	2015	Cross-sectional, Population	Depression module of the Structured Clinical Interview for DSM-IV (SCID)	NR	English, seTsawa	Age ≥ 18 y, clinic attendance for routine chronic disease services (e.g., HIV, hypertension, diabetes) and ability to comprehend and complete study components in Tswana or English.	NR	2014	South Africa	345
Geldsetzer	2019	Cross-sectional, Population	Center for Epidemiological Studies Depression (CES-D) screening tool	NR	English, Shangaan	Age ≥ 40 y and continuously living in the area during the 12 months prior to study enrolment	%Males: 37.4 Mean age : NR	2014-2015	South Africa	1822
Grimsrud	2009	Cross-sectional, Population	Composite International Diagnostic Interview Version 3.0 (CIDI-3.0)	NR	NR	South Africans ≥ 18 y who lived in households and hostels during the field period of the study	%Males: 28.0; Mean age: 50.3	2002-2004	South Africa	767
Hamer	2012	Cross-sectional, Population	Patient Health Questionnaire 9 (PHQ-9)	Validated	English and local language	Age: 25-60 y with hypertension	NR	2008-2009	South Africa	254
Igwe	2013	Cross-sectional, Hospital	Mini International Neuro-psychiatric Interview (MINI)	NR	NR	Age: 18 - 64 y. Hypertension for at least 1 year and stable without need for hospital admission for 3 months prior to assessment	%Males: 53.7; Mean age: 50.4	2010-2011	Nigeria	270
Iloh	2018	Cross-sectional, Hospital	Patient Health Questionnaire 9 (PHQ-9)	Validated	NR	Age ≥18 y with hypertension	%Males: 40.7; Mean age : NR	2017	Nigeria	142

Kretchy	2014	Cross-sectional, Hospital	Depression Anxiety Stress Scale (DASS) – 21	NR	NR	Age ≥ 18 y, a diagnosis of hypertension, reporting prescription of at least one antihypertensive medication for a minimum of two months	%Males: 37.3; Mean age : NR	2012	Ghana	400
Okunrinboye	2019	Cross-sectional, Hospital	Mini International Neuro-psychiatric Interview (MINI)	NR	Yoruba, English	Age: 18 and 64 y who were diagnosed by a consultant physician at the Centre as suffering from hypertension and have been on anti-hypertensive medication for at least 6 months, spoke Yoruba or English language fluently	%Males: 38.0; Mean age: 59.6y	2012	Nigeria	400
Umer	2019	Cross-sectional, Hospital	Patient Health Questionnaire 9 (PHQ-9)	Validated	English, Afan Oromo, Amharic	Age ≥ 18 y, follow-up for hypertension	%Males: 52.8; Mean age : NR	2014	Ethiopia	128
Yaméogo	2015	Cross-sectional, Hospital	Hospital Anxiety and Depression Scale (HADS)	NR	NR	Hypertensive consenting adult outpatients	%Males: 40.1; Mean age: 54.6y	2010-2011	Burkina-Faso	414

NR: not reported.

Author, Year	Cases	Total	Prevalence, %	[95% C.I.]	Weight
A. Depressive disorders					
Bhana, 2015	34	345	9.9	[6.9; 13.5]	19.9%
Yaméogo, 2015	69	414	16.7	[13.2; 20.6]	20.0%
Okunrinboye, 2019	81	400	20.2	[16.4; 24.5]	20.0%
Grimsrud, 2009	163	767	21.3	[18.4; 24.3]	20.2%
Igwe, 2013	72	270	26.7	[21.5; 32.4]	19.8%
Subgroup prevalence		**2196**	**18.6**	**[13.8; 23.9]**	**100.0%**
Heterogeneity: I^2 = 89.2%, p < 0.0001					
B. Depressive symptoms					
Kretchy, 2014	39	400	9.8	[7.0; 13.1]	17.0%
Geldsetzer, 2019	317	1822	17.4	[15.7; 19.2]	17.3%
Ademola, 2019	62	237	26.2	[20.7; 32.2]	16.8%
Ademola, 2019	50	120	41.7	[32.7; 51.0]	16.2%
Umer, 2019	69	128	53.9	[44.9; 62.8]	16.3%
Iloh, 2018	118	142	83.1	[75.9; 88.9]	16.4%
Subgroup prevalence		**2849**	**37.3**	**[19.3; 57.3]**	**100.0%**
Heterogeneity: I^2 = 98.7%, p < 0.0001					
C. Major depressive symptoms					
Kretchy, 2014	17	400	4.2	[2.5; 6.7]	50.3%
Hamer, 2012	32	254	12.6	[8.8; 17.3]	49.7%
Subgroup prevalence		**654**	**7.9**	**[1.7; 17.9]**	**100.0%**
Heterogeneity: I^2 = 93.3%, p = 0.0001					



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

Francky Teddy **Endomba**, Mazou N. **Temgoua**, Jean Joel **Bigna**

APPENDIX

Supplementary Table 1. Search strategy

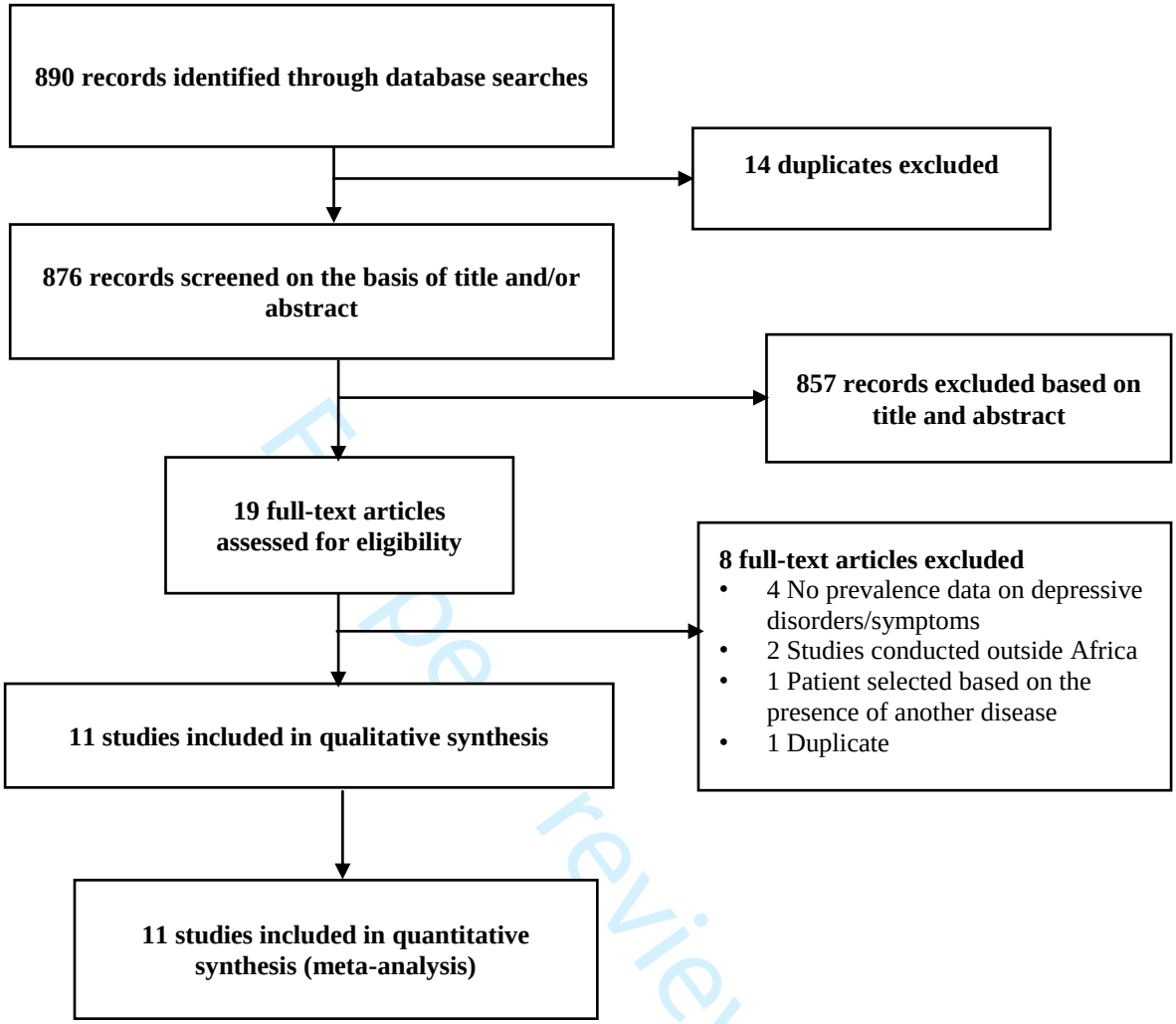
Search	Search terms
#1	'africa'/exp OR africa OR 'algeria'/exp OR algeria OR 'angola'/exp OR angola OR 'benin'/exp OR benin OR 'botswana'/exp OR botswana OR 'burkina faso'/exp OR 'burkina faso' OR 'burundi'/exp OR burundi OR 'cameroon'/exp OR cameroon OR 'canary islands'/exp OR 'canary islands' OR 'cape verde'/exp OR 'cape verde' OR 'central african republic'/exp OR 'central african republic' OR 'chad'/exp OR chad OR 'comoros'/exp OR comoros OR 'congo'/exp OR congo OR 'democratic republic of congo' OR 'djibouti'/exp OR djibouti OR 'egypt'/exp OR egypt OR 'equatorial guinea'/exp OR 'equatorial guinea' OR 'eritrea'/exp OR eritrea OR 'ethiopia'/exp OR ethiopia OR 'gabon'/exp OR gabon OR 'gambia'/exp OR gambia OR 'ghana'/exp OR ghana OR 'guinea'/exp OR guinea OR 'guinea bissau'/exp OR 'guinea bissau' OR 'ivory coast'/exp OR 'ivory coast' OR 'cote ivoire' OR jamahiriya OR 'kenya'/exp OR kenya OR 'lesotho'/exp OR lesotho OR 'liberia'/exp OR liberia OR 'libya'/exp OR libya OR 'madagascar'/exp OR madagascar OR 'malawi'/exp OR malawi OR 'mali'/exp OR mali OR 'mauritania'/exp OR mauritania OR 'mauritius'/exp OR mauritius OR 'mayotte'/exp OR mayotte OR 'morocco'/exp OR morocco OR 'mozambique'/exp OR mozambique OR 'namibia'/exp OR namibia OR 'niger'/exp OR niger OR 'nigeria'/exp OR nigeria OR principe OR 'reunion'/exp OR reunion OR 'rwanda'/exp OR rwanda OR 'sao tome' OR 'senegal'/exp OR senegal OR 'seychelles'/exp OR seychelles OR 'sierra leone'/exp OR 'sierra leone' OR 'somalia'/exp OR somalia OR 'south africa'/exp OR 'south africa' OR 'st helena'/exp OR 'st helena' OR 'sudan'/exp OR sudan OR 'swaziland'/exp OR swaziland OR 'tanzania'/exp OR tanzania OR 'togo'/exp OR togo OR 'tunisia'/exp OR tunisia OR 'uganda'/exp OR uganda OR 'western sahara'/exp OR 'western sahara' OR 'zaire'/exp OR zaire OR 'zambia'/exp OR zambia OR 'zimbabwe'/exp OR zimbabwe OR 'central africa'/exp OR 'central africa' OR 'central african'/exp OR 'central african' OR 'west africa'/exp OR 'west africa' OR 'west african'/exp OR 'west african' OR 'western africa'/exp OR 'western africa' OR 'western african'/exp OR 'western african' OR 'east africa'/exp OR 'east africa' OR 'east african'/exp OR 'east african' OR 'eastern africa'/exp OR 'eastern africa' OR 'eastern african'/exp OR 'eastern african' OR 'north africa'/exp OR 'north africa' OR 'north african'/exp OR 'north african' OR 'northern africa'/exp OR 'northern africa' OR 'northern african'/exp OR 'northern african' OR 'south african'/exp OR 'south african' OR 'southern africa'/exp OR 'southern africa' OR 'southern african'/exp OR 'southern african' OR 'sub saharan africa'/exp OR 'sub saharan africa' OR 'sub saharan african'/exp OR 'sub saharan african' OR 'subsaharan africa'/exp OR 'subsaharan africa' OR 'subsaharan african'
#2	'depression'/exp OR depression OR 'depressive disorder'/exp OR 'depressive disorder' OR 'depressive symptom'/exp OR 'depressive symptom' OR 'depressive neuros*' OR 'depressive syndrome*'

#3	'hypertension'/exp OR hypertension OR 'high blood pressure'/exp OR 'high blood pressure' OR (high AND ('blood'/exp OR blood) AND ('pressure'/exp OR pressure))
#4	#1 AND #2 AND #3

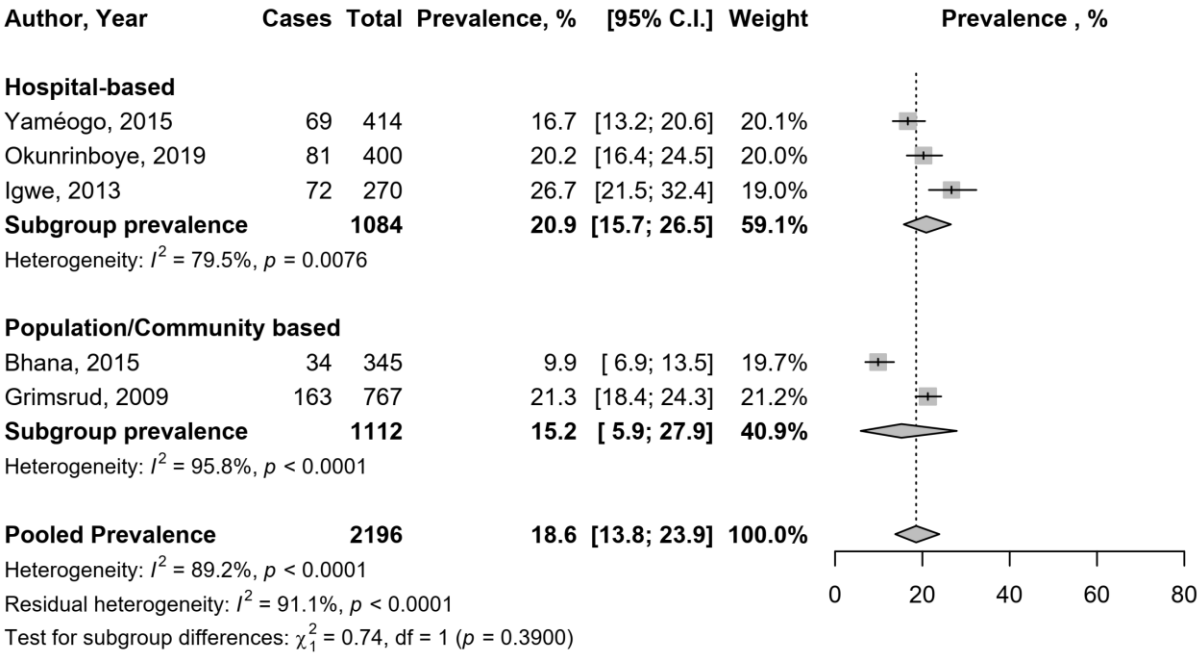
Supplementary Table 2. Methodological quality of included studies

Author, Year	Sampling method	Timing of data collection	Sample size adequate	Response rate	Same method of data collection for all participants	SUMMARY (Risk of bias)
Ademola, 2019	Convenience	Prospectively	No	Not described	Yes	Moderate
Bhana, 2015	Convenience	Prospectively	Yes	Not described	Yes	Moderate
Geldsetzer, 2019	Stratified Random	Prospectively	Yes	Adequate	Yes	Low
Grimsrud, 2009	Stratified Multistage	Prospectively	Yes	Not described	Yes	Low
Hamer, 2012	Convenience	Prospectively	Yes	Not described	Yes	Moderate
Igwe, 2013	Convenience	Prospectively	Yes	Not described	Yes	Moderate
Iloh, 2018	Convenience	Prospectively	Yes	Not described	Yes	Moderate
Kretchy, 2014	Time-Location	Prospectively	Yes	Not described	Yes	Moderate
Okunrinboye, 2019	Systematic Random	Prospectively	Yes	Not described	Yes	Low
Umer, 2019	Convenience	Prospectively	No	Adequate	Yes	Moderate
Yaméogo, 2015	Convenience	Prospectively	Yes	Not described	Yes	Moderate

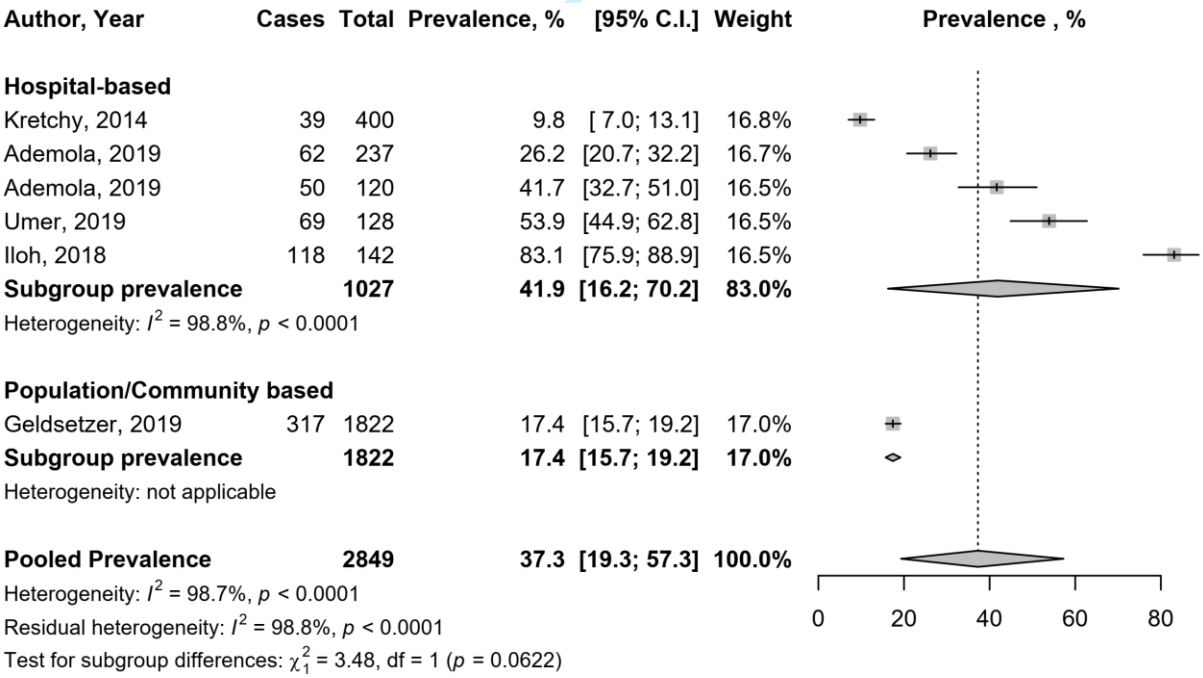
Supplementary Figure 1. PRISMA flow diagram



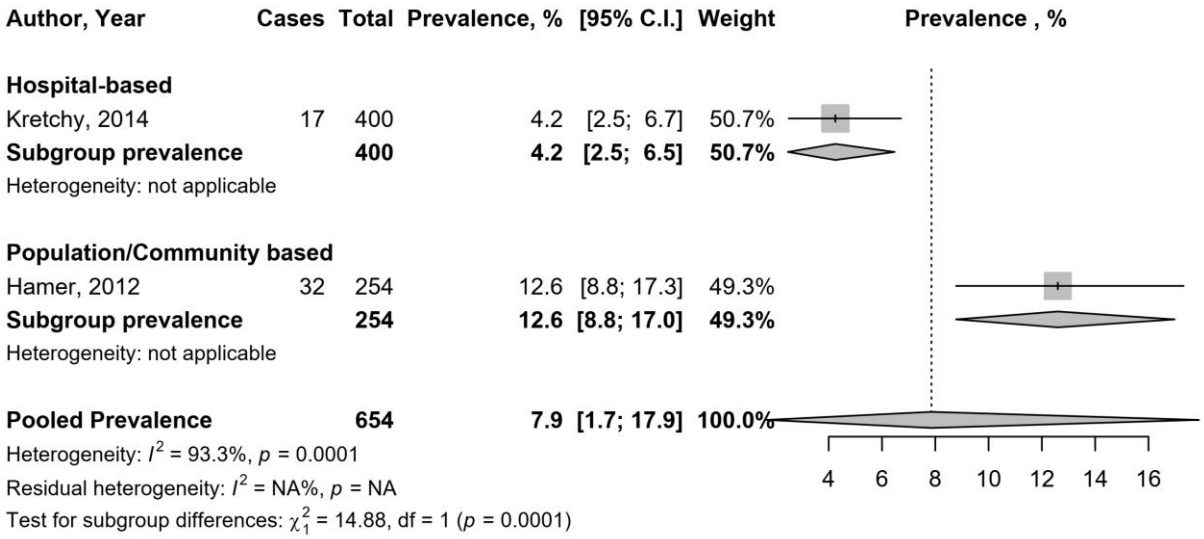
Supplementary Figure 2. Meta-analysis prevalence of depressive disorders by setting



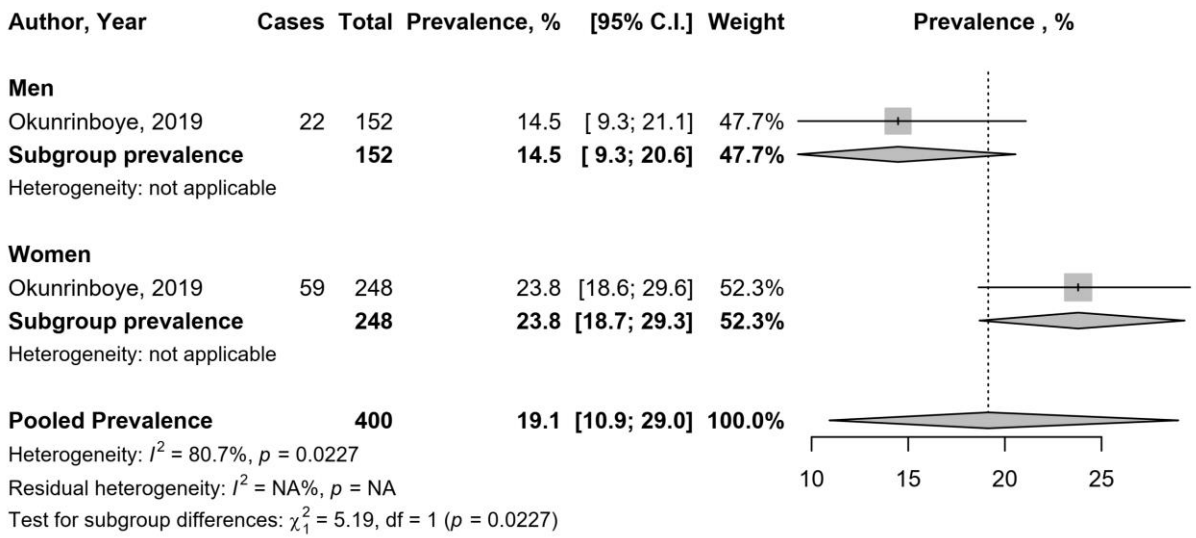
Supplementary Figure 3. Meta-analysis prevalence of depressive symptoms by setting



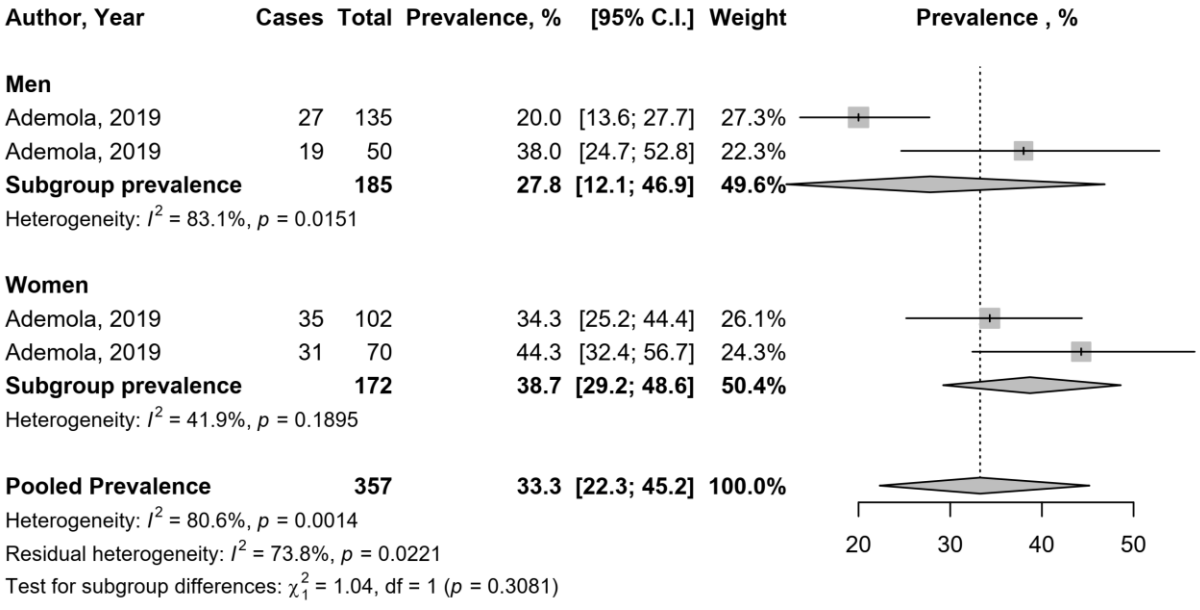
Supplementary Figure 4. Meta-analysis prevalence of major depressive disorders by setting



Supplementary Figure 5. Meta-analysis prevalence of depressive disorders by sex



Supplementary Figure 6. Meta-analysis prevalence of depressive symptoms by sex



PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5-6
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	6
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6-7
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	7
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	7, Appendix
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	7
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	7-8
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	7-8
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	8
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	8
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	8

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	8
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	8
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	9
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	9
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	9, Appendix
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	9, Table 1
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	9-10
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	9-10
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	9-10
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	10
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	12
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	12
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	13

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