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Prevalence of uncontrolled hypertension in people with comorbidities in sub-Saharan Africa: a systematic review and meta-analysis

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Abstract

Background: The burden of uncontrolled hypertension in sub-Saharan Africa (SSA) is high and hypertension is known to co-exist with other chronic diseases such as kidney disease, diabetes among others. This is the first systematic review and meta-analysis to determine the burden ofuncontrolled hypertension among patients with comorbidities in SSA.

Methods: A comprehensive search was conducted on MEDLINE, Excerpta Medica Database (Embase), and Web of Science to identify all relevant articles published between January 1st, 2000 and June 15th, 2019. We included studies that reported on the prevalence of uncontrolled hypertension among people in SSA who report taking antihypertensive treatment and have another chronic condition A random-effects meta-analysis was performed to obtain the pooled estimate of the prevalence of uncontrolled hypertension among patients with comorbid conditions while on treatment across studies in SSA.

Results: In all 18 articles were included for meta-analyses. Eleven articles were among diabetic patients, three articles among HIV patients, two were among stroke patients while chronic kidney disease and atrial fibrillation had one article each. The pooled prevalence of uncontrolled hypertension among patients with comorbidities was 75.9% (95% CI, 67.9%-83.0%); I^2 96.0%), varying from 66.4% in patients with HIV to 100.0% in patients with atrial fibrillation. Subgroup analysis showed differences in uncontrolled hypertension prevalence by various study-level characteristics

Conclusion: This study suggests a high burden of uncontrolled hypertension in people with comorbidities in SSA. Strategies to improve the control of hypertension among people with comorbidities are needed. PROSPERO registration number CRD42019108218.

Word count – 240

Key word – Uncontrolled hypertension, comorbidities, sub-Saharan Africa

Strengths and limitations of this study

- A published comprehensive protocol was used to identify all available evidence without language restriction, reporting in accordance with PRISMA guidelines, search using multiple electronic databases, searching grey literature, contacting experts in the field for additional data sources to reduce study selection bias, and heterogeneity test by subgroup analyses and sensitivity analyses.
- Two independent reviewers were used in data extraction and the assessment of the risk of bias.
- The prevalence of uncontrolled hypertension (UHTN) in some comorbidities such as atrial fibrillation and chronic kidney disease were reported in single studies.
- Most of the studies included in the meta-analysis were hospital based studies that used non-random sampling procedures.
- There was substantial heterogeneity between the studies.

Introduction

Hypertension is an important risk factor for cardiovascular diseases (CVDs) and a leading contributor to death globally (1). An estimated 1.4 billion people have hypertension globally with three quarter (75%) of this population living in low-and –middle-income countries (2, 3). Worldwide trends analysis based on a large dataset from multiple studies conducted between 1975 and 2015 in 200 countries showed no change in global mean blood pressure, but a a substantial downward trend in high income countries and a rise in low and middle income countries (4). Levels of hypertension awareness, treatment and control improved by 2.9% in high income countries while in low-middle-income countries neglible improvement in awareness, treatment, and control were observed (3, 4). Sub-Saharan African (SSA) countries have the highest (30%) prevalence of hypertension in the world (5). In the lastest systematic review and meta-analysis on hypertension in SSA, Ataklte et al (5), reported a (93%) high prevalence of uncontrolled hypertension (UHTN).

Hypertension often co-exists with comorbidities such as chronic kidney disease, diabetes, and hypercholesterolemia among others (6-9). These comorbidities could explain part of the inadequacy in blood pressure control. Some studies conducted in Europe and the US found that patients with diabetes mellitus had a significantly increased risk of uncontrolled blood pressure (10, 11). Another study conducted in the UK has shown that achieving optimal blood pressure control in patients with hypertension and type 2 diabetes produces an important decrease in the risks associated with diabetes (12). This study provides evidence that optimal blood pressure control in type 2 diabetes has implications for the management of blood pressure in diabetic patients.

In recent years, public health efforts to promote prevention, awareness and treatment of hypertension in SSA have intensified (13-16) but hypertension control remains low (17-21). Despite several studies conducted on UHTN in people with comorbidities, pooled estimations of the burden are not available for comorbidities such as diabetes, dyslipidaemia, stroke, HIV, obesity, atrial fibrillation. From a clinical perspective, it is important to understand why patients on treatment are

not attaining optimal blood control and whether their pre-existing comorbidities contribute to the lack of control of blood pressure. Therefore, to inform policy, practice and the development of guidelines for hypertension for integrated care among patients with comorbid conditions, it is critical to understand the burden of UHTN in people with comorbidities. The purpose of this review is to summarize the evidence on and estimate the prevalence of UHTN in patients with comorbidities in SSA and to explore factors associated with UHTN in people with comorbidities .

Methods

Protocol and registration

The protocol for this systemic review and meta-analysis was registered on the International Prospective Register of Systematic Reviews (PROSPERO CRD42019108218) and published (22). The reporting was done according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA-P) guidelines (23).

Search Strategy

We systematically searched MEDLINE via Ovid, Excerpta Medica Database (Embase), and Web of Science from January 1st, 2000 to June 15th, 2019**.** The search strategy included the following relevant terms: *uncontrolled hypertension, hypertension, uncontrolled blood pressure, high blood pressure , a list of comorbidities, and sub-Saharan Africa (Detailed search strategy list is attached as supplement (Supplement file S1).* Additionally, the reference lists of the included studies were reviewed to identify other relevant studies.

Eligibility criteria

Studies were included if (1) they provided primary data on the prevalence of hypertension in accordance with the sevent report of the Joint National Committee (JNC7) among those who reported taking antihypertensive treatment and had a comorbid condition, (2) participants had been diagnosed with one of the comorbidities of interest – diabetes, dyslipidemia, obesity, chronic kidney disease,

stroke or transient ischemic attack, coronary heart disease, heart failure, peripheral vascular disease, atrial fibrillation, depression and HIV (Table S1), (3) participants were 15 and above years, (4) the study was published in any language, and (5) the study was conducted in a sub-Saharan Africa. The following types of study designs were excluded: (1) case studies, commentaries, editorials, letters, qualitative studies, and systematic reviews; (2) studies that included hypertension prevalence but did not report on the prevalence of hypertension among those on antihypertensive medication; and (3) studies of pregnancy-related hypertension and secondary hypertension.

Study selection

Two researchers independently screened the titles and abstracts (SFM & ASM). Two researchers (SFM & ASM) also assessed full-text reviews of the articles independently for final inclusion. The reference lists of potentially relevant publications were manually searched for additional publications. Disagreements were resolved by consensus. For multi-national studies, data were separated to show the estimate at the country level.

Data items and collection process

SFM and ASM independently screened the full texts of included studies. SFM extracted data from the selected studies, and ASM checked the data for accuracy. A standardized data extraction table was created (Table 1) and included the following data from all eligible articles: first author name, year of publication, language, country of the study, study design, sample size, study period, study setting, sampling method, the timing of data collection, data source, use of comorbidity specific hypertension control cuttoff, male proportion, age of participants (mean or median), type of comorbidity (diabetes, stroke, HIV, chronic kidney disease, atrial fibrillation), and main outcome of interest uncontrolled hypertension proportion or the data to cumpute it.

Risk of bias in individual studies

A tool developed by Hoy et.al (24) for prevalence studies was adapted and used to assess the methodological quality of included studies by evaluating the extent to which they addressed bias in 9 areas of internal and external validity (Table S2). Each of the nine areas was scored one if yes (high quality) and zero if no (poor quality), and a total quality score was calculated by summing the individual scores. Total scores ranged from 0 to 9, with higher scores indicating higher quality. Studies were then classified as having a low (>8), moderate (6–8), or high (≤5) risk of bias. Two researchers (SFM and MKM) independently assessed each of the included publications and disagreements was resolved through discussion.

Patient and Public Involvement

This research was done without patient involvement. There was no involvement of patients or members of the public in the design, or conduct, or reporting, or dissemination plans of this research.

Synthesis of results

The statistical approach used in this meta-analysis followed the study protocol (22). Crude numerators and denominators from the individual studies were used to recalculate the study-specific unadjusted prevalence estimates. Variances of the study-specific estimates were stabilized using the double arcsine transformation to minimise the effect of studies with very small or very large prevalence estimates on the overall estimate (16) and then a random-effects meta-analysis was performed (17) to determine the pooled estimate of the prevalence of UHTN among patients with comorbidities overall and also among people with diabetes, HIV and stroke separately while on antihypertensive treatment across the included studies in SSA. Prevalence estimates were also summarised by comorbidities, publication year, sample size, study setting, sampling, risk of bias, gender proportionmean age and geographic regions.

Heterogeneity was explored using Cochrane's Q and quantified by I^2 statistics (25, 26). Subgroup analyses were performed based on the following; mean age, gender proportion of participants, patient comorbidities, study design, study setting, sample size, use of recommended comorbidity specific blood pressure control cut-offs, countries, regions (Eastern, Western, Central, and Southern Africa), and by Gross National Income (GNI) were be performed to identify the possible sources of heterogeneity. Sensitivity analyses were performed to assess the robustness of the findings by excluding studies with a high risk of bias.

Funnel plots and Egger asymmetry test were used to assess publication bias, with $P < .10$ considered to be statistically significant for publication bias (27). Inter-rater agreements between the researchers involved in study inclusion and those involved in the identification of risk of bias were assessed using κ Cohen's coefficient (20).

All analyses were performed using 'metaprop' routine using StataSE version 16 (StataCorp LLC).

Results

Study selection

From the electronic database search, 7365 records were identified. An additional 35 articles were identified through reference tracing and from other sources. After duplicate removal, 4776 remained for the title and abstract screening. After screening, we found 4267 records to be irrelevant and excluded them. The full texts of 509 articles and reports were retrieved and assessed for eligibility, resulting in the inclusion of 18 studies for the meta-analysis (figure 1). The inter-rater agreement for study selection was 0.77.

Study characteristics

Table 1 and Table S3 provide detailed information on the included studies. In total, 3,469 participants were included across 18 studies. Most of the studies were cross-sectional (17, 94%), in English (17, 94%), hospital-based (11, 52%), used consecutive sampling (14, 78%), and prospectively collected data (12, 67%). The mean (SD) participant age from the 18 studies (28-45) providing this information was

56.7 (0.11) years. Study sample sizes ranged from 35 to 567 participants. The proportion of male participants in the included studies was reported in all studies and it ranged from 25.5% to 60.9% (28-45). Of the included studies, 11 (29-31, 33, 34, 38-42, 45) reported on diabetes, three (32, 35, 37, 43) reported on HIV, two (28, 44) reported on stroke, and one each reported on chronic kidney disease (32) and atrial fibrillation (36). None of the included studies reported on obesity, dyslipidaemia, coronary heart disease, heart failure, peripheral heart disease, and depression.

Table 1: Characteristics of the Included Studies

Study	Country	Age (Mean/Median)	Study period	Study site	Sampling	Male %	Sample size	UHTN%	Risk of bias
Atrial Fibrilation									
Jardine et.al,2014	South Africa	67±13	Feb 2010 - Mar 2011	Health center	Consecutive	59.9	198	100.0	High
Chronic Kidney Disease									
Babua et.al 2015	Uganda	42.8	Jun - Feb 2013	Hospital	Consecutive	51.2	191	76.0	Low
Diabetes									
Abera et.al, 2016	Ethiopia	56.3±10	Aug - Jan 2015	Hospital	Consecutive	59.9	382	85.0	Low
Adeniyi et.al, 2016	South Africa	61.3±11.8	Jul to Nov 2013	Hospital	Consecutive	28.3	265	75.5	Low
Agaba et.al, 2009	Nigeria	51±12	Jun - Sept 2004	Hospital	Consecutive	40.2	79	70.9	Moderate
Choukem et.al 2006	Cameroon	56.6±13.3	6 months	Hospital	Consecutive	50.5	98	79.6	Low
Cohen et.al, 2010	Malawi	53.2±14.0	Mar - Jun 2007	Hospital	Consecutive	39.8	253	72.7	Low
Mwita et.al, 2012	Tanzania	51.6±11.2	Feb - Sep 2010	Health center	Consecutive	38.0	67	66.0	Low
Pinchevsky et.al, 2017	South Africa	53.9±11.5	May - Aug 2015	Health center	Consecutive	46.1	459	78.0	Low
Pinchevsky et.al, 2013	South Africa	63 ± 11.9	July 2008-2009	Hospital	Random	44.6	567	54.2	Low
Rotchford,2002	South Africa	56.5±10.4	2 months in 1999	Hospital	Consecutive	26.9	129	86.0	Low
Soetedjo et.al 2018	South Africa	53±9.9	Dec 2013 - Jun 2016	Health center	Consecutive	35.9	48	66.7	Low
Yameogo et.al,2012	Senegal	58.2±9.2	Mar 2007 - Jul 2008	Hospital	NR	25.5	52	80.8	High
HIV									
Hyle et.al, 2019	South Africa	38.4±8.3	2015	Health center	Consecutive	33.0	54	83.0	Low
Muddu et.al, 2019	Uganda	43.6±11.5	Jan 2014 - Jan 2017	Health center	Consecutive	39.4	91	41.8	Low
Steffen et.al, 2017	Malawi	36±9.3	Not indicated	Health center	NR	42.8	35	77.1	Moderate
Stroke									
Abboud et.al, 2013	South Africa	63.5±11.3	Jan 2007 - Dec 2008	Hospital	Random	58.5	217	88.0	Low
Wahab et.al, 2017	Nigeria	59±13.1	Feb 2009 - Apr 2011	Hospital	Consecutive	60.9	284	60.2	Low

NR=Not reported

Risk of Bias Assessment

The risk of bias was assessed in all included studies of the 18 included studies. Most studies were categorized as having some concern for bias with two (11.1%) (36, 45) studies being deemed to have high risk of bias. Two studies (31, 43) (11.1%) had a moderate risk of biaswhile 14 studies (28-30, 32-35, 37-42, 44) (77.8%) had a low risk of bias. The inter-rater agreement for the risk of bias assessment was 0.65. Additional details on the domains assessed are included in the risk of bias summary table in the supplement (Table S2).

Prevalence of uncontrolled hypertension among patients with comorbidities

Eighteen publications reported on uncontrolled hypertension among patients with comorbidities (Table 1). The majority of the studies were from South Africa (8, 44.4%) (28, 30, 35, 36, 39-42). Uganda (32, 37), Nigeria (31, 44), and Malawi (34, 43) had two (11.1%) studies each while Ethiopia (29), Tanzania (38), and Senegal (45) had one study (5.6%) each. The reported prevalence of UHTN among people with comorbidities ranged from 41.8% (95% CI, 32.2%-52.0%) in Uganda to 100.0% (95% CI, 98.1%-100.0%) in South Africa. The pooled uncontrolled hypertension prevalence estimate in patients with comorbidities from the random-effects meta-analysis was 75.9% (95% CI, 67.9%-83.0%). Substantial heterogeneity (I^2 = 96.1%; P < .0001) existed in the included studies (Table 2). Absence of publication bias is suggested by the symmetrical visual inspection of the funnel plot, confirmed by the Egger's test (P < .001) (Figure 2).

Table 2: Meta-analysis results for the prevalence of uncontrolled hypertension in people with comorbidities in sub-Saharan Africa

	Prevalence (95%CI)	No of studies	Number of Participants	I^2 (95%CI)	$p^{heterogeneneity}$
Overall	75.9 (67.9-83.0)	18	3469	96.1	<0.0001
By comorbidity					
Atrial fibrillation	100.0 (98.1-100.0)	1	198	-	-
Chronic kidney disease	75.9 (69.4-81.4)	1	191	-	-
Diabetes	74.5 (67.1-81.3)	11	2399	93.1	<0.001
HIV	66.2 (38.3-89.3)	3	180	-	-

Stroke	73.1 (69.1-76.9)	2	501	-	-
By region					
Eastern	68.4 (49.7-84.4)	4	731	95.6	<0.001
Western	69.8 (57.0-81.2)	3	415	-	-
Central	79.6 (70.6-86.4)	1	98	-	-
Southern	79.8 (68.1-89.4)	10	2225	97.3	<0.001
By risk of bias					
Low	72.9 (65.7-79.5)	14	3105	94.5	<0.001
Moderate	72.0 (63.3-80.0)	2	114	-	-
High	99.0 (97.1-100.0)	2	250	-	-
By study size					
Small studies	70.4 (60.1-79.8)	8	524	83.4	<0.001
Large studies	79.5 (69.0-83.0)	10	2945	97.7	<0.001
By period of publication					
Before 2015	79.4 (66.5-89.9)	10	1851	97.3	<0.001
After 2015	71.1 (61.6-79.8)	8	1618	93.1	<0.001
By gender proportion					
More females	71.0 (63.3-78.1)	12	2099	91.9	<0.001
More males	84.1 (69.5-94.7)	6	1370	97.6	<0.001
By sampling					
Consecutive	76.1 (67.6-83.7)	14	2598	95.6	<0.001
Random	64.5 (61.1-67.9)	2	784	-	-
By setting					
Hospital	75.5 (67.7-82.3)	11	2517	94.7	<0.001
Health center	76.0 (55.7-91.6)	7	952	97.3	<0.001
By comorbidity HTN target					
Comorbidity target used	70.7 (61.3-79.2)	11	1735	93.3	<0.001
Comorbidity target not used	83.0 (72.4-91.4)	7	1734	96.3	<0.001
By Gross National Income					
Below SSA Average	72.7 (63.4-81.0)	8	1169	97.5	<0.001
Above SSA average	78.3 (66.1-88.4)	10	2300	90.2	<0.001

SSA=sub-Saharan Africa **P^{egger}= 0.623**

Subgroup analysis revealed differences in uncontrolled hypertension prevalence by comorbidity (Figure 3). Adults with atrial fibrillation reported the highest uncontrolled hypertension estimate (100.0% [95% CI, 98.1%- 100.0%]), followed by adults with chronic kidney disease (75.9% [95% CI, 69.4%-81.4%]). The lowest pooled uncontrolled hypertension prevalence estimate was found in adults with HIV (66.2% [95% CI, 38.3%-89.3%]). Pooled UHTN prevalence differed by geographic regions; studies conducted in the Southern and Central region reported higher prevalence's (79.8% [95% CI,

68.2%-89.3%]) and (79.6% [95% CI, 70.6%-86.4%]) respectively than studies conducted in Eastern and Western regions (68.4% [95% CI, 49.7%-84.4%]) and (69.8% [95% CI, 57.0%-81.2%]) respectively. Prevalence varied by sample size; large studies reported a higher prevalence (79.5% [95% CI, 69.1%-88.2%]) compared to small studies (70.4% [95% CI, 60.1%-79.8%]) (table 2). Studies that used the recomended hypertension control value for each comorbidity reported lower pooled prevalence of uncontrolled hypertension (70.1 [95% CI, 57.4-81.5]) compared to those that did not use the recomemded comorbidity specific blood pressure control value (78.2 [95% CI, 73.1-82.9]). Studies that had below the average SSA GNI reported a lower prevalence of UHTN (72.7 [95% CI, 63.4-81.0]) compared to studies above the average SSA GNI (78.3 [95% CI, 66.1-88.4]).

The univariable analysis of the UHTN prevalence association with comorbidities explained 14.4% of the heterogeneity (Table S4). The use of the recommended comorbidity specific blood pressure control explained 26.6% of the heterogeneity but this was only marginally significant at 10%. The multivariable meta-regression analysis, comorbidities and the recomended hypertension control value for each comorbidity explained 32.4% of the 96.1% residual heterogeneity. However, the differences noted in the final multivariable meta-regression were not statistically significant.

Sensitivity analysis done by excluding studies with high risk of bias from the analysis did not show any influence on the robustness of the findings in the pooled analysis.

Prevalence of uncontrolled hypertension among patients with diabetes

The prevalence of uncontrolled hypertension prevalence estimate among patients with diabetes was reported in 11 studies (29-31, 33, 34, 38-42, 45), with a total of 2399 participants. Uncontrolled hypertension prevalence in this group ranged from 54% (95% CI, 50%- 58%) to 85% (95% CI, 78%-90%), with a pooled estimate of 74.5% (95% CI, 67.1%-81.3%) (Table 2). Substantial heterogeneity (I^2 = 93.1%; P < .001) was observed in the included studies (Figure 2). Publication bias was not evident from the visual inspection of the funnel plot (Figure 4).

Subgroup analysis revealed differences in uncontrolled hypertension prevalence among people with diabetes. Table 3). There were differences noted by sample size; large studies reported a higher prevalence (75.5% [95% CI, 67.1%-81.3%]) compared to small studies (73.3% [95% CI, 68.2%-79.3%]) (table 2). Pooled UHTN prevalence differed by geographic regions; studies conducted in the Eastern reported the highest pooled prevalence (82.5% [95% CI, 80.4%-87.1%]) while studies in conducted in the Southern region reported the lowest pooled prevalence (72.5% [95% CI, 62.0%-81.8%]). Gender differences were also noted; studies with more male participants had higher pooled prevalence (72.5% [95% CI, 64.4%-79.9%]) compared to studies with more female participants. Studies conducted after 2015 had higher pooled prevalence of UHTN among people with diabetes compared to studies conducted before 2015. Studies that used the recommended diabetes hypertension cuttoff (BP<130/85 mmHg) to define blood pressure control reported lower UHTN prevalences compared to those that did not use the recommended hypertension control value. Studies that had below the average SSA GNI reported a higher prevalence of UHTN (77.3 [95% CI, 69.7-84.2]) compared to studies with above the average SSA GNI (72.3 [95% CI, 61.0-82.3]).

In the univariable analysis, the use of the recomended hypertension control value for diabetes explained the most of the heterogeneity (56.7%) observed while sampling explained 100% of the heterogeneity (Table S5). In the final multivariable model, the sampling method used was associated with uncontrolled hypertension and explained most of the heterogeneity.

Table 3: Meta-analysis results for the prevalence of uncontrolled hypertension in people with diabetes in sub-Saharan Africa

	Prevalence (95%CI)	No of studies	Number of Participants	I^2 (95%CI)	$p^{heterogeneneity}$
Overall	74.5 (67.1-81.3)	11	2399	93.1	<0.001
By region					
Eastern	82.5 (78.8-85.9)	2	449	-	-
Western	75.0 (67.1-82.1)	2	131	-	-
Central	79.6 (70.6-86.4)	1	98	-	-
Southern	72.5 (62.0-81.8)	6	1721	94.9	<0.001
By risk of bias					
Low	74.2 (65.8-81.9)	9	2268	94.4	<0.001

Moderate	70.9 (60.1-78.8)	1	79	-	-
High	80.8 (68.1-89.2)	1	52	-	-
By study size					
Small studies	73.25 (66.8-79.3)	5	344	40.6	0.15
Large studies	75.5 (64.82-84.8)	6	2055	96.4	<0.001
By period of publication					
Before 2015	72.9 (62.4-82.3)	4	1245	92.4	<0.001
After 2015	78.0 (71.9-83.6)	7	1154	79.6	<0.001
By gender proportion					
More females	72.5 (64.4-79.9)	9	1919	92.2	<0.001
More males	83.9 (80.4-87.1)	2	480	-	-
By sampling					
Consecutive	76.7 (72.3-80.9)	9	1780	75.2	<0.001
Random	54.1 (50.0-58.2)	1	567	-	-
By setting					
Hospital	75.7 (66.0-84.3)	8	1825	94.9	<0.001
Health center	71.6 (61.5-80.8)	3	574	-	-
By comorbidity HTN target					
Comorbidity target used	70.1 (57.4-81.5)	5	863	90.1	<0.001
Comorbidity target not used	78.2 (73.1-82.9)	6	1536	79.3	<0.001
By Gross National Income					
Below SSA Average	77.3 (69.7-84.2)	5	852	81.1	<0.001
Above SSA average	72.3 (61.0-82.3)	6	1547	94.9	<0.001

SSA=sub-Saharan Africa $P^{egger} < 0.001$

Discussion

To our knowledge, this is the first systematic review and meta-analysis on the pooled prevalence of UHTN among patients with comorbidities in SSA. Our findings indicate more than three-quarters of the hypertensive people with coormodities have uncontrolled hypertension. These findings support the literature describing the challenges in controlling blood pressure among those on treatment and living with comorbidities while highlighting the fact that recognition of patient comorbidities' should be a core aspect of the care and support offered to patients with hypertension.

The prevalence of uncontrolled hypertension varied with the type of comorbidity. The highest pooled UHTN prevalence estimate (75.9%) was observed in people with chronic kidney disease (75.9%) and diabetes (74.5%). Reduced risk associated with diabetes were observed in people who achieved

optimal blood pressure in a UK study (12). Another study conducted in Kenya found that 80% of diabetic patients from rural and semi-urban areas had hypertension (46). Since hypertension is common among people with diabetes, there is need to focus on integrated care for diabetes and hypertension. These findings support literature describing the challenge in blood pressure control among those on treatment and with comorbidities.

The high prevalence of UHTN in people with comorbidities is concerning and requires further understanding. There are several factors affecting UHTN among patients on treatment. Non-adherence to antihypertensive is an important cause of uncontrolled hypertension. A systematic review conducted by Abegaz et al found 45% of patients on antihypertensive were non-adherent to medications with a higher proportion (84%) being among those with uncontrolled blood pressures (47). Barriers to adherence are mainly related to medication side effects, low perception of the risks involved with having uncontrolled blood pressure, out-of-pocket costs and pill burden due to comorbidities. Provider related factors also affect the UHTN rates. A study conducted by Rose et al. concluded that inadequate treatment regimens are to blame for a majority of uncontrolled hypertension (7). Provider lack of adherence to hypertension guidelines in regards to dose escalation and use of multiple drug regimens are a barrier to hypertension control. Chow et al revealed the use of multiple drug regimens to treat hypertension was lower in low-income countries compared the higher-, upper middle- or the lower middle-income countries (9).

The prevalence of uncontrolled hypertension has declined significantly in studies published after 2015 compared to those published before 2015 probably because of adherence to the changing guidelines promoting tighter blood pressure control for people with comorbidities. However, despite the observed decline, the prevalence of uncontrolled hypertension among people with comorbidities is very high and needs further research to understand the interventions that can reduce the uncontrolled hypertension rate so it can be adapted in other countries.

Our findings have the potential to inform public health strategies to reduce the burden of uncontrolled hypertension in SSA. Addressing the barriers identified is essential in achieving optimal blood pressure levels. The World Health Organization's global target on hypertension control action plan recommends integrated care programmes for the management of hypertension and comorbidities, a recommendation supported by the results of the current study (1).

Strengths and Limitations

Strengths of our systematic review and meta-analysis include the use of a published comprehensive protocol (22) to identify all available evidence without language restriction, reporting in accordance with PRISMA guidelines, search using multiple electronic databases, searching grey literature, contacting experts in the field for additional data sources to reduce study selection bias, and heterogeneity test by subgroup analyses and sensitivity analyses. The use of two independent reviewers in data extraction and the assessment of the risk of bias further reduced assessor bias.

This study should however, be interpreted in the context of the following limitations. First, it is important to note that control of hypertension among those on treatment was not the main outcome of most of the included studies. Secondly, the prevalence of UHTN in some comorbidities such as atrial fibrillation and chronic kidney disease were reported in single studies probably because these conditions are understudied in SSA thus limiting the generalizeability of such findings. Fourth, most of the studies included in the meta-analysis were hospital based studies that used non-random sampling procedures. Therefore, the prevalence of UHTN in these populations needs to be confirmed by further studies. Lastly, we found substantial heterogeneity between the studies and conducted meta-regression analysis, which did not explain most of the heterogeneity. The lack of uniformity and variance in the blood pressure cut-off points for the different comorbidities may have resulted in this heterogeneity.

Conclusion

In conclusion, the prevalence of uncontrolled hypertension is high in people with comorbid conditions in sub-Saharan Africa, particularly among people with diabetes. These findings strengthen the case for action to implement integrated care in the control of hypertension more effectively in African populations and other low-and-middle-income countries. Such efforts include improved access to blood pressure testing among people with cormbodities, strategies to improve adherence, reviewing treatment guidelines and training of healthcare workers in managing people with hypertension comorbidities, and monitoring blood pressure control among all patients on treatment.

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Disclosures

None.

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Contributors

SFM conceived the study. SFM, OAU, MKM, GA, ASM, and PG designed the search strategy. SFM and ASM conducted the searches, retrieved articles, screened abstract and title, and the full text of

potentially relevant articles. SFM wrote the first draft of the manuscript. All authors critically revised the manuscript and contributed to subsequent iterations.

List of figures

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Figure 1: Study selection flow diagram

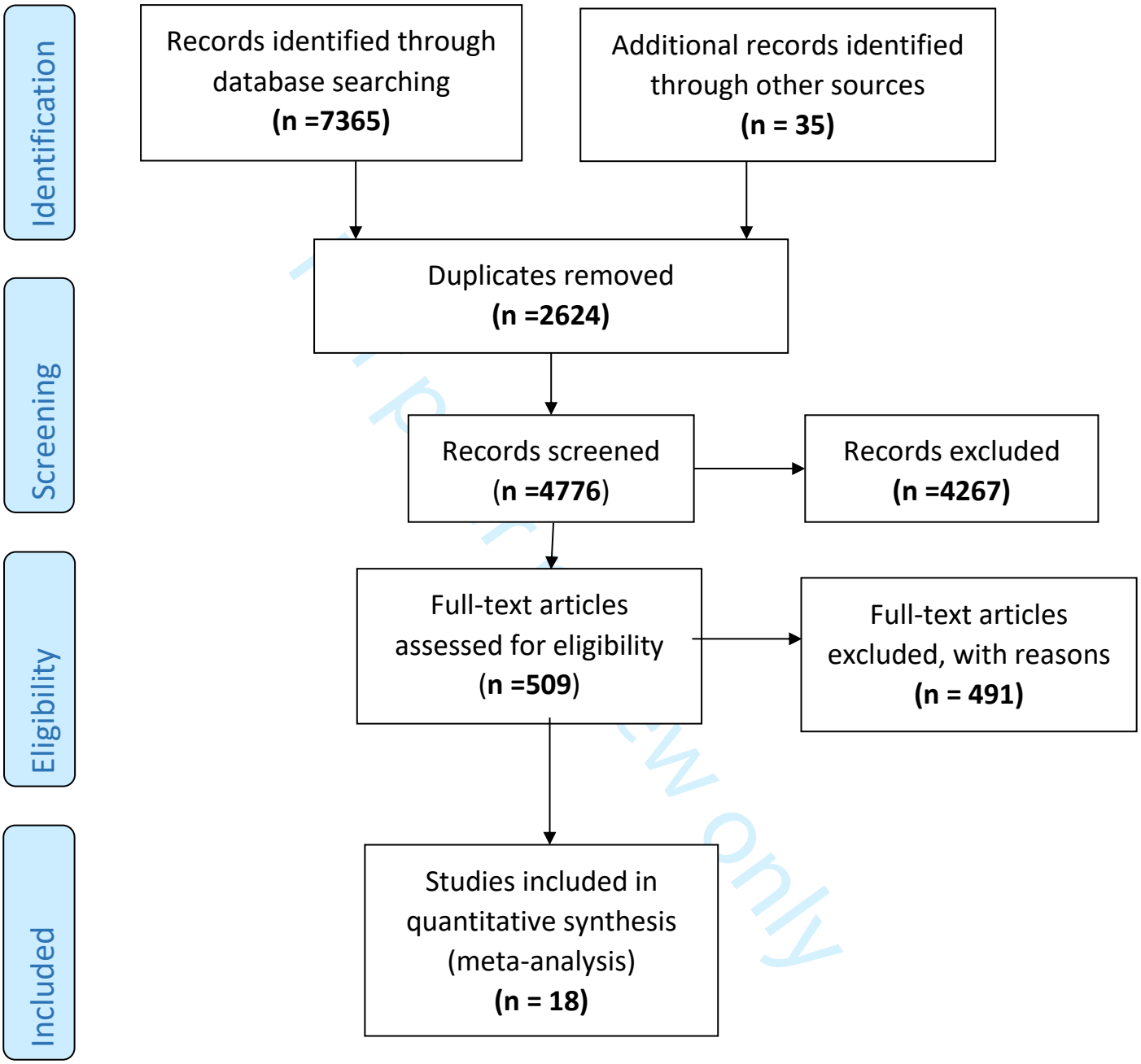


Figure 2: Funnel plot of the prevalence of uncontrolled hypertension in people with comorbidities in sub-Saharan Africa

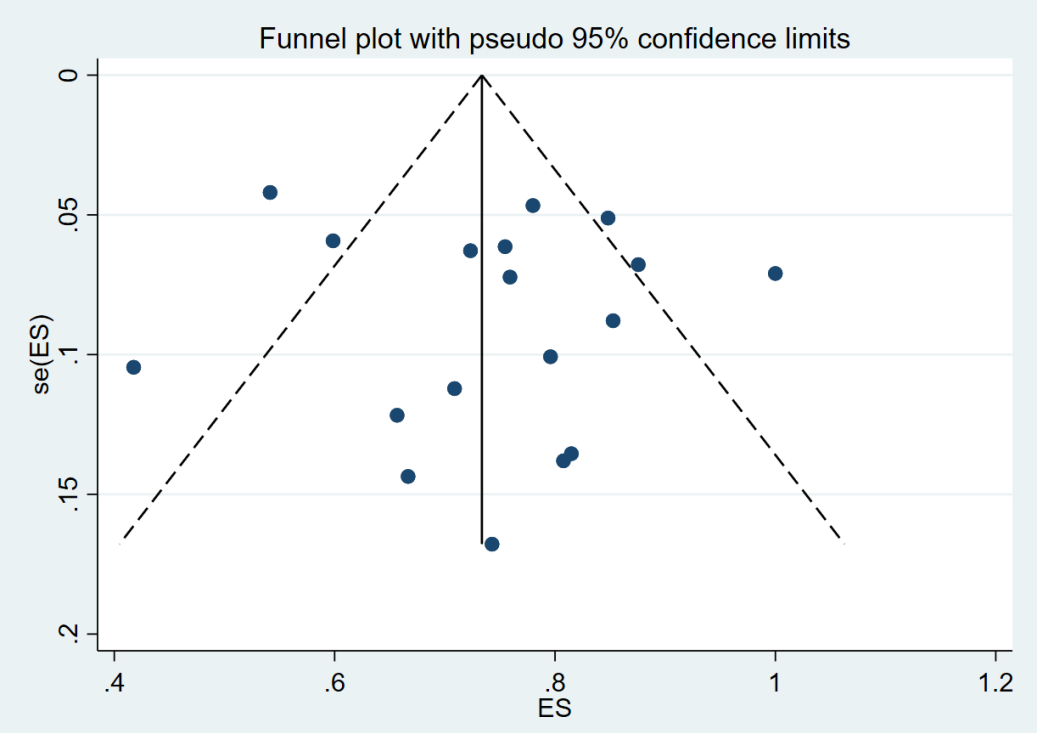


Figure 3: Pooled prevalence of uncontrolled hypertension in people with comorbidities in sub-Saharan Africa, by comorbidities

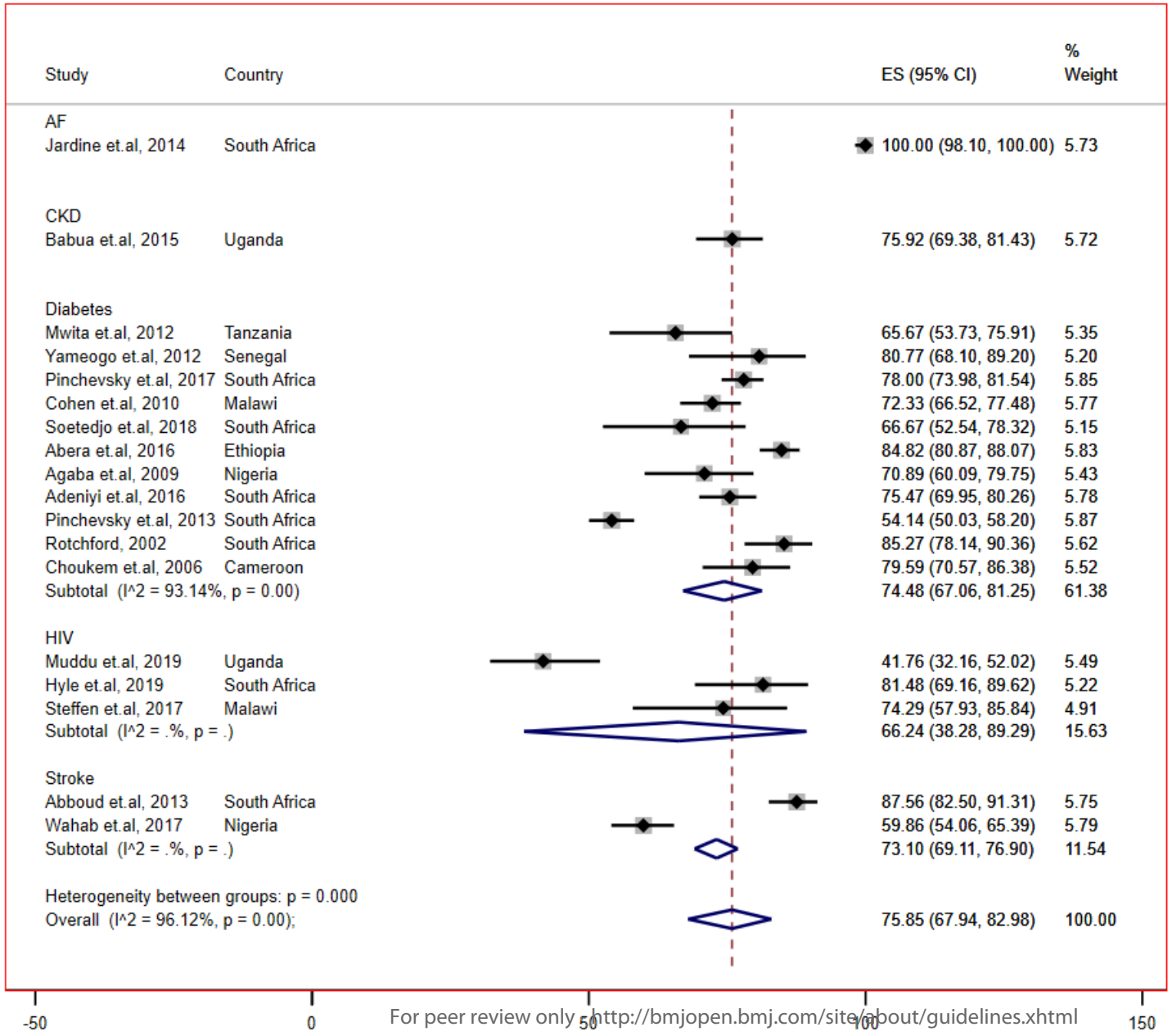
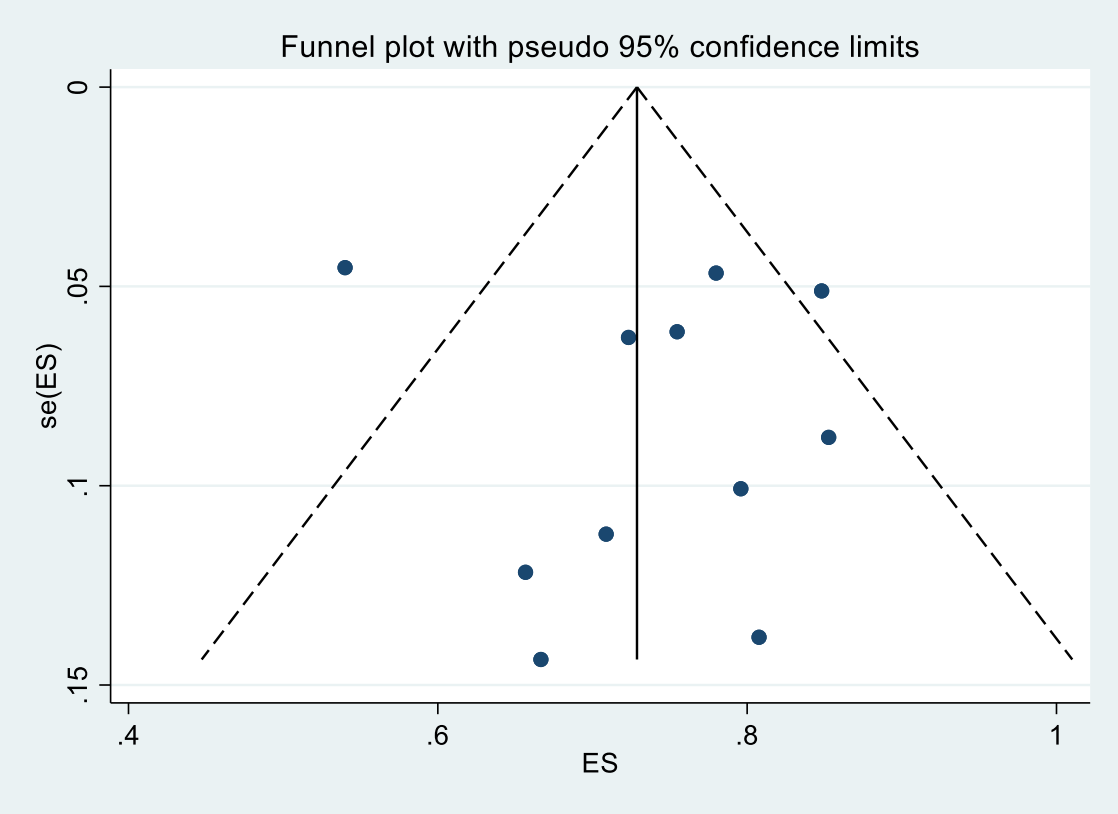


Figure 4: Funnel plot of the prevalence of uncontrolled hypertension in people with diabetes in sub-Saharan Africa



Supplementary file S1 – Search strategy

Medline - search

1. exp Hypertension/ or hypertension.mp.
2. exp Hypertension/ or uncontrolled hypertension.mp.
3. exp Hypertension/ or uncontrolled blood pressure.mp.
4. high blood pressure.mp. or exp Hypertension/
5. 1 or 2 or 3 or 4
6. type 2 diabetes mellitus.mp. or exp Diabetes Mellitus, Type 2/
7. type 2 diabetes.mp. or exp Diabetes Mellitus, Type 2/
8. exp Diabetes Mellitus, Type 2/ or type II diabetes.mp.
9. dyslipidemia.mp. or exp Dyslipidemias/
10. exp Dyslipidemias/ or dyslipidimia.mp.
11. exp Dyslipidemias/ or dyslipidaemia.mp.
12. Hypercholesterolemia.mp. or exp Hypercholesterolemia/
13. Hypercholesterolaemia.mp. or exp Hypercholesterolemia/
14. Hypercholesterolimia.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
15. hypertriglyceridemia.mp. or exp Hypertriglyceridemia/
16. exp Hypertriglyceridemia/ or hypertriglyceridaemia.mp.
17. hypertriglyceridimia.mp.
18. hyperlipidemia.mp. or exp Hyperlipidemias/
19. exp Hyperlipidemias/ or hyperlipidaemia.mp.
20. hyperlipidimia.mp.
21. obesity.mp. or exp Obesity/
22. chronic kidney disease.mp. or exp Renal Insufficiency, Chronic/
23. stroke.mp. or exp Stroke/
24. transient ischemic attack.mp. or exp Ischemic Attack, Transient/
25. Stroke/ or exp Ischemic Attack, Transient/ or transient ischaemic attack.mp.
26. coronary heart disease.mp. or exp Coronary Disease/
27. Heart failure.mp. or exp Heart Failure/
28. peripheral vascular disease.mp. or exp Peripheral Vascular Diseases/
29. atrial fibrillation.mp. or exp Atrial Fibrillation/
30. depression.mp. or exp Depression/
31. HIV/ or HIV.mp.
32. human immunodeficiency virus.mp. or exp HIV/
33. 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32
34. (Angola or Benin or Botswana or "Burkina Faso" or "Upper Volta" or Burundi or Urundi or Cameroon or Cameroons or "Cape Verde" or "Central African Republic" or Chad or Comoros or "Comoro Islands" or Comores or Mayotte or Congo or Zaire or "Cote d'Ivoire" or "Ivory Coast" or ("Democratic Republic of the Congo" or Djibouti or "French Somaliland" or Eritrea or Ethiopia or Gabon or "Gabonese Republic" or Gambia or Ghana or "Gold Coast" or Guinea or Kenya or Lesotho or Basutoland or Liberia) or (Madagascar or "Malagasy Republic" or Malawi or Nyasaland or Mali or Mauritania or Mauritius or Mozambique or Namibia or Niger or Nigeria) or (Rwanda or "Sao Tome" or Seychelles or Senegal or "Sierra Leone" or Somalia or "South Africa" or Sudan or Swaziland or Tanzania or Togo or "Togolese Republic" or Uganda or Zambia or Zimbabwe or Rhodesia)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
35. sub-Saharan africa.mp. or exp "Africa South of the Sahara"/
36. subsaharan africa.mp. or exp "Africa South of the Sahara"/
37. 34 or 35 or 36
38. 5 and 33 and 37
39. limit 38 to (humans and yr="2000 - 2019")

Embase - search

1. hypertension.mp. or exp hypertension/
2. exp hypertension/ or uncontrolled hypertension.mp. or exp antihypertensive agent/
3. exp antihypertensive agent/ or exp hypertension/ or uncontrolled blood pressure.mp.
4. high blood pressure.mp. or exp hypertension/
5. 1 or 2 or 3 or 4
6. type 2 diabetes mellitus.mp. or exp non insulin dependent diabetes mellitus/
7. type 2 diabetes.mp. or exp non insulin dependent diabetes mellitus/
8. type II diabetes.mp. or exp non insulin dependent diabetes mellitus/
9. dyslipidemia.mp. or exp dyslipidemia/
10. dyslipidimia.mp.
11. dyslipidaemia.mp. or exp dyslipidemia/
12. exp hypercholesterolemia/ or Hypercholesterolemia.mp.
13. Hypercholesterolaemia.mp. or exp hypercholesterolemia/
14. Hypercholesterolimia.mp.
15. hypertriglyceridemia.mp. or exp hypertriglyceridemia/
16. hypertriglyceridaemia.mp. or exp hypertriglyceridemia/
17. hypertriglyceridimia.mp. or exp hypertriglyceridemia/
18. hyperlipidemia.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
19. hyperlipidaemia.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
20. hyperlipidimia.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
21. obesity.mp. or exp obesity/
22. chronic kidney disease.mp. or exp chronic kidney failure/
23. stroke.mp. or exp cerebrovascular accident/
24. transient ischemic attack.mp. or exp transient ischemic attack/
25. transient ischaemic attack.mp. or exp transient ischemic attack/
26. coronary heart disease.mp. or exp ischemic heart disease/
27. Heart failure.mp. or exp heart failure/
28. peripheral vascular disease.mp. or exp peripheral vascular disease/
29. atrial fibrillation.mp. or exp atrial fibrillation/
30. exp depression/ or depression.mp.
31. HIV.mp. or exp Human immunodeficiency virus/
32. 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31
33. (Angola or Benin or Botswana or "Burkina Faso" or "Upper Volta" or Burundi or Urundi or Cameroon or Cameroons or "Cape Verde" or "Central African Republic" or Chad or Comoros or "Comoro Islands" or Comores or Mayotte or Congo or Zaire or "Cote d'Ivoire" or "Ivory Coast" or ("Democratic Republic of the Congo" or Djibouti or "French Somaliland" or Eritrea or Ethiopia or Gabon or "Gabonese Republic" or Gambia or Ghana or "Gold Coast" or Guinea or Kenya or Lesotho or Basutoland or Liberia) or (Madagascar or "Malagasy Republic" or Malawi or Nyasaland or Mali or Mauritania or Mauritius or Mozambique or Namibia or Niger or Nigeria) or (Rwanda or "Sao Tome" or Seychelles or Senegal or "Sierra Leone" or Somalia or "South Africa" or Sudan or Swaziland or Tanzania or Togo or "Togolese Republic" or Uganda or Zambia or Zimbabwe or Rhodesia)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
34. sub-Saharan africa.mp. or exp "Africa south of the Sahara"/
35. subsaharan africa.mp. or exp "Africa south of the Sahara"/

36. 33 or 34 or 35
37. 5 and 32 and 36
38. limit 37 to (human and yr="2000 - 2019")

Web of Science - search

# 38	2,114	#37 AND #33 AND #5 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 37	421,085	#36 OR #35 OR #34 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 36	301	TS=(subsaharan Africa) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 35	33,673	TS=(sub-Saharan Africa) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 34	407,520	TS=(Angola OR Benin OR Botswana OR "Burkina Faso" OR "Upper Volta" OR Burundi OR Urundi OR Cameroon OR Cameroons OR "Cape Verde" OR "Central African Republic" OR Chad OR Comoros OR "Comoro Islands" OR Comores OR Mayotte OR Congo OR Zaire OR "Cote d'Ivoire" OR "Ivory Coast" OR "Democratic Republic of the Congo" OR Djibouti OR "French Somaliland" OR Eritrea OR Ethiopia OR Gabon OR "Gabonese Republic" OR Gambia OR Ghana OR "Gold Coast" OR Guinea OR Kenya OR Lesotho OR Basutoland OR Liberia OR Madagascar OR "Malagasy Republic" OR Malawi OR Nyasaland OR Mali OR Mauritania OR Mauritius OR Mozambique OR Namibia OR Niger OR Nigeria OR Rwanda OR "Sao Tome" OR Seychelles OR Senegal OR "Sierra Leone" OR Somalia OR "South Africa" OR Sudan OR Swaziland OR Tanzania OR Togo OR "Togolese Republic" OR Uganda OR Zambia OR Zimbabwe OR Rhodesia) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 33	1,764,519	#32 OR #31 OR #30 OR #29 OR #28 OR #27 OR #26 OR #25 OR #24 OR #23 OR #22 OR #21 OR #20 OR #19 OR #18 OR #17 OR #16 OR #15 OR #14 OR #13 OR #12 OR #11 OR #10 OR #9 OR #8 OR #7 OR #6 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 32	85,771	TS=(Human immunodeficiency virus) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 31	272,497	TS=(HIV) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 30	369,094	TS=(depression) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit

# 29	80,988	TS=(atrial fibrillation) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 28	20,886	TS=(peripheral vascular disease) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 27	226,090	TS=(heart failure) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 26	144,037	TS=(coronary heart disease) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 25	1,959	TS=(transient ischaemic attack) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 24	11,095	TS=(transient ischemic attack) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 23	278,508	TS=(stroke) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 22	75,433	TS=(chronic kidney disease) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 21	280,562	TS=(obesity) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 20	5	TS=(hyperlipidimia) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 19	2,534	TS=(hyperlipidaemia) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 18	21,065	TS=(hyperlipidemia) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 17	2	TS=(hypertriglyceridimia) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 16	1,000	TS=(hypertriglyceridaemia) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 15	8,591	TS=(hypertriglyceridemia)	Edit

		Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI *Timespan=2000-2019*	
# 14	**0**	TS=(hypercholesterolimia) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 13	**3,188**	TS=(hypercholesterolaemia) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 12	**27,232**	TS=(hypercholesterolemia) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 11	**4,539**	TS=(dyslipidaemia) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 10	**6**	TS=(dyslipidimia) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 9	**25,588**	TS=(dyslipidemia) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 8	**16,630**	TS=(type II diabetes) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 7	**173,805**	TS=(type 2 diabetes) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 6	**94,317**	TS=(Type 2 diabetes mellitus) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 5	**375,418**	#4 OR #3 OR #2 OR #1 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 4	**113,713**	TS=(high blood pressure) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 3	**3,503**	TS=(uncontrolled blood pressure) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 2	**4,063**	TS=(uncontrolled hypertension) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 1	**307,652**	**TOPIC:** (hypertension) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	

Table S1: List of 11 conditions included as comorbidity

	Conditions
1	Diabetes
2	Hypercholesterolemia/dyslipidemia/hyperlipidemia/hypertriglyceridemia
3	Obesity
4	Chronic kidney disease
5	Stroke and or transient Ischemic attack
6	Coronary heart disease
7	Heart failure
8	Peripheral vascular disease
9	Atrial fibrillation
10	Depression
11	HIV

Table S2: Assessment of Risk of Bias (RoB)

	External validity	Yes/No		Internal validity	Yes/No
1	Was the target population representative of the population in relation to relevant variables?		5	Were data collected directly from the subjects (as opposed to a proxy)?	
2	Was the sampling frame a true or close representation of the target population?		6	Was an acceptable case definition used in the study?	
3	Was some form of random selection used to select the sample, OR was a census undertaken?		7	Was the study instrument that measured the parameter of interest shown to have validity and reliability?	
4	Was the likelihood of nonresponse bias minimal in the study?		8	Was the same mode of data collection used for all subjects?	
			9	Were the numerator(s) and denominator(s) for the parameter of interest appropriate?	
10	Summary item on the overall risk of study bias				

Adapted from Hoy D, Brooks P, Woolf A, Blyth F, March L, Bain C, et al. Assessing risk of bias in prevalence studies: modification of an existing tool and evidence of interrater agreement. Journal of clinical epidemiology. 2012;65(9):934-9.

Table S3: Characteristics of studies in the prevalence of Uncontrolled hypertension in sub-Saharan Africa

Year of publication (n = 18)	2002-2019
Period of inclusion (n = 18)	2000-2019
Mean age, years (n = 18)	56.7(±0.11)
% of males (n = 18)	46.9(±0.18)
Comorbidities	**N studies**

Diabetes	11
HIV	3
Stroke	2
Atrial fibrillation	1
Chronic Kidney Disease (CKD)	1
sub-Saharan African regions	
Eastern Africa	4
Western Africa	3
Central Africa	1
Central Africa	10
Study design	
Cross sectional	17
Not reported	1
Sampling	
Consecutive	14
Random	2
Not reported	2
Timing of data collection	
Retrospectively	5
Prospectively	12
Not reported	1
Data sources	
Medical records	5
Participants	9
from both medical records and participants	3
Not reported	1
Study site	
Hospital	11
Health Center	7

Table S4: **Meta-regression analysis for the variation of the prevalence of uncontrolled hypertension in people with comorbidity in SSA**

Variables (reference)	Univariate analysis				Multivariate analysis	
	N studies	P value	Coefficient (95% CI)	R^2, %	P-value	Adjusted coefficient (95% CI)
Year of publication (after 2015)	18	0.402	-0.0600 (-0.2080; 0.0879)	-5.40		
More females	18	0.114	0.1106 (-0.0297; 0.2508)	14.45		
Risk of bias (low)	18			19.80		
Moderate		0.990	-0.0016 (-0.2682; 0.2649)			
High		0.067	0.2106 (-0.0167; 0.4378)			
Sample size (small studies)	18			-0.31		
Large studies		0.328	0.0736 (-0.0810; 0,2282)			
SSA regions (Eastern)	18			-15.88		
Western		0.929	-0.0107 (-0.2650; 0.2435)			
Central		0.572	0.1017 (-0.1102; 0.2706)			
Southern		0.381	0.0802 (-0.1101; 0.2706)			
Comorbidities (atrial fibrillation)	18			14.44		
Chronic kidney disease		0.205	-0.2408 (-0.6310; 0.1493)		0.483	-0.1333 (-0.5346; 0.2681)
Diabetes		0.073	-0.2610 (-0.5499; 0.0278)		0.110	-0.2199 (-0.4972; 0.0574)
HIV		**0.036**	-0.3746 (-0.7215; -0.0277)		0.136	-0.2703 (-0.6389; 0.0983)
Stroke		0.106	-0.2678 (-0.6013; 0.0656)		0.340	-0.1612 (-0.5146; 0.1922)
Setting (Health center)	18			-8.45		
Hospital		0.974	0.0025 (-0.1550;0.1600)			
Sampling (Consecutive)	16					
Random		0.614	-0.0534 (-0.2755; 0.1687)	-5.95		
BP target used (recommended comorbidity target not used)	18			26.48		
Recommended BP control used		**0.064**	-0.1228 (-.2538; 0 .0082)		0.190	-0.1076 (-0.2764; 0.0612)
GNI (Below SSA average)	18					

Above SSA average		0.675	0 .0303 (-0.1204; 0.1810)	-8.67		
Mean age	18	0.299	-0.0097 (-0.0296; 0.0101)	19.04		

BP=Blood pressure

Table S5: **Meta-regression analysis for the variation of the prevalence of uncontrolled hypertension in people with comorbidity in SSA**

Variables (reference)	Univariate analysis				Multivariate analysis	
	N studies	P value	Coefficient (95% CI)	R^2, %	P-value	Adjusted coefficient (95% CI)
Year of publication (after 2015)	18	0.402	-0.0600 (-0.2080; 0.0879)	-5.40		
More females	18	0.114	0.1106 (-0.0297; 0.2508)	14.45		
Risk of bias (low)	16			-6.67		
Moderate		0.990	-0.0016 (-0.2706; 0.2674)			
Sample size (small studies)	18			-0.31		
Large studies		0.328	0.0736 (-0.0810; 0,2282)			
SSA regions (Eastern)	18			-15.88		
Western		0.929	-0.0107 (-0.2650; 0.2435)			
Central		0.572	0.1017 (-0.1102; 0.2706)			
Southern		0.381	0.0802 (-0.1101; 0.2706)			
Comorbidities (atrial fibrillation)	18			14.44		
Chronic kidney disease		0.205	-0.2408 (-0.6310; 0.1493)		0.483	-0.1333 (-0.5346; 0.2681)
Diabetes		0.073	-0.2610 (-0.5499; 0.0278)		0.110	-0.2199 (-0.4972; 0.0574)
HIV		**0.036**	-0.3746 (-0.7215; -0.0277)		0.136	-0.2703 (-0.6389; 0.0983)
Stroke		0.106	-0.2678 (-0.6013; 0.0656)		0.340	-0.1612 (-0.5146; 0.1922)
Setting (Health center)	18			-8.45		
Hospital		0.974	0.0025 (-0.1550;0.1600)			
Sampling (Consecutive)	16					
Random		0.614	-0.0534 (-0.2755; 0.1687)	-5.95		
BP target used (recommended comorbidity target not used)	18			26.48		
Recommended BP control used		**0.064**	-0.1228 (-.2538; 0 .0082)		0.190	-0.1076 (-0.2764; 0.0612)
GNI (Below SSA average)	18					
Above SSA average		0.675	0 .0303 (-0.1204; 0.1810)	-8.67		
Mean age	18	0.299	-0.0097 (-0.0296; 0.0101)	19.04		

BP=Blood pressure

Table S6: **Meta-regression analysis for the variation of the prevalence of uncontrolled hypertension in people with diabetes in SSA**

Variables (reference)	Univariate analysis				Multivariate analysis	
	N studies	P value	Coefficient (95% CI)	R^2, %	P value	Adjusted coefficient (95% CI)
Year of publication (after 2015)	11	0.274	0.0793 (-0.0748; 0.2334)	18.20		
More females	11	0.205	0.1157 (-0.0758; 0.3072)	16.26		
Risk of bias (low)	11			-15.57		
Moderate		0.858	-0.0278 (-0.3753; 0.3198)			
High		0.688	0.0711 (-0.3228; 0.4650)			
Sample size (small studies)	11			-11.04		
Large studies		0.89	.0115 (-0.1714; 0.1943)			
SSA regions (Eastern)	11			-18.36		
Western		0.815	-.0341 (-0.3664; 0.2982)			
Central		0.952	.0101 (-0.3755; 0.3956)			
Southern		0.500	-0.0709 (-0.3067; 0.1649)			
Setting (Health center)	11			-15.43		
Hospital		0.860	.0160 (-0.1825; 0.2144)			
Sampling (Consecutive)	10					
Random		**0.001**	-0.2366 (-0.3477 -0.1255)	100.00	**0.043**	-0.1880 (-0.3686; -0.0074)
BP target used (recommended diabetes BP target not used)	11			56.66	0.439	-0.0563 (-0.2188; 0.1062)
Recommended diabetes BP control target used		**0.054**	-0.1320 (-0.2671; 0.0030)			
GNI (Below SSA average)	11					
Above SSA average		0.401	-0.0633 (-0.2256; 0.0991)	3.10		
Mean age	11	0.296	0.0047 (-.0046; 0.0139)	-0.16		

BP=Blood pressure

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.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
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.	4
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.	4-5
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.	4-5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplement file 1
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).	5
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.	5
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5
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.	5-6
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	6
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.	6

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).	7
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	6
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.	7 and figure 1
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.	7-8
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).	10
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.	9-12 and figure 3
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	10-14
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	10
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	11-13
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).	14-16
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).	17
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	17
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.	17

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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Prevalence of uncontrolled hypertension in people with comorbidities in sub-Saharan Africa: a systematic review and meta-analysis

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Prevalence of uncontrolled hypertension in people with comorbidities in sub-Saharan Africa: a systematic review and meta-analysis

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Word Count: 3231

Abstract

Background: The burden of uncontrolled hypertension in sub-Saharan Africa (SSA) is high and hypertension is known to co-exist with other chronic diseases such as kidney disease, diabetes among others. This is the first systematic review and meta-analysis to determine the burden of uncontrolled hypertension among patients with comorbidities in SSA.

Methods: A comprehensive search was conducted on MEDLINE, Excerpta Medica Database (Embase), and Web of Science to identify all relevant articles published between January 1st, 2000 and June 17th, 2021. We included studies that reported on the prevalence of uncontrolled hypertension among people in SSA who report taking antihypertensive treatment and have another chronic condition A random-effects meta-analysis was performed to obtain the pooled estimate of the prevalence of uncontrolled hypertension among patients with comorbid conditions while on treatment across studies in SSA.

Results: In all 20 articles were included for meta-analyses. Eleven articles were among diabetic patients, five articles were among HIV patients, two were among stroke patients while chronic kidney disease and atrial fibrillation had one article each. The pooled prevalence of uncontrolled hypertension among patients with comorbidities was 78.6% (95% CI, 71.1%-85.3%); I^2 95.9%), varying from 73.1% in patients with stroke to 100.0% in patients with atrial fibrillation. Subgroup analysis showed differences in uncontrolled hypertension prevalence by various study-level characteristics

Conclusion: This study suggests a high burden of uncontrolled hypertension in people with comorbidities in SSA. Strategies to improve the control of hypertension among people with comorbidities are needed. PROSPERO registration number CRD42019108218.

Word count – 241

Key word – Uncontrolled hypertension, comorbidities, sub-Saharan Africa

Strengths and limitations of this study

- A published comprehensive protocol was used to identify all available evidence without language restriction, reporting in accordance with PRISMA guidelines, search using multiple electronic databases, searching grey literature, contacting experts in the field for additional data sources to reduce study selection bias, and heterogeneity test by subgroup analyses and sensitivity analyses.
- The prevalence of uncontrolled hypertension (UHTN) in some comorbidities such as atrial fibrillation and chronic kidney disease were reported in single studies.
- Most of the studies included in the meta-analysis were hospital based studies that used non-random sampling procedures.
- There was substantial heterogeneity between the studies.

Introduction

Hypertension is an important risk factor for cardiovascular diseases (CVDs) and a leading contributor to death globally [1]. An estimated 1.4 billion people have hypertension globally with three quarter (75%) of this population living in low-and –middle-income countries [2, 3]. Worldwide trends analysis based on a large dataset from multiple studies conducted between 1975 and 2015 in 200 countries showed no change in global mean blood pressure, but a a substantial downward trend in high income countries and a rise in low and middle income countries [4]. Levels of hypertension awareness, treatment and control improved by 2.9% in high income countries while in low-middle-income countries neglible improvement in awareness, treatment, and control were observed [3, 4]. The African region has the highest (30%) prevalence of hypertension compared to 18% in the Americas region [5]. In a systematic review and meta-analysis on hypertension in SSA, Ataklte et al [6], reported a (93%) high prevalence of uncontrolled hypertension (UHTN).

Hypertension often co-exists with comorbidities such as chronic kidney disease, diabetes, and hypercholesterolemia among others [7-10]. These comorbidities could explain part of the inadequacy in blood pressure control. Some studies conducted in Europe and the US found that patients with diabetes mellitus had a significantly increased risk of uncontrolled blood pressure [11, 12]. Another study conducted in the UK has shown that achieving optimal blood pressure control in patients with hypertension and type 2 diabetes produces an important decrease in the risks associated with diabetes [13].

In recent years, public health efforts to promote prevention, awareness and treatment of hypertension in SSA have intensified [14-17] but hypertension control remains low [18-22]. Despite several studies conducted on UHTN in people with comorbidities, pooled estimations of the burden are not available for comorbidities such as diabetes, dyslipidaemia, stroke, HIV, obesity, atrial fibrillation. From a clinical perspective, it is important to understand why patients on treatment are not attaining optimal blood control and whether their pre-existing comorbidities contribute to the

lack of control of blood pressure. Therefore, to inform policy, practice and the development of guidelines for hypertension for integrated care among patients with comorbid conditions, it is critical to understand the burden of UHTN in people with comorbidities. The purpose of this review is to summarize the evidence on and estimate the prevalence of UHTN in patients with comorbidities in SSA and to explore factors associated with UHTN in people with comorbidities .

Methods

Protocol and registration

The protocol for this systemic review and meta-analysis was registered on the International Prospective Register of Systematic Reviews (PROSPERO CRD42019108218) and published [23]. The reporting was done according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA-P) guidelines [24].

Search Strategy

We systematically searched MEDLINE via Ovid, Excerpta Medica Database (Embase), and Web of Science from January 1st, 2000 to June 17th, 2021**.** The search strategy included the following relevant terms: *uncontrolled hypertension, hypertension, uncontrolled blood pressure, high blood pressure , a list of comorbidities, and sub-Saharan Africa (Detailed search strategy list is attached as supplement (Supplement file S1).* Additionally, the reference lists of the included studies were reviewed to identify other relevant studies.

Eligibility criteria

Studies were included if (1) they provided primary data on the prevalence of hypertension in accordance with the sevent report of the Joint National Committee (JNC7) among those who reported taking antihypertensive treatment and had a comorbid condition, (2) participants had been diagnosed with one of the comorbidities of interest – diabetes, dyslipidemia, obesity, chronic kidney disease, stroke or transient ischemic attack, coronary heart disease, heart failure, peripheral vascular disease,

atrial fibrillation, depression and HIV (Table S2), (3) participants were 15 and above years, (4) the study was published in any language, and (5) the study was conducted in a sub-Saharan Africa. The following types of study designs were excluded: (1) case-control studies, commentaries, editorials, letters, qualitative studies, and systematic reviews; (2) studies that included hypertension prevalence but did not report on the prevalence of hypertension among those on antihypertensive medication; and (3) studies of pregnancy-related hypertension.

Study selection

Two researchers independently screened the titles and abstracts (SFM & ASM). Two researchers (SFM & ASM) also assessed full-text reviews of the articles independently for final inclusion. The reference lists of potentially relevant publications were manually searched for additional publications. Disagreements were resolved by consensus. For multi-national studies, data were separated to show the estimate at the country level.

Data items and collection process

SFM and ASM independently screened the full texts of included studies. SFM extracted data from the selected studies, and ASM checked the data for accuracy. A standardized data extraction table was created (Table 1) and included the following data from all eligible articles: first author name, year of publication, language, country of the study, study design, sample size, study period, study setting, sampling method, the timing of data collection, data source, use of comorbidity specific hypertension control cuttoff, male proportion, age of participants (mean or median), type of comorbidity (diabetes, stroke, HIV, chronic kidney disease, atrial fibrillation), and main outcome of interest uncontrolled hypertension proportion or the data to cumpute it.

Risk of bias in individual studies

A tool developed by Hoy et.al [25] for prevalence studies was adapted and used to assess the methodological quality of included studies by evaluating the extent to which they addressed bias in 9

areas of internal and external validity (Table S3). Each of the nine areas was scored one if yes (high quality) and zero if no (poor quality), and a total quality score was calculated by summing the individual scores. Total scores ranged from 0 to 9, with higher scores indicating higher quality. Studies were then classified as having a low (>8), moderate (6–8), or high (≤5) risk of bias. Two researchers (SFM and MKM) independently assessed each of the included publications and disagreements was resolved through discussion.

Patient and Public Involvement

This research was done without patient involvement. There was no involvement of patients or members of the public in the design, or conduct, or reporting, or dissemination plans of this research.

Synthesis of results

The statistical approach used in this meta-analysis followed the study protocol [23]. Crude numerators and denominators from the individual studies were used to recalculate the study-specific unadjusted prevalence estimates. Variances of the study-specific estimates were stabilized using the double arcsine transformation to minimise the effect of studies with very small or very large prevalence estimates on the overall estimate (16) and then a random-effects meta-analysis was performed (17) to determine the pooled estimate of the prevalence of UHTN among patients with comorbidities overall and also among people with diabetes, HIV and stroke separately while on antihypertensive treatment across the included studies in SSA. Prevalence estimates were also summarised by comorbidities, publication year, sample size, study setting, sampling, risk of bias, gender proportionmean age and geographic regions.

Heterogeneity was explored using Cochrane's Q and quantified by I^2 statistics [26, 27]. Subgroup analyses were performed based on the following; gender proportion of participants, patient comorbidities, study design, study setting, sample size, use of recommended comorbidity specific

blood pressure control cut-offs, countries, regions (Eastern, Western, Central, and Southern Africa), and by Gross National Income (GNI) were be performed to identify the possible sources of heterogeneity. Sensitivity analyses were performed to assess the robustness of the findings by excluding studies with a high risk of bias.

Funnel plots and Egger asymmetry test were used to assess publication bias, with $P < .10$ considered to be statistically significant for publication bias [28]. Inter-rater agreements between the researchers involved in study inclusion and those involved in the identification of risk of bias were assessed using κ Cohen's coefficient (20).

All analyses were performed using 'metaprop' routine using StataSE version 16 (StataCorp LLC).

Results

Study selection

From the electronic database search, 8492 records were identified. An additional 35 articles were identified through reference tracing and from other sources. After duplicate removal, 5610 remained for the title and abstract screening. After screening, we found 5085 records to be irrelevant and excluded them. The full texts of 525 articles and reports were retrieved and assessed for eligibility, resulting in the inclusion of 20 studies for the meta-analysis (figure 1). The inter-rater agreement for study selection was 0.77.

Study characteristics

Table 1 and Table S4 provide detailed information on the included studies. In total, 3,510 participants were included across 20 studies. Most of the studies were cross-sectional (19, 95%), in English (19, 95%), hospital-based (12, 60%), used consecutive sampling (16, 80%), and prospectively collected data (14, 70%). The mean (SD) participant age from the 20 studies [29-48] providing this information was 56.8 (0.12) years. Study sample sizes ranged from 10 to 567 participants. The proportion of male participants in the included studies was reported in all studies and it ranged from 21.4% to 60.9% [29-48]. Of the included studies, 11 [30-32, 34, 35, 39-43, 46] reported on diabetes, five [36, 38, 44, 47,

48] reported on HIV, two [29, 45] reported on stroke, and one each reported on chronic kidney disease [33] and atrial fibrillation [37]. None of the included studies reported on obesity, dyslipidaemia, coronary heart disease, heart failure, peripheral heart disease, and depression.

Table 1: Characteristics of the Included Studies

Study	Country	Age (Mean/Median)	Study period	Study site	Sampling	Male %	Sample size	UHTN%	Risk of bias
Atrial Fibrilation									
Jardine et.al,2014	South Africa	67±13	Feb 2010 - Mar 2011	Health center	Consecutive	59.9	198	100.0	High
Chronic Kidney Disease									
Babua et.al 2015	Uganda	42.8	Jun - Feb 2013	Hospital	Consecutive	51.2	191	76.0	Low
Diabetes									
Abera et.al, 2016	Ethiopia	56.3±10	Aug - Jan 2015	Hospital	Consecutive	59.9	382	85.0	Low
Adeniyi et.al, 2016	South Africa	61.3±11.8	Jul to Nov 2013	Hospital	Consecutive	28.3	265	75.5	Low
Agaba et.al, 2009	Nigeria	51±12	Jun - Sept 2004	Hospital	Consecutive	40.2	79	70.9	Moderate
Choukem et.al 2006	Cameroon	56.6±13.3	6 months	Hospital	Consecutive	50.5	98	79.6	Low
Cohen et.al, 2010	Malawi	53.2±14.0	Mar - Jun 2007	Hospital	Consecutive	39.8	253	72.7	Low
Mwita et.al, 2012	Tanzania	51.6±11.2	Feb - Sep 2010	Health center	Consecutive	38.0	67	66.0	Low
Pinchevsky et.al, 2017	South Africa	53.9±11.5	May - Aug 2015	Health center	Consecutive	46.1	459	78.0	Low
Pinchevsky et.al, 2013	South Africa	63 ± 11.9	July 2008-2009	Hospital	Random	44.6	567	54.2	Low
Rotchford,2002	South Africa	56.5±10.4	2 months in 1999	Hospital	Consecutive	26.9	129	86.0	Low
Soetedjo et.al 2018	South Africa	53±9.9	Dec 2013 - Jun 2016	Health center	Consecutive	35.9	48	66.7	Low
Yameogo et.al,2012	Senegal	58.2±9.2	Mar 2007 - Jul 2008	Hospital	NR	25.5	52	80.8	High
HIV									
Fiseha et.al, 2019	Ethiopia	37±10.3	Jan - May 2018	Hospital	Consecutive	33.1	31	100.0	Low
Hyle et.al, 2019	South Africa	38.4±8.3	2015	Health center	Consecutive	33.0	54	83.0	Low
Manavalan et.al, 2020	Tanzania	NR	Oct 2016 - Dec 2018	Health center	Consecutive	21.4	10	100.0	Low
Muddu et.al, 2019	Uganda	43.6±11.5	Jan 2014 - Jan 2017	Health center	Consecutive	39.4	91	41.8	Low
Steffen et.al, 2017	Malawi	36±9.3	Not indicated	Health center	NR	42.8	35	77.1	Moderate
Stroke									
Abboud et.al, 2013	South Africa	63.5±11.3	Jan 2007 - Dec 2008	Hospital	Random	58.5	217	88.0	Low
Wahab et.al, 2017	Nigeria	59±13.1	Feb 2009 - Apr 2011	Hospital	Consecutive	60.9	284	60.2	Low

NR=Not reported

Risk of Bias Assessment

The risk of bias was assessed in all included studies of the 20 included studies. Most studies were categorized as having some concern for bias with two (10%) [37, 46] studies being deemed to have high risk of bias. Two studies [32, 44] (11.1%) had a moderate risk of bias while 16 studies [29-31, 33-36, 38-43, 45, 47, 48] (80%) had a low risk of bias. The inter-rater agreement for the risk of bias assessment was 0.65. Additional details on the domains assessed are included in the risk of bias summary table in the supplement (Table S3).

Prevalence of uncontrolled hypertension among patients with comorbidities

Twenty publications reported on uncontrolled hypertension among patients with comorbidities (Table 1). The majority of the studies were from South Africa (8, 40%) [29, 31, 36, 37, 40-43]. Uganda [33, 38], Nigeria [32, 45], Malawi [35, 44] Ethiopia [30, 47], and Tanzania [39, 48], had two (10%) studies each while Senegal [46] and Cameroon [34] had one study (5%) each. The reported prevalence of UHTN among people with comorbidities ranged from 41.8% (95% CI, 32.2%-52.0%) in Uganda to 100.0% (95% CI, 98.1%-100.0%) in South Africa. The pooled uncontrolled hypertension prevalence estimate in patients with comorbidities from the random-effects meta-analysis was 78.6% (95% CI, 71.1%-85.3%). Substantial heterogeneity (I^2 = 95.9%; P < .0001) existed in the included studies (Table 2). Absence of publication bias is suggested by the symmetrical visual inspection of the funnel plot, confirmed by the Egger's test (P < .001) (Figure 2).

Table 2: Meta-analysis results for the prevalence of uncontrolled hypertension in people with comorbidities in sub-Saharan Africa

	Prevalence (95%CI)	No of studies	Number of Participants	I^2 (95%CI)	$P^{heterogeneneity}$
Overall	78.6 (67.9-83.0)	20	3510	96.1	<0.0001
By comorbidity					
Atrial fibrillation	100.0 (98.1-100.0)	1	198	-	-
Chronic kidney disease	75.9 (69.4-81.4)	1	191	-	-
Diabetes	74.5 (67.1-81.3)	11	2399	93.1	<0.001

HIV	83.7 (56.0-99.5)	5	221	94.4	<0.001
Stroke	73.1 (69.1-76.9)	2	501	-	-
By region					
Eastern	80.8 (64.6-93.1)	6	772	94.7	<0.001
Western	69.8 (57.0-81.2)	3	415	-	-
Central	79.6 (70.6-86.4)	1	98	-	-
Southern	79.8 (68.1-89.4)	10	2225	97.3	<0.001
By risk of bias					
Low	76.4 (69.3-82.8)	16	3146	94.4	<0.001
Moderate	72.0 (63.3-80.0)	2	114	-	-
High	99.0 (97.1-100.0)	2	250	-	-
By study size					
Small studies	77.6 (66.0-87.4)	10	565	88.6	<0.001
Large studies	79.5 (69.0-83.0)	10	2945	97.7	<0.001
By period of publication					
Before 2015	79.4 (66.5-89.9)	10	1851	97.3	<0.001
After 2015	77.3 (68.0-85.4)	10	1659	93.1	<0.001
By gender proportion					
More females	75.4 (67.6-82.5)	14	2140	92.5	<0.001
More males	84.1 (69.5-94.7)	6	1370	97.6	<0.001
By sampling					
Consecutive	76.1 (67.6-83.7)	18	2639	95.6	<0.001
Random	64.5 (61.1-67.9)	2	784	-	-
By setting					
Hospital	78.4 (69.8-86.0)	12	2548	95.3	<0.001
Health center	79.4(60.7-93.4)	8	962	96.8	<0.001
By comorbidity HTN target					
Comorbidity target used	70.7 (61.3-79.2)	13	1776	93.3	<0.001
Comorbidity target not used	83.0 (72.4-91.4)	7	1734	96.3	<0.001
By Gross National Income					
Below SSA Average	78.6 (68.2-87.4)	9	1179	91.9	<0.001
Above SSA average	78.3 (66.1-88.4)	11	2331	97.3	<0.001
SSA=sub-Saharan Africa	**P^{egger}= 0.381**				

Subgroup analysis revealed differences in uncontrolled hypertension prevalence by comorbidity (Figure 3). Adults with atrial fibrillation reported the highest uncontrolled hypertension estimate (100.0% [95% CI, 98.1%- 100.0%]), followed by adults with HIV (83.7% [95% CI, 56.0%-99.5%]). The lowest pooled uncontrolled hypertension prevalence estimate was found in adults with stroke (73.1% [95% CI, 69.1%-76.9%]). Pooled UHTN prevalence differed by geographic regions; studies conducted in the Eastern, Southern and Central region reported higher prevalence's (80.8% [95% CI, 64.6%-

93.1%]), (79.8% [95% CI, 68.2%-89.3%]) and (79.6% [95% CI, 70.6%-86.4%]) respectively than studies conducted in the Western region (69.8% [95% CI, 57.0%-81.2%]). Prevalence varied by sample size; large studies reported a slightly higher prevalence (79.5% [95% CI, 69.1%-88.2%]) compared to small studies (77.6% [95% CI, 66.0%-87.4%]) (table 2). Studies that used the recomended hypertension control value for each comorbidity reported lower pooled prevalence of uncontrolled hypertension (75.8 [95% CI, 66.4-84.1]) compared to those that did not use the recomemded comorbidity specific blood pressure control value (83.0 [95% CI, 72.4-91.4]).

In the univariable analysis, heterogeneity was explained by being female (11.3%), risk of bias (18.4%), by regions (15.8%), comorbidities (3.5%), and using target blood pressure (21.3%) (Table S5). However only comorbidities and risk of bias were significant at 10% and these were added to the multivariable meta-regression analysis. The results from the multivariable meta-regression were not statistically significant. Sensitivity analysis conducted by excluding studies that had high risk of bias from the analysis did not show any influence on the robustness of the findings in the pooled analyses.

Sensitivity analysis done by excluding studies with high risk of bias from the analysis did not show any influence on the robustness of the findings in the pooled analysis.

Prevalence of uncontrolled hypertension among patients with diabetes

The prevalence of uncontrolled hypertension prevalence estimate among patients with diabetes was reported in 11 studies [30-32, 34, 35, 39-43, 46], with a total of 2399 participants. Uncontrolled hypertension prevalence in this group ranged from 54% (95% CI, 50%- 58%) to 85% (95% CI, 78%-90%), with a pooled estimate of 74.5% (95% CI, 67.1%-81.3%) (Table 2). Substantial heterogeneity (I^2 = 93.1%; P < .001) was observed in the included studies (Figure 2). Publication bias was not evident from the visual inspection of the funnel plot (Figure 4).

Subgroup analysis revealed differences in uncontrolled hypertension prevalence among people with diabetes(Table 3). There were differences noted by sample size; large studies reported a higher

prevalence (75.5% [95% CI, 67.1%-81.3%]) compared to small studies (73.3% [95% CI, 68.2%-79.3%]) (table 2). Pooled UHTN prevalence differed by geographic regions; studies conducted in the Eastern reported the highest pooled prevalence (82.5% [95% CI, 80.4%-87.1%]) while studies in conducted in the Southern region reported the lowest pooled prevalence (72.5% [95% CI, 62.0%-81.8%]). Gender differences were also noted; studies with more male participants had higher pooled prevalence (72.5% [95% CI, 64.4%-79.9%]) compared to studies with more female participants. Studies conducted after 2015 had higher pooled prevalence of UHTN among people with diabetes compared to studies conducted before 2015. Studies that used the recommended diabetes hypertension cuttoff (BP<130/85 mmHg) to define blood pressure control reported lower UHTN prevalences compared to those that did not use the recommended hypertension control value. Studies that had below the average SSA GNI reported a higher prevalence of UHTN (77.3 [95% CI, 69.7-84.2]) compared to studies with above the average SSA GNI (72.3 [95% CI, 61.0-82.3]).

In the univariable analysis, the use of the recomended hypertension control value for diabetes explained the most of the heterogeneity (56.7%) observed while sampling explained 100% of the heterogeneity (Table S6). In the final multivariable model, the sampling method used was associated with uncontrolled hypertension and explained most of the heterogeneity.

Table 3: Meta-analysis results for the prevalence of uncontrolled hypertension in people with diabetes in sub-Saharan Africa

	Prevalence (95%CI)	**No of studies**	**Number of Participants**	**I^2 (95%CI)**	**$p_{heterogeneneity}$**
Overall	74.5 (67.1-81.3)	11	2399	93.1	<0.001
By region					
Eastern	82.5 (78.8-85.9)	2	449	-	-
Western	75.0 (67.1-82.1)	2	131	-	-
Central	79.6 (70.6-86.4)	1	98	-	-
Southern	72.5 (62.0-81.8)	6	1721	94.9	<0.001
By risk of bias					
Low	74.2 (65.8-81.9)	9	2268	94.4	<0.001
Moderate	70.9 (60.1-78.8)	1	79	-	-
High	80.8 (68.1-89.2)	1	52	-	-
By study size					
Small studies	73.25 (66.8-79.3)	5	344	40.6	0.15

Large studies	75.5 (64.82-84.8)	6	2055	96.4	<0.001
By period of publication					
Before 2015	72.9 (62.4-82.3)	4	1245	92.4	<0.001
After 2015	78.0 (71.9-83.6)	7	1154	79.6	<0.001
By gender proportion					
More females	72.5 (64.4-79.9)	9	1919	92.2	<0.001
More males	83.9 (80.4-87.1)	2	480	-	-
By sampling					
Consecutive	76.7 (72.3-80.9)	9	1780	75.2	<0.001
Random	54.1 (50.0-58.2)	1	567	-	-
By setting					
Hospital	75.7 (66.0-84.3)	8	1825	94.9	<0.001
Health center	71.6 (61.5-80.8)	3	574	-	-
By comorbidity HTN target					
Comorbidity target used	70.1 (57.4-81.5)	5	863	90.1	<0.001
Comorbidity target not used	78.2 (73.1-82.9)	6	1536	79.3	<0.001
By Gross National Income					
Below SSA Average	77.3 (69.7-84.2)	5	852	81.1	<0.001
Above SSA average	72.3 (61.0-82.3)	6	1547	94.9	<0.001

SSA=sub-Saharan Africa $P^{egger} < 0.001$

Discussion

To our knowledge, this is the first systematic review and meta-analysis on the pooled prevalence of UHTN among patients with comorbidities in SSA. Our findings indicate more than three-quarters of the hypertensive people with coormodities have uncontrolled hypertension. These findings support the literature describing the challenges in controlling blood pressure among those on treatment and living with comorbidities while highlighting the fact that recognition of patient comorbidities' should be a core aspect of the care and support offered to patients with hypertension.

The prevalence of uncontrolled hypertension varied with the type of comorbidity. The highest pooled UHTN prevalence estimate (83.7%) was observed in people with HIV (83.7%), chronic kidney disease (75.9%) and diabetes (74.5%). A systematic review and meta-analysis on the prevalence of hypertension among people with HIV showed that about 25% of people with HIV had hypertension [49]. Also important to note is that the majority of people living with HIV are in SSA. Similarly, a UK

study found reduced risk associated with diabetes in people who achieved optimal blood pressure [13]. Another study conducted in Kenya found that 80% of diabetic patients from rural and semi-urban areas had hypertension [50]. Since hypertension is common among people with comorbidities, there is need to focus on integrated care for comorbidities and hypertension. These findings support literature describing the challenge in blood pressure control among those on treatment and with comorbidities.

The high prevalence of UHTN in people with comorbidities is concerning and requires further understanding. There are several factors affecting UHTN among patients on treatment. Non-adherence to antihypertensive is an important cause of uncontrolled hypertension. A systematic review conducted by Abegaz et al found 45% of patients on antihypertensive were non-adherent to medications with a higher proportion (84%) being among those with uncontrolled blood pressures [51]. Barriers to adherence are mainly related to limited accessibility to medications, medication side effects, low perception of the risks involved with having uncontrolled blood pressure, out-of-pocket costs and pill burden due to comorbidities. Provider related factors also affect the UHTN rates. A study conducted by Rose et al. concluded that inadequate treatment regimens are to blame for a majority of uncontrolled hypertension [8]. Provider lack of adherence to hypertension guidelines in regards to dose escalation and use of multiple drug regimens are a barrier to hypertension control. Chow et al revealed the use of multiple drug regimens to treat hypertension was lower in low-income countries compared the higher-, upper middle- or the lower middle-income countries [10].

The prevalence of uncontrolled hypertension has declined significantly in studies published after 2015 compared to those published before 2015 probably because of adherence to the changing guidelines promoting tighter blood pressure control for people with comorbidities. However, despite the observed decline, the prevalence of uncontrolled hypertension among people with comorbidities is very high and needs further research to understand the interventions that can reduce the uncontrolled hypertension rate so it can be adapted in other countries.

Our findings have the potential to inform public health strategies to reduce the burden of uncontrolled hypertension in SSA. Addressing the barriers identified is essential in achieving optimal blood pressure levels. The World Health Organization's global target on hypertension control action plan recommends integrated care programmes for the management of hypertension and comorbidities, a recommendation supported by the results of the current study [1].

Strengths and Limitations

Strengths of our systematic review and meta-analysis include the use of a published comprehensive protocol [23] to identify all available evidence without language restriction, reporting in accordance with PRISMA guidelines, search using multiple electronic databases, searching grey literature, contacting experts in the field for additional data sources to reduce study selection bias, and heterogeneity test by subgroup analyses and sensitivity analyses.

This study should however, be interpreted in the context of the following limitations. First, it is important to note that control of hypertension among those on treatment was not the main outcome of most of the included studies. Secondly, the prevalence of UHTN in some comorbidities such as atrial fibrillation and chronic kidney disease were reported in single studies probably because these conditions are understudied in SSA thus limiting the generalizeability of such findings. Fourth, most of the studies included in the meta-analysis were hospital based studies (60%) that used non-random sampling procedures (80%). Therefore, population based studies are warranted. Lastly, we found substantial heterogeneity between the studies and conducted meta-regression analysis, which did not explain the heterogeneity. The lack of uniformity and variance in the blood pressure cut-off points for the different comorbidities may have resulted in this heterogeneity.

Conclusion

In conclusion, the prevalence of uncontrolled hypertension is high in people with comorbid conditions in sub-Saharan Africa, particularly among people with diabetes. These findings strengthen the case for action to implement integrated care in the control of hypertension more effectively in African

populations and other low-and-middle-income countries. Such efforts include improved access to blood pressure testing among people with cormbodities, strategies to improve adherence, reviewing treatment guidelines and training of healthcare workers in managing people with hypertension comorbidities, and monitoring blood pressure control among all patients on treatment.

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Disclosures

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Data availability

All data relevant to the study are included in the article or uploaded as supplementary information.

No additional data available.

Ethics Approval

No ethics approval was sought for this study. This study only used published material.

Contributors

SFM conceived the study. SFM, OAU, MKM, GA, ASM, and PG designed the search strategy. SFM and ASM conducted the searches, retrieved articles, screened abstract and title, and the full text of potentially relevant articles. SFM wrote the first draft of the manuscript. All authors critically revised the manuscript and contributed to subsequent iterations.

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Figure 1: Study selection flow diagram

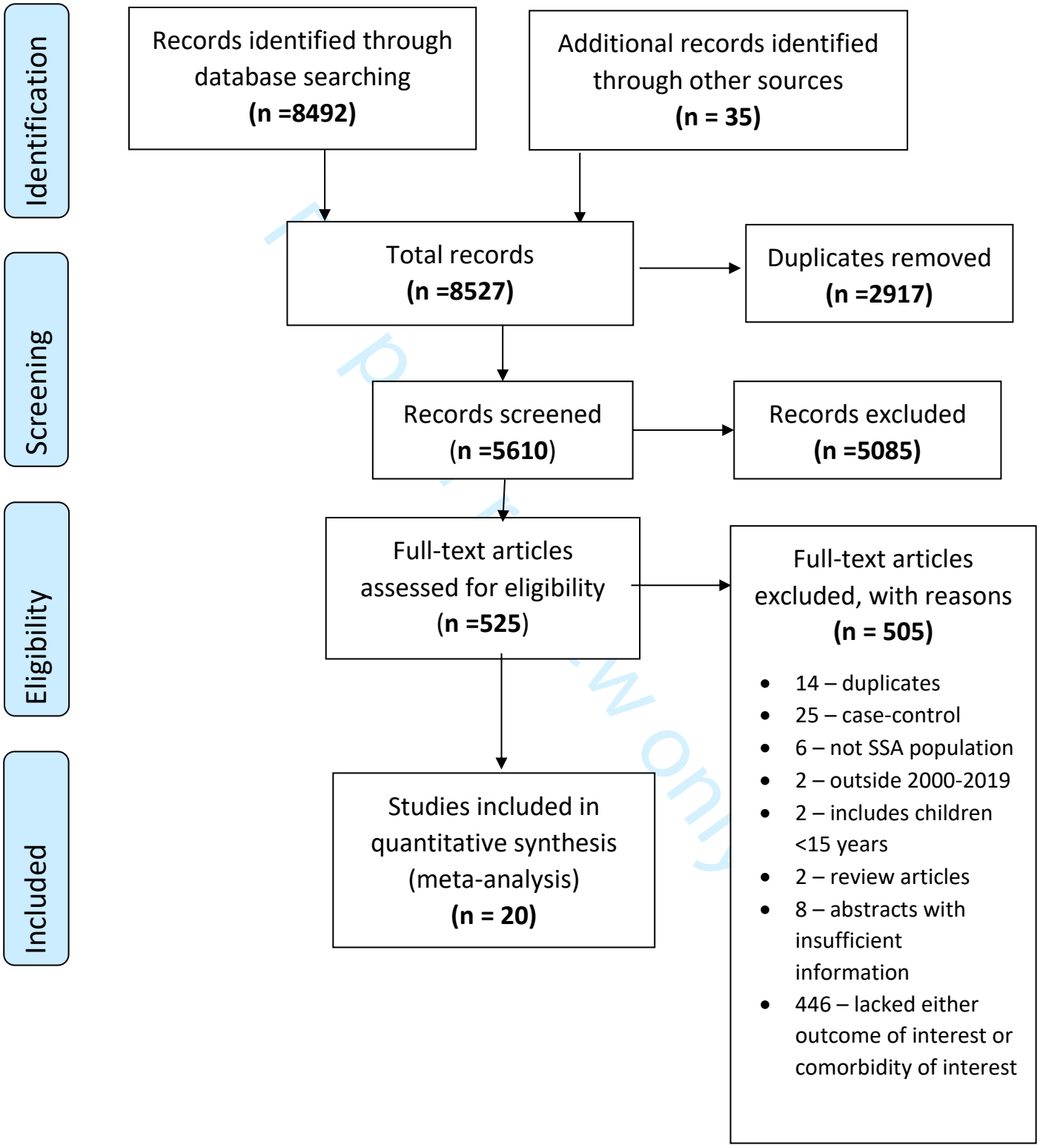


Figure 2: Funnel plot of the prevalence of uncontrolled hypertension in people with comorbidities in sub-Saharan Africa

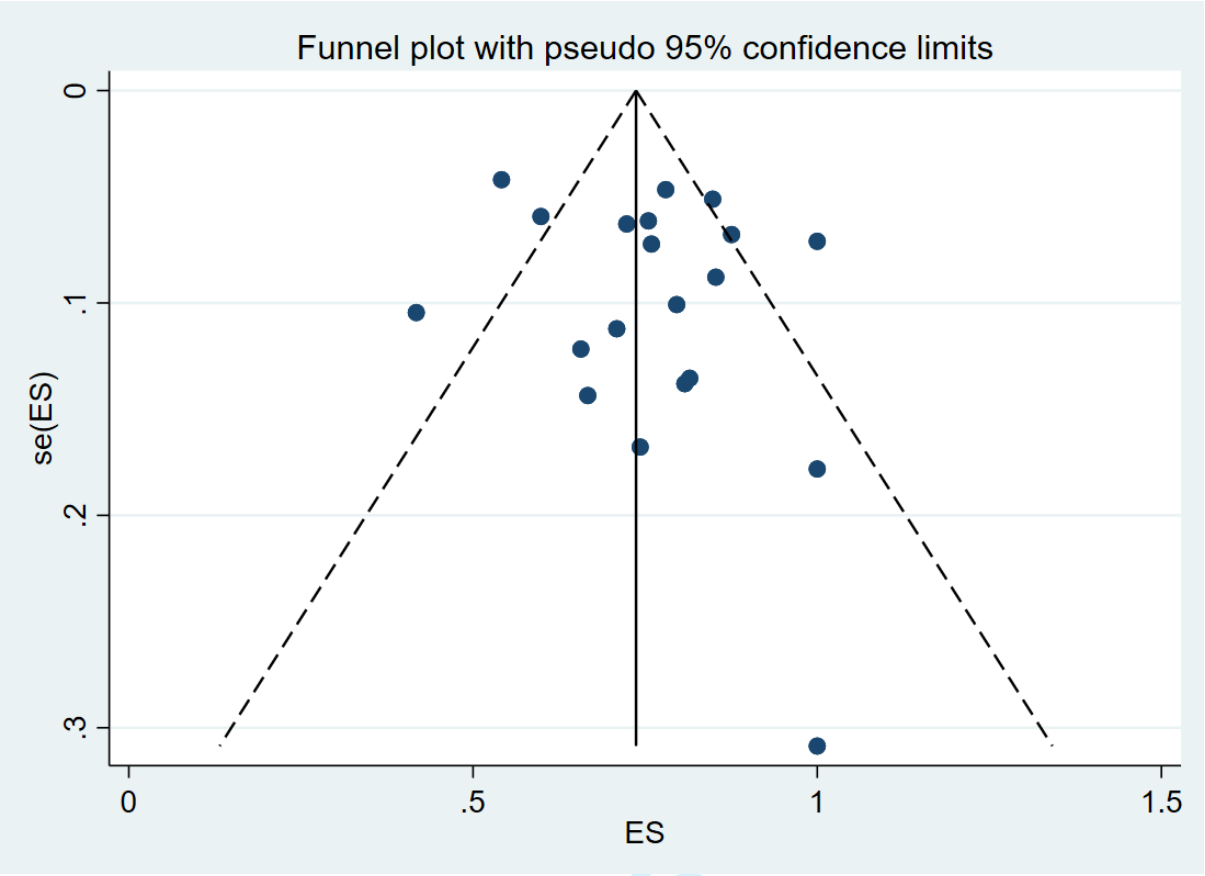


Figure 3: Pooled prevalence of uncontrolled hypertension in people with comorbidities in sub-Saharan Africa, by comorbidities

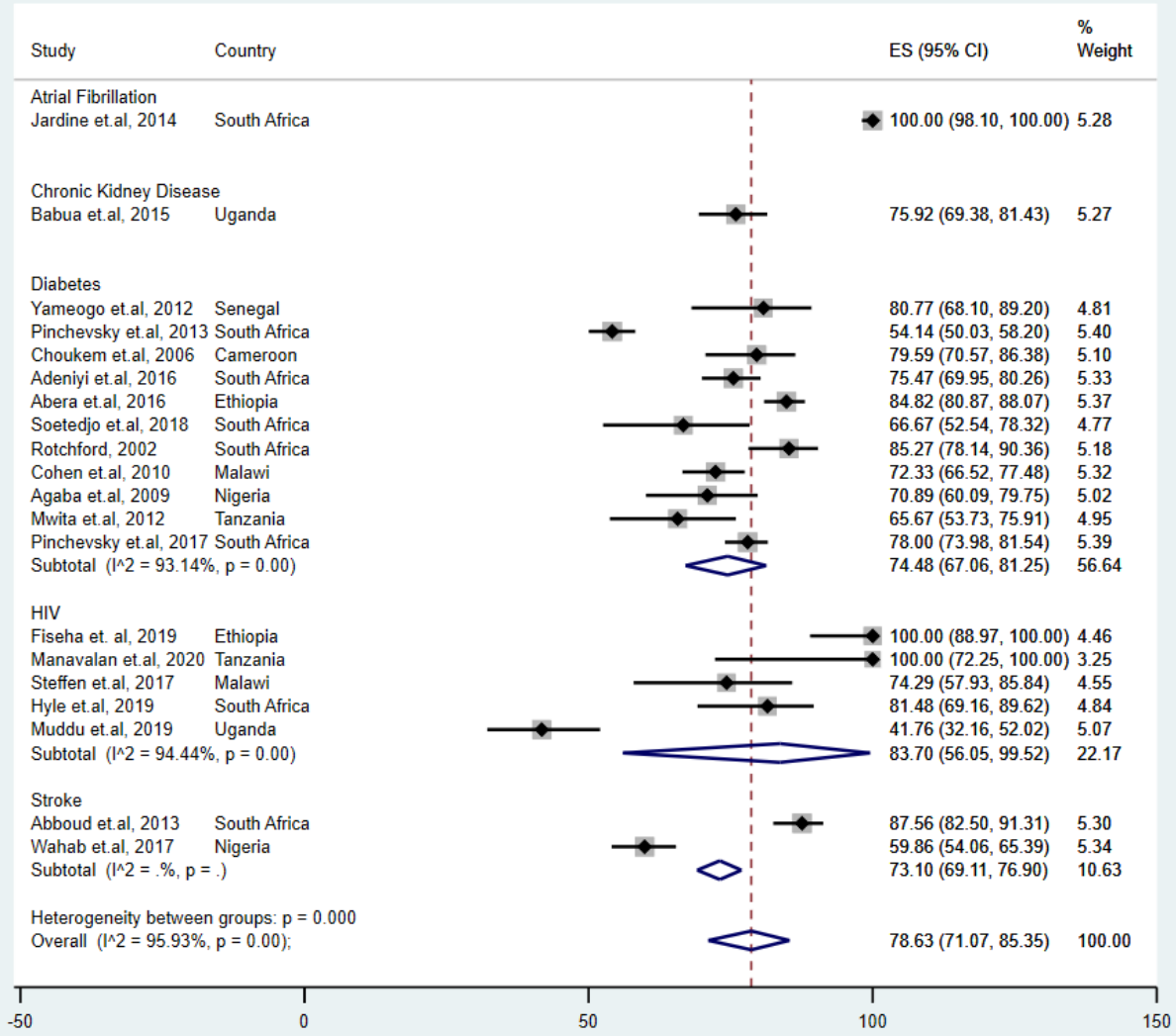
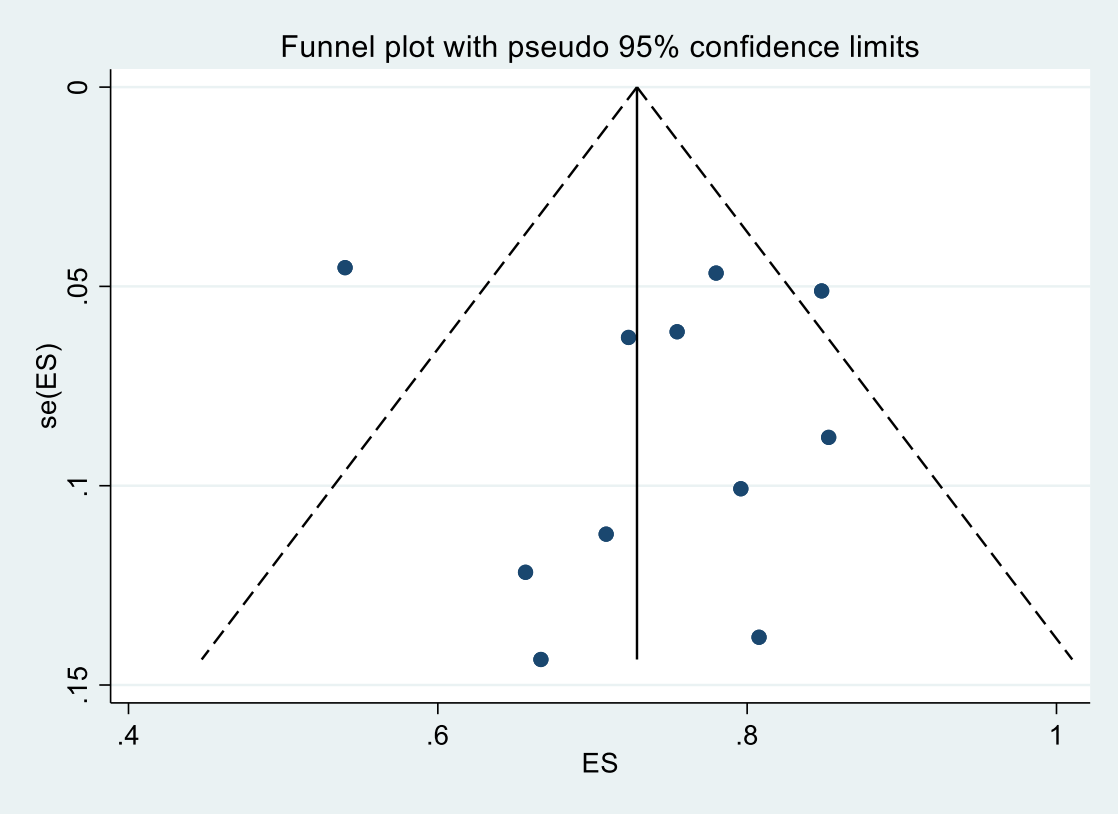


Figure 4: Funnel plot of the prevalence of uncontrolled hypertension in people with diabetes in sub-Saharan Africa



Supplementary file S1 – Search strategy

Medline - search

1. exp Hypertension/ or hypertension.mp.
2. exp Hypertension/ or uncontrolled hypertension.mp.
3. exp Hypertension/ or uncontrolled blood pressure.mp.
4. high blood pressure.mp. or exp Hypertension/
5. 1 or 2 or 3 or 4
6. type 2 diabetes mellitus.mp. or exp Diabetes Mellitus, Type 2/
7. type 2 diabetes.mp. or exp Diabetes Mellitus, Type 2/
8. exp Diabetes Mellitus, Type 2/ or type II diabetes.mp.
9. dyslipidemia.mp. or exp Dyslipidemias/
10. exp Dyslipidemias/ or dyslipidimia.mp.
11. exp Dyslipidemias/ or dyslipidaemia.mp.
12. Hypercholesterolemia.mp. or exp Hypercholesterolemia/
13. Hypercholesterolaemia.mp. or exp Hypercholesterolemia/
14. Hypercholesterolimia.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
15. hypertriglyceridemia.mp. or exp Hypertriglyceridemia/
16. exp Hypertriglyceridemia/ or hypertriglyceridaemia.mp.
17. hypertriglyceridimia.mp.
18. hyperlipidemia.mp. or exp Hyperlipidemias/
19. exp Hyperlipidemias/ or hyperlipidaemia.mp.
20. hyperlipidimia.mp.
21. obesity.mp. or exp Obesity/
22. chronic kidney disease.mp. or exp Renal Insufficiency, Chronic/
23. stroke.mp. or exp Stroke/
24. transient ischemic attack.mp. or exp Ischemic Attack, Transient/
25. Stroke/ or exp Ischemic Attack, Transient/ or transient ischaemic attack.mp.
26. coronary heart disease.mp. or exp Coronary Disease/
27. Heart failure.mp. or exp Heart Failure/
28. peripheral vascular disease.mp. or exp Peripheral Vascular Diseases/
29. atrial fibrillation.mp. or exp Atrial Fibrillation/
30. depression.mp. or exp Depression/
31. HIV/ or HIV.mp.
32. human immunodeficiency virus.mp. or exp HIV/
33. 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32
34. (Angola or Benin or Botswana or "Burkina Faso" or "Upper Volta" or Burundi or Urundi or Cameroon or Cameroons or "Cape Verde" or "Central African Republic" or Chad or Comoros or "Comoro Islands" or Comores or Mayotte or Congo or Zaire or "Cote d'Ivoire" or "Ivory Coast" or ("Democratic Republic of the Congo" or Djibouti or "French Somaliland" or Eritrea or Ethiopia or Gabon or "Gabonese Republic" or Gambia or Ghana or "Gold Coast" or Guinea or Kenya or Lesotho or Basutoland or Liberia) or (Madagascar or "Malagasy Republic" or Malawi or Nyasaland or Mali or Mauritania or Mauritius or Mozambique or Namibia or Niger or Nigeria) or (Rwanda or "Sao Tome" or Seychelles or Senegal or "Sierra Leone" or Somalia or "South Africa" or Sudan or Swaziland or Tanzania or Togo or "Togolese Republic" or Uganda or Zambia or Zimbabwe or Rhodesia)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
35. sub-Saharan africa.mp. or exp "Africa South of the Sahara"/
36. subsaharan africa.mp. or exp "Africa South of the Sahara"/
37. 34 or 35 or 36
38. 5 and 33 and 37
39. limit 38 to (humans and yr="2000 - 2021")

Embase - search

1. hypertension.mp. or exp hypertension/
2. exp hypertension/ or uncontrolled hypertension.mp. or exp antihypertensive agent/
3. exp antihypertensive agent/ or exp hypertension/ or uncontrolled blood pressure.mp.
4. high blood pressure.mp. or exp hypertension/
5. 1 or 2 or 3 or 4
6. type 2 diabetes mellitus.mp. or exp non insulin dependent diabetes mellitus/
7. type 2 diabetes.mp. or exp non insulin dependent diabetes mellitus/
8. type II diabetes.mp. or exp non insulin dependent diabetes mellitus/
9. dyslipidemia.mp. or exp dyslipidemia/
10. dyslipidimia.mp.
11. dyslipidaemia.mp. or exp dyslipidemia/
12. exp hypercholesterolemia/ or Hypercholesterolemia.mp.
13. Hypercholesterolaemia.mp. or exp hypercholesterolemia/
14. Hypercholesterolimia.mp.
15. hypertriglyceridemia.mp. or exp hypertriglyceridemia/
16. hypertriglyceridaemia.mp. or exp hypertriglyceridemia/
17. hypertriglyceridimia.mp. or exp hypertriglyceridemia/
18. hyperlipidemia.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
19. hyperlipidaemia.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
20. hyperlipidimia.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
21. obesity.mp. or exp obesity/
22. chronic kidney disease.mp. or exp chronic kidney failure/
23. stroke.mp. or exp cerebrovascular accident/
24. transient ischemic attack.mp. or exp transient ischemic attack/
25. transient ischaemic attack.mp. or exp transient ischemic attack/
26. coronary heart disease.mp. or exp ischemic heart disease/
27. Heart failure.mp. or exp heart failure/
28. peripheral vascular disease.mp. or exp peripheral vascular disease/
29. atrial fibrillation.mp. or exp atrial fibrillation/
30. exp depression/ or depression.mp.
31. HIV.mp. or exp Human immunodeficiency virus/
32. 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31
33. (Angola or Benin or Botswana or "Burkina Faso" or "Upper Volta" or Burundi or Urundi or Cameroon or Cameroons or "Cape Verde" or "Central African Republic" or Chad or Comoros or "Comoro Islands" or Comores or Mayotte or Congo or Zaire or "Cote d'Ivoire" or "Ivory Coast" or ("Democratic Republic of the Congo" or Djibouti or "French Somaliland" or Eritrea or Ethiopia or Gabon or "Gabonese Republic" or Gambia or Ghana or "Gold Coast" or Guinea or Kenya or Lesotho or Basutoland or Liberia) or (Madagascar or "Malagasy Republic" or Malawi or Nyasaland or Mali or Mauritania or Mauritius or Mozambique or Namibia or Niger or Nigeria) or (Rwanda or "Sao Tome" or Seychelles or Senegal or "Sierra Leone" or Somalia or "South Africa" or Sudan or Swaziland or Tanzania or Togo or "Togolese Republic" or Uganda or Zambia or Zimbabwe or Rhodesia)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
34. sub-Saharan africa.mp. or exp "Africa south of the Sahara"/
35. subsaharan africa.mp. or exp "Africa south of the Sahara"/

36. 33 or 34 or 35
37. 5 and 32 and 36
38. limit 37 to (human and yr="2000 - 2021")

Web of Science - search

# 38	**2,114**	#37 AND #33 AND #5 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 37	**421,085**	#36 OR #35 OR #34 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 36	**301**	TS=(subsaharan Africa) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 35	**33,673**	TS=(sub-Saharan Africa) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 34	**407,520**	TS=(Angola OR Benin OR Botswana OR "Burkina Faso" OR "Upper Volta" OR Burundi OR Urundi OR Cameroon OR Cameroons OR "Cape Verde" OR "Central African Republic" OR Chad OR Comoros OR "Comoro Islands" OR Comores OR Mayotte OR Congo OR Zaire OR "Cote d'Ivoire" OR "Ivory Coast" OR "Democratic Republic of the Congo" OR Djibouti OR "French Somaliland" OR Eritrea OR Ethiopia OR Gabon OR "Gabonese Republic" OR Gambia OR Ghana OR "Gold Coast" OR Guinea OR Kenya OR Lesotho OR Basutoland OR Liberia OR Madagascar OR "Malagasy Republic" OR Malawi OR Nyasaland OR Mali OR Mauritania OR Mauritius OR Mozambique OR Namibia OR Niger OR Nigeria OR Rwanda OR "Sao Tome" OR Seychelles OR Senegal OR "Sierra Leone" OR Somalia OR "South Africa" OR Sudan OR Swaziland OR Tanzania OR Togo OR "Togolese Republic" OR Uganda OR Zambia OR Zimbabwe OR Rhodesia) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 33	**1,764,519**	#32 OR #31 OR #30 OR #29 OR #28 OR #27 OR #26 OR #25 OR #24 OR #23 OR #22 OR #21 OR #20 OR #19 OR #18 OR #17 OR #16 OR #15 OR #14 OR #13 OR #12 OR #11 OR #10 OR #9 OR #8 OR #7 OR #6 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 32	**85,771**	TS=(Human immunodeficiency virus) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 31	**272,497**	TS=(HIV) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 30	**369,094**	TS=(depression)	Edit

		Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI *Timespan=2000-2019*	
# 29	**80,988**	TS=(atrial fibrillation) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 28	**20,886**	TS=(peripheral vascular disease) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 27	**226,090**	TS=(heart failure) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 26	**144,037**	TS=(coronary heart disease) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 25	**1,959**	TS=(transient ischaemic attack) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 24	**11,095**	TS=(transient ischemic attack) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 23	**278,508**	TS=(stroke) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 22	**75,433**	TS=(chronic kidney disease) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 21	**280,562**	TS=(obesity) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 20	**5**	TS=(hyperlipidimia) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 19	**2,534**	TS=(hyperlipidaemia) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 18	**21,065**	TS=(hyperlipidemia) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 17	**2**	TS=(hypertriglyceridimia) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit

# 16	1,000	TS=(hypertriglyceridaemia) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 15	8,591	TS=(hypertriglyceridemia) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 14	0	TS=(hypercholesterolimia) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 13	3,188	TS=(hypercholesterolaemia) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 12	27,232	TS=(hypercholesterolemia) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 11	4,539	TS=(dyslipidaemia) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 10	6	TS=(dyslipidimia) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 9	25,588	TS=(dyslipidemia) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 8	16,630	TS=(type II diabetes) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 7	173,805	TS=(type 2 diabetes) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 6	94,317	TS=(Type 2 diabetes mellitus) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 5	375,418	#4 OR #3 OR #2 OR #1 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 4	113,713	TS=(high blood pressure) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 3	3,503	TS=(uncontrolled blood pressure) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit

# 2	**4,063**	TS=(uncontrolled hypertension) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 1	**307,652**	**TOPIC:** (hypertension) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	

Table S2: List of 11 conditions included as comorbidity

	Conditions
1	Diabetes
2	Hypercholesterolemia/dyslipidemia/hyperlipidemia/hypertriglyceridemia
3	Obesity
4	Chronic kidney disease
5	Stroke and or transient Ischemic attack
6	Coronary heart disease
7	Heart failure
8	Peripheral vascular disease
9	Atrial fibrillation
10	Depression
11	HIV

Table S3: Assessment of Risk of Bias (RoB)

	External validity	Yes/No		Internal validity	Yes/No
1	Was the target population representative of the population in relation to relevant variables?		5	Were data collected directly from the subjects (as opposed to a proxy)?	
2	Was the sampling frame a true or close representation of the target population?		6	Was an acceptable case definition used in the study?	
3	Was some form of random selection used to select the sample, OR was a census undertaken?		7	Was the study instrument that measured the parameter of interest shown to have validity and reliability?	
4	Was the likelihood of nonresponse bias minimal in the study?		8	Was the same mode of data collection used for all subjects?	
			9	Were the numerator(s) and denominator(s) for the parameter of interest appropriate?	
10	Summary item on the overall risk of study bias				

Adapted from Hoy D, Brooks P, Woolf A, Blyth F, March L, Bain C, et al. Assessing risk of bias in prevalence studies: modification of an existing tool and evidence of interrater agreement. Journal of clinical epidemiology. 2012;65(9):934-9.

Supplement Table S4: Characteristics of studies in the prevalence of uncontrolled hypertension in sub-Saharan Africa

Year of publication (n = 20)	2002-2020
Period of inclusion (n = 20)	2000-2021
Mean age, years (n = 20)	56.8(±0.12)
% of males (n = 20)	41.8(±0.27)
Comorbidities	**N studies**
Diabetes	11
HIV	5
Stroke	2
Atrial fibrillation	1
Chronic Kidney Disease (CKD)	1
sub-Saharan African regions	
Eastern Africa	6
Western Africa	3
Central Africa	1
Central Africa	10
Study design	
Cross sectional	19
Not reported	1
Sampling	
Consecutive	16
Random	2
Not reported	2
Timing of data collection	
Retrospectively	5
Prospectively	14
Not reported	1
Data sources	
Medical records	5
Participants	11
from both medical records and participants	3
Not reported	1
Study site	
Hospital	12
Health Center	8
Gross National Income (GNI)	
Below sub-Saharan Africa average	9
Above sub-Saharan Africa average	11

Supplement table 5: **Meta-regression analysis for the variation of the prevalence of uncontrolled hypertension in people with comorbidity in SSA**

Variables (reference)	Univariate analysis				Multivariate analysis	
	N studies	P value	Odds ratio (95% CI)	R^2, %	P-value	Odds ratio (95% CI)
Year of publication (after 2015)	20	0.595	0.96 (0.83; 1.11)	0.00		
More females	20	0.172	0.09 (-0.04; 0.23)	11.35		
Risk of bias (low)	20			18.41		
Moderate		0.923	0.99 (0.76; 1.29)			
High		**0.080**	1.22 (0.97; 1.53)			
Sample size (small studies)	20			0		
Large studies		0.563	1.04 (0.90; 1.21)			
SSA regions (Eastern)	20			0.00		
Western		0.636	0.95 (0.74; 1.21)			
Central		0.747	1.06 (0.73; 1.53)			
Southern		0.679	1.04 (0.87; 1.24)			
Comorbidities (atrial fibrilation)	20			3.50		
Chroninc kidney disease		0.222	0.78 (0.53; 1.16)			
Diabetes		0.082	0.77 (0.58; 1.03)			
HIV		0.097	0.75 (0.53; 1.06)			
Stroke		0.119	0.76 (0.54; 1.08)			
Setting (Health center)	20			0		
Hospital		0.958	1.00 (0.86; 1.17)			
Sampling (Consecutive)	18			0		
Random		0.536	0.94 (0.75; 1.16)			
BP target used (recommended comorbidity target not used)	20			21.34		
Recommended BP control used		0.111	0.90 (0.79; 1.03)			
GNI (Below SSA average)	20					
Above SSA average		0.821	1.02 (0.88; 1.18)	0		

BP=Blood pressure

Table S6: **Meta-regression analysis for the variation of the prevalence of uncontrolled hypertension in people with diabetes in SSA**

Variables (reference)	Univariate analysis				Multivariate analysis	
	N studies	P value	Coefficient (95% CI)	R^2, %	P value	Adjusted coefficient (95% CI)
Year of publication (after 2015)	11	0.274	0.0793 (-0.0748; 0.2334)	18.20		
More females	11	0.205	0.1157 (-0.0758; 0.3072)	16.26		
Risk of bias (low)	11			-15.57		
Moderate		0.858	-0.0278 (-0.3753; 0.3198)			
High		0.688	0.0711 (-0.3228; 0.4650)			
Sample size (small studies)	11			-11.04		
Large studies		0.89	.0115 (-0.1714; 0.1943)			
SSA regions (Eastern)	11			-18.36		
Western		0.815	-.0341 (-0.3664; 0.2982)			
Central		0.952	.0101 (-0.3755; 0.3956)			
Southern		0.500	-0.0709 (-0.3067; 0.1649)			
Setting (Health center)	11			-15.43		
Hospital		0.860	.0160 (-0.1825; 0.2144)			
Sampling (Consecutive)	10					
Random		**0.001**	-0.2366 (-0.3477 -0.1255)	100.00	**0.043**	-0.1880 (-0.3686; -0.0074)
BP target used (recommended diabetes BP target not used)	11			56.66	0.439	-0.0563 (-0.2188; 0.1062)
Recommended diabetes BP control target used		**0.054**	-0.1320 (-0.2671; 0.0030)			
GNI (Below SSA average)	11					
Above SSA average		0.401	-0.0633 (-0.2256; 0.0991)	3.10		
Mean age	11	0.296	0.0047 (-.0046; 0.0139)	-0.16		

BP=Blood pressure

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.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
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.	4
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.	4-5
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.	4-5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplement file 1
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).	5
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.	5
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5
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.	5-6
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	6
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.	6

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).	7
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	6
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.	7 and figure 1
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.	7-8
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).	10
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.	9-12 and figure 3
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	10-14
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	10
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	11-13
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).	14-16
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).	17
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	17
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.	17

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Prevalence of uncontrolled hypertension in people with comorbidities in sub-Saharan Africa: a systematic review and meta-analysis

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Prevalence of uncontrolled hypertension in people with comorbidities in sub-Saharan Africa: a systematic review and meta-analysis

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Abstract

Background: The burden of uncontrolled hypertension in sub-Saharan Africa (SSA) is high and hypertension is known to co-exist with other chronic diseases such as kidney disease, diabetes among others. This is the first systematic review and meta-analysis to determine the burden of uncontrolled hypertension among patients with comorbidities in SSA.

Methods: A comprehensive search was conducted on MEDLINE, Excerpta Medica Database (Embase), and Web of Science to identify all relevant articles published between January 1st, 2000 and June 17th, 2021. We included studies that reported on the prevalence of uncontrolled hypertension among people in SSA who report taking antihypertensive treatment and have another chronic condition A random-effects meta-analysis was performed to obtain the pooled estimate of the prevalence of uncontrolled hypertension among patients with comorbid conditions while on treatment across studies in SSA.

Results: In all 20 articles were included for meta-analyses. Eleven articles were among diabetic patients, five articles were among HIV patients, two were among stroke patients while chronic kidney disease and atrial fibrillation had one article each. The pooled prevalence of uncontrolled hypertension among patients with comorbidities was 78.6% (95% CI, 71.1%-85.3%); I^2 95.9%), varying from 73.1% in patients with stroke to 100.0% in patients with atrial fibrillation. Subgroup analysis showed differences in uncontrolled hypertension prevalence by various study-level characteristics

Conclusion: This study suggests a high burden of uncontrolled hypertension in people with comorbidities in SSA. Strategies to improve the control of hypertension among people with comorbidities are needed. PROSPERO registration number CRD42019108218.

Word count – 241

Key word – Uncontrolled hypertension, comorbidities, sub-Saharan Africa

Strengths and limitations of this study

- A published comprehensive protocol was used to identify all available evidence without language restriction, reporting in accordance with PRISMA guidelines, search using multiple electronic databases, searching grey literature, contacting experts in the field for additional data sources to reduce study selection bias, and heterogeneity test by subgroup analyses and sensitivity analyses.
- The prevalence of uncontrolled hypertension (UHTN) in some comorbidities such as atrial fibrillation and chronic kidney disease were reported in single studies.
- Most of the studies included in the meta-analysis were hospital based studies that used non-random sampling procedures.
- There was substantial heterogeneity between the studies.

Introduction

Hypertension is an important risk factor for cardiovascular diseases (CVDs) and a leading contributor to death globally [1]. An estimated 1.4 billion people have hypertension globally with three quarter (75%) of this population living in low-and –middle-income countries [2, 3]. Worldwide trends analysis based on a large dataset from multiple studies conducted between 1975 and 2015 in 200 countries showed no change in global mean blood pressure, but a a substantial downward trend in high income countries and a rise in low and middle income countries [4]. Levels of hypertension awareness, treatment and control improved by 2.9% in high income countries while in low-middle-income countries neglible improvement in awareness, treatment, and control were observed [3, 4]. Africa is one of the regions in the world with the highest rates of uncontrolled blood pressure [5]. In a systematic review and meta-analysis on hypertension in SSA, Ataklte et al [6], reported a (93%) high prevalence of uncontrolled hypertension (UHTN).

Hypertension often co-exists with comorbidities such as chronic kidney disease, diabetes, and hypercholesterolemia among others [7-10]. These comorbidities could explain part of the inadequacy in blood pressure control. Some studies conducted in Europe and the US found that patients with diabetes mellitus had a significantly increased risk of uncontrolled blood pressure [11, 12]. Another study conducted in the UK has shown that achieving optimal blood pressure control in patients with hypertension and type 2 diabetes produces an important decrease in the risks associated with diabetes [13].

In recent years, public health efforts to promote prevention, awareness and treatment of hypertension in SSA have intensified [14-17] but hypertension control remains low [18-22]. Despite several studies conducted on UHTN in people with comorbidities, pooled estimations of the burden are not available for comorbidities such as diabetes, dyslipidaemia, stroke, HIV, obesity, atrial fibrillation. From a clinical perspective, it is important to understand why patients on treatment are not attaining optimal blood control and whether their pre-existing comorbidities contribute to the

lack of control of blood pressure. Therefore, to inform policy, practice and the development of guidelines for hypertension for integrated care among patients with comorbid conditions, it is critical to understand the burden of UHTN in people with comorbidities. The purpose of this review is to summarize the evidence on and estimate the prevalence of UHTN in patients with comorbidities in SSA and to explore factors associated with UHTN in people with comorbidities .

Methods

Protocol and registration

The protocol for this systemic review and meta-analysis was registered on the International Prospective Register of Systematic Reviews (PROSPERO CRD42019108218) and published [23]. The reporting was done according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA-P) guidelines [24].

Search Strategy

We systematically searched MEDLINE via Ovid, Excerpta Medica Database (Embase), and Web of Science from January 1st, 2000 to June 17th, 2021**.** The search strategy included the following relevant terms: *uncontrolled hypertension, hypertension, uncontrolled blood pressure, high blood pressure , a list of comorbidities, and sub-Saharan Africa (Detailed search strategy list is attached as supplement (Supplement file S1).* Additionally, the reference lists of the included studies were reviewed to identify other relevant studies.

Eligibility criteria

Studies were included if (1) they provided primary data on the prevalence of hypertension in accordance with the sevent report of the Joint National Committee (JNC7) among those who reported taking antihypertensive treatment and had a comorbid condition, (2) participants had been diagnosed with one of the comorbidities of interest – diabetes, dyslipidemia, obesity, chronic kidney disease, stroke or transient ischemic attack, coronary heart disease, heart failure, peripheral vascular disease,

atrial fibrillation, depression and HIV (Table S1), (3) participants were 15 and above years, (4) the study was published in any language, and (5) the study was conducted in a sub-Saharan Africa. The following types of study designs were excluded: (1) case-control studies, commentaries, editorials, letters, qualitative studies, and systematic reviews; (2) studies that included hypertension prevalence but did not report on the prevalence of hypertension among those on antihypertensive medication; and (3) studies of pregnancy-related hypertension.

Study selection

Two researchers independently screened the titles and abstracts (SFM & ASM). Two researchers (SFM & ASM) also assessed full-text reviews of the articles independently for final inclusion. The reference lists of potentially relevant publications were manually searched for additional publications. Disagreements were resolved by consensus. For multi-national studies, data were separated to show the estimate at the country level.

Data items and collection process

SFM and ASM independently screened the full texts of included studies. SFM extracted data from the selected studies, and ASM checked the data for accuracy. A standardized data extraction table was created (Table 1) and included the following data from all eligible articles: first author name, year of publication, language, country of the study, study design, sample size, study period, study setting, sampling method, the timing of data collection, data source, use of comorbidity specific hypertension control cuttoff, male proportion, age of participants (mean or median), type of comorbidity (diabetes, stroke, HIV, chronic kidney disease, atrial fibrillation), and main outcome of interest uncontrolled hypertension proportion or the data to cumpute it.

Risk of bias in individual studies

A tool developed by Hoy et.al [25] for prevalence studies was adapted and used to assess the methodological quality of included studies by evaluating the extent to which they addressed bias in 9

areas of internal and external validity (Table S2). Each of the nine areas was scored one if yes (high quality) and zero if no (poor quality), and a total quality score was calculated by summing the individual scores. Total scores ranged from 0 to 9, with higher scores indicating higher quality. Studies were then classified as having a low (>8), moderate (6–8), or high (≤5) risk of bias. Two researchers (SFM and MKM) independently assessed each of the included publications and disagreements was resolved through discussion.

Patient and Public Involvement

This research was done without patient involvement. There was no involvement of patients or members of the public in the design, or conduct, or reporting, or dissemination plans of this research.

Synthesis of results

The statistical approach used in this meta-analysis followed the study protocol [23]. Crude numerators and denominators from the individual studies were used to recalculate the study-specific unadjusted prevalence estimates. Variances of the study-specific estimates were stabilized using the double arcsine transformation to minimise the effect of studies with very small or very large prevalence estimates on the overall estimate (16) and then a random-effects meta-analysis was performed (17) to determine the pooled estimate of the prevalence of UHTN among patients with comorbidities overall and also among people with diabetes, HIV and stroke separately while on antihypertensive treatment across the included studies in SSA. Prevalence estimates were also summarised by comorbidities, publication year, sample size, study setting, sampling, risk of bias, gender proportionmean age and geographic regions.

Heterogeneity was explored using Cochrane's Q and quantified by I^2 statistics [26, 27]. Subgroup analyses were performed based on the following; gender proportion of participants, patient comorbidities, study design, study setting, sample size, use of recommended comorbidity specific

blood pressure control cut-offs, countries, regions (Eastern, Western, Central, and Southern Africa), and by Gross National Income (GNI) were be performed to identify the possible sources of heterogeneity. Sensitivity analyses were performed to assess the robustness of the findings by excluding studies with a high risk of bias.

Funnel plots and Egger asymmetry test were used to assess publication bias, with $P < .10$ considered to be statistically significant for publication bias [28]. Inter-rater agreements between the researchers involved in study inclusion and those involved in the identification of risk of bias were assessed using κ Cohen's coefficient (20).

All analyses were performed using 'metaprop' routine using StataSE version 16 (StataCorp LLC).

Results

Study selection

From the electronic database search, 8492 records were identified. An additional 35 articles were identified through reference tracing and from other sources. After duplicate removal, 5610 remained for the title and abstract screening. After screening, we found 5085 records to be irrelevant and excluded them. The full texts of 525 articles and reports were retrieved and assessed for eligibility, resulting in the inclusion of 20 studies for the meta-analysis (figure 1). The inter-rater agreement for study selection was 0.77.

Study characteristics

Table 1 and Table S3 provide detailed information on the included studies. In total, 3,510 participants were included across 20 studies. Most of the studies were cross-sectional (19, 95%), in English (19, 95%), hospital-based (12, 60%), used consecutive sampling (16, 80%), and prospectively collected data (14, 70%). The mean (SD) participant age from the 20 studies [29-48] providing this information was 56.8 (0.12) years. Study sample sizes ranged from 10 to 567 participants. The proportion of male participants in the included studies was reported in all studies and it ranged from 21.4% to 60.9% [29-48]. Of the included studies, 11 [30-32, 34, 35, 39-43, 46] reported on diabetes, five [36, 38, 44, 47,

48] reported on HIV, two [29, 45] reported on stroke, and one each reported on chronic kidney disease [33] and atrial fibrillation [37]. None of the included studies reported on obesity, dyslipidaemia, coronary heart disease, heart failure, peripheral heart disease, and depression.

Table 1: Characteristics of the Included Studies

Study	Country	Age (Mean/Median)	Study period	Study site	Sampling	Male %	Sample size	UHTN%	Risk of bias
Atrial Fibrillation									
Jardine et.al,2014	South Africa	67±13	Feb 2010 - Mar 2011	Health center	Consecutive	59.9	198	100.0	High
Chronic Kidney Disease									
Babua et.al 2015	Uganda	42.8	Jun - Feb 2013	Hospital	Consecutive	51.2	191	76.0	Low
Diabetes									
Abera et.al, 2016	Ethiopia	56.3±10	Aug - Jan 2015	Hospital	Consecutive	59.9	382	85.0	Low
Adeniyi et.al, 2016	South Africa	61.3±11.8	Jul to Nov 2013	Hospital	Consecutive	28.3	265	75.5	Low
Agaba et.al, 2009	Nigeria	51±12	Jun - Sept 2004	Hospital	Consecutive	40.2	79	70.9	Moderate
Choukem et.al 2006	Cameroon	56.6±13.3	6 months	Hospital	Consecutive	50.5	98	79.6	Low
Cohen et.al, 2010	Malawi	53.2±14.0	Mar - Jun 2007	Hospital	Consecutive	39.8	253	72.7	Low
Mwita et.al, 2012	Tanzania	51.6±11.2	Feb - Sep 2010	Health center	Consecutive	38.0	67	66.0	Low
Pinchevsky et.al, 2017	South Africa	53.9±11.5	May - Aug 2015	Health center	Consecutive	46.1	459	78.0	Low
Pinchevsky et.al, 2013	South Africa	63 ± 11.9	July 2008-2009	Hospital	Random	44.6	567	54.2	Low
Rotchford,2002	South Africa	56.5±10.4	2 months in 1999	Hospital	Consecutive	26.9	129	86.0	Low
Soetedjo et.al 2018	South Africa	53±9.9	Dec 2013 - Jun 2016	Health center	Consecutive	35.9	48	66.7	Low
Yameogo et.al,2012	Senegal	58.2±9.2	Mar 2007 - Jul 2008	Hospital	NR	25.5	52	80.8	High
HIV									
Fiseha et.al, 2019	Ethiopia	37±10.3	Jan - May 2018	Hospital	Consecutive	33.1	31	100.0	Low
Hyle et.al, 2019	South Africa	38.4±8.3	2015	Health center	Consecutive	33.0	54	83.0	Low
Manavalan et.al, 2020	Tanzania	NR	Oct 2016 - Dec 2018	Health center	Consecutive	21.4	10	100.0	Low
Muddu et.al, 2019	Uganda	43.6±11.5	Jan 2014 - Jan 2017	Health center	Consecutive	39.4	91	41.8	Low
Steffen et.al, 2017	Malawi	36±9.3	Not indicated	Health center	NR	42.8	35	77.1	Moderate
Stroke									
Abboud et.al, 2013	South Africa	63.5±11.3	Jan 2007 - Dec 2008	Hospital	Random	58.5	217	88.0	Low
Wahab et.al, 2017	Nigeria	59±13.1	Feb 2009 - Apr 2011	Hospital	Consecutive	60.9	284	60.2	Low

NR=Not reported

Risk of Bias Assessment

The risk of bias was assessed in all included studies of the 20 included studies. Most studies were categorized as having some concern for bias with two (10%) [37, 46] studies being deemed to have high risk of bias. Two studies [32, 44] (11.1%) had a moderate risk of bias while 16 studies [29-31, 33-36, 38-43, 45, 47, 48] (80%) had a low risk of bias. The inter-rater agreement for the risk of bias assessment was 0.65. Additional details on the domains assessed are included in the risk of bias summary table in the supplement (Table S2).

Prevalence of uncontrolled hypertension among patients with comorbidities

Twenty publications reported on uncontrolled hypertension among patients with comorbidities (Table 1). The majority of the studies were from South Africa (8, 40%) [29, 31, 36, 37, 40-43]. Uganda [33, 38], Nigeria [32, 45], Malawi [35, 44] Ethiopia [30, 47], and Tanzania [39, 48], had two (10%) studies each while Senegal [46] and Cameroon [34] had one study (5%) each. The reported prevalence of UHTN among people with comorbidities ranged from 41.8% (95% CI, 32.2%-52.0%) in Uganda to 100.0% (95% CI, 98.1%-100.0%) in South Africa. The pooled uncontrolled hypertension prevalence estimate in patients with comorbidities from the random-effects meta-analysis was 78.6% (95% CI, 71.1%-85.3%). Substantial heterogeneity (I^2 = 95.9%; P < .0001) existed in the included studies (Table 2). Absence of publication bias is suggested by the symmetrical visual inspection of the funnel plot, confirmed by the Egger's test (P < .001) (Figure 2).

Table 2: Meta-analysis results for the prevalence of uncontrolled hypertension in people with comorbidities in sub-Saharan Africa

	Prevalence (95%CI)	No of studies	Number of Participants	I^2 (95%CI)	$P^{heterogeneneity}$
Overall	78.6 (67.9-83.0)	20	3510	96.1	<0.0001
By comorbidity					
Atrial fibrillation	100.0 (98.1-100.0)	1	198	-	-
Chronic kidney disease	75.9 (69.4-81.4)	1	191	-	-
Diabetes	74.5 (67.1-81.3)	11	2399	93.1	<0.001

HIV	83.7 (56.0-99.5)	5	221	94.4	<0.001
Stroke	73.1 (69.1-76.9)	2	501	-	-
By region					
Eastern	80.8 (64.6-93.1)	6	772	94.7	<0.001
Western	69.8 (57.0-81.2)	3	415	-	-
Central	79.6 (70.6-86.4)	1	98	-	-
Southern	79.8 (68.1-89.4)	10	2225	97.3	<0.001
By risk of bias					
Low	76.4 (69.3-82.8)	16	3146	94.4	<0.001
Moderate	72.0 (63.3-80.0)	2	114	-	-
High	99.0 (97.1-100.0)	2	250	-	-
By study size					
Small studies	77.6 (66.0-87.4)	10	565	88.6	<0.001
Large studies	79.5 (69.0-83.0)	10	2945	97.7	<0.001
By period of publication					
Before 2015	79.4 (66.5-89.9)	10	1851	97.3	<0.001
After 2015	77.3 (68.0-85.4)	10	1659	93.1	<0.001
By gender proportion					
More females	75.4 (67.6-82.5)	14	2140	92.5	<0.001
More males	84.1 (69.5-94.7)	6	1370	97.6	<0.001
By sampling					
Consecutive	76.1 (67.6-83.7)	18	2639	95.6	<0.001
Random	64.5 (61.1-67.9)	2	784	-	-
By setting					
Hospital	78.4 (69.8-86.0)	12	2548	95.3	<0.001
Health center	79.4(60.7-93.4)	8	962	96.8	<0.001
By comorbidity HTN target					
Comorbidity target used	70.7 (61.3-79.2)	13	1776	93.3	<0.001
Comorbidity target not used	83.0 (72.4-91.4)	7	1734	96.3	<0.001
By Gross National Income					
Below SSA Average	78.6 (68.2-87.4)	9	1179	91.9	<0.001
Above SSA average	78.3 (66.1-88.4)	11	2331	97.3	<0.001
SSA=sub-Saharan Africa	**P^{egger}= 0.381**				

Subgroup analysis revealed differences in uncontrolled hypertension prevalence by comorbidity (Figure 3). Adults with atrial fibrillation reported the highest uncontrolled hypertension estimate (100.0% [95% CI, 98.1%- 100.0%]), followed by adults with HIV (83.7% [95% CI, 56.0%-99.5%]). The lowest pooled uncontrolled hypertension prevalence estimate was found in adults with stroke (73.1% [95% CI, 69.1%-76.9%]). Pooled UHTN prevalence differed by geographic regions; studies conducted in the Eastern, Southern and Central region reported higher prevalence's (80.8% [95% CI, 64.6%-

93.1%]), (79.8% [95% CI, 68.2%-89.3%]) and (79.6% [95% CI, 70.6%-86.4%]) respectively than studies conducted in the Western region (69.8% [95% CI, 57.0%-81.2%]). Prevalence varied by sample size; large studies reported a slightly higher prevalence (79.5% [95% CI, 69.1%-88.2%]) compared to small studies (77.6% [95% CI, 66.0%-87.4%]) (table 2). Studies that used the recomended hypertension control value for each comorbidity reported lower pooled prevalence of uncontrolled hypertension (75.8 [95% CI, 66.4-84.1]) compared to those that did not use the recomemded comorbidity specific blood pressure control value (83.0 [95% CI, 72.4-91.4]).

In the univariable analysis, heterogeneity was explained by being female (11.3%), risk of bias (18.4%), by regions (15.8%), comorbidities (3.5%), and using target blood pressure (21.3%) (Table S4). However only comorbidities and risk of bias were significant at 10% and these were added to the multivariable meta-regression analysis. The results from the multivariable meta-regression were not statistically significant. Sensitivity analysis conducted by excluding studies that had high risk of bias from the analysis did not show any influence on the robustness of the findings in the pooled analyses.

Sensitivity analysis done by excluding studies with high risk of bias from the analysis did not show any influence on the robustness of the findings in the pooled analysis.

Prevalence of uncontrolled hypertension among patients with diabetes

The prevalence of uncontrolled hypertension prevalence estimate among patients with diabetes was reported in 11 studies [30-32, 34, 35, 39-43, 46], with a total of 2399 participants. Uncontrolled hypertension prevalence in this group ranged from 54% (95% CI, 50%- 58%) to 85% (95% CI, 78%-90%), with a pooled estimate of 74.5% (95% CI, 67.1%-81.3%) (Table 2). Substantial heterogeneity (I^2 = 93.1%; P < .001) was observed in the included studies (Figure 2). Publication bias was not evident from the visual inspection of the funnel plot (Figure 4).

Subgroup analysis revealed differences in uncontrolled hypertension prevalence among people with diabetes(Table 3). There were differences noted by sample size; large studies reported a higher

prevalence (75.5% [95% CI, 67.1%-81.3%]) compared to small studies (73.3% [95% CI, 68.2%-79.3%]) (table 2). Pooled UHTN prevalence differed by geographic regions; studies conducted in the Eastern reported the highest pooled prevalence (82.5% [95% CI, 80.4%-87.1%]) while studies in conducted in the Southern region reported the lowest pooled prevalence (72.5% [95% CI, 62.0%-81.8%]). Gender differences were also noted; studies with more male participants had higher pooled prevalence (72.5% [95% CI, 64.4%-79.9%]) compared to studies with more female participants. Studies conducted after 2015 had higher pooled prevalence of UHTN among people with diabetes compared to studies conducted before 2015. Studies that used the recommended diabetes hypertension cuttoff (BP<130/85 mmHg) to define blood pressure control reported lower UHTN prevalences compared to those that did not use the recommended hypertension control value. Studies that had below the average SSA GNI reported a higher prevalence of UHTN (77.3 [95% CI, 69.7-84.2]) compared to studies with above the average SSA GNI (72.3 [95% CI, 61.0-82.3]).

In the univariable analysis, the use of the recomended hypertension control value for diabetes explained the most of the heterogeneity (56.7%) observed while sampling explained 100% of the heterogeneity (Table S5). In the final multivariable model, the sampling method used was associated with uncontrolled hypertension and explained most of the heterogeneity.

Table 3: Meta-analysis results for the prevalence of uncontrolled hypertension in people with diabetes in sub-Saharan Africa

	Prevalence (95%CI)	**No of studies**	**Number of Participants**	**I^2 (95%CI)**	**$p_{heterogeneneity}$**
Overall	74.5 (67.1-81.3)	11	2399	93.1	<0.001
By region					
Eastern	82.5 (78.8-85.9)	2	449	-	-
Western	75.0 (67.1-82.1)	2	131	-	-
Central	79.6 (70.6-86.4)	1	98	-	-
Southern	72.5 (62.0-81.8)	6	1721	94.9	<0.001
By risk of bias					
Low	74.2 (65.8-81.9)	9	2268	94.4	<0.001
Moderate	70.9 (60.1-78.8)	1	79	-	-
High	80.8 (68.1-89.2)	1	52	-	-
By study size					
Small studies	73.25 (66.8-79.3)	5	344	40.6	0.15

Large studies	75.5 (64.82-84.8)	6	2055	96.4	<0.001
By period of publication					
Before 2015	72.9 (62.4-82.3)	4	1245	92.4	<0.001
After 2015	78.0 (71.9-83.6)	7	1154	79.6	<0.001
By gender proportion					
More females	72.5 (64.4-79.9)	9	1919	92.2	<0.001
More males	83.9 (80.4-87.1)	2	480	-	-
By sampling					
Consecutive	76.7 (72.3-80.9)	9	1780	75.2	<0.001
Random	54.1 (50.0-58.2)	1	567	-	-
By setting					
Hospital	75.7 (66.0-84.3)	8	1825	94.9	<0.001
Health center	71.6 (61.5-80.8)	3	574	-	-
By comorbidity HTN target					
Comorbidity target used	70.1 (57.4-81.5)	5	863	90.1	<0.001
Comorbidity target not used	78.2 (73.1-82.9)	6	1536	79.3	<0.001
By Gross National Income					
Below SSA Average	77.3 (69.7-84.2)	5	852	81.1	<0.001
Above SSA average	72.3 (61.0-82.3)	6	1547	94.9	<0.001

SSA=sub-Saharan Africa $P^{egger} < 0.001$

Discussion

To our knowledge, this is the first systematic review and meta-analysis on the pooled prevalence of UHTN among patients with comorbidities in SSA. Our findings indicate more than three-quarters of the hypertensive people with coormodities have uncontrolled hypertension. These findings support the literature describing the challenges in controlling blood pressure among those on treatment and living with comorbidities while highlighting the fact that recognition of patient comorbidities' should be a core aspect of the care and support offered to patients with hypertension.

The prevalence of uncontrolled hypertension varied with the type of comorbidity. The highest pooled UHTN prevalence estimate (83.7%) was observed in people with HIV (83.7%), chronic kidney disease (75.9%) and diabetes (74.5%). A systematic review and meta-analysis on the prevalence of hypertension among people with HIV showed that about 25% of people with HIV had hypertension [49]. Also important to note is that the majority of people living with HIV are in SSA. Similarly, a UK

study found reduced risk associated with diabetes in people who achieved optimal blood pressure [13]. Another study conducted in Kenya found that 80% of diabetic patients from rural and semi-urban areas had hypertension [50]. Since hypertension is common among people with comorbidities, there is need to focus on integrated care for comorbidities and hypertension. These findings support literature describing the challenge in blood pressure control among those on treatment and with comorbidities.

The high prevalence of UHTN in people with comorbidities is concerning and requires further understanding. There are several factors affecting UHTN among patients on treatment. Non-adherence to antihypertensive is an important cause of uncontrolled hypertension. A systematic review conducted by Abegaz et al found 45% of patients on antihypertensive were non-adherent to medications with a higher proportion (84%) being among those with uncontrolled blood pressures [51]. Barriers to adherence are mainly related to limited accessibility to medications, medication side effects, low perception of the risks involved with having uncontrolled blood pressure, out-of-pocket costs and pill burden due to comorbidities. Provider related factors also affect the UHTN rates. A study conducted by Rose et al. concluded that inadequate treatment regimens are to blame for a majority of uncontrolled hypertension [8]. Provider lack of adherence to hypertension guidelines in regards to dose escalation and use of multiple drug regimens are a barrier to hypertension control. Chow et al revealed the use of multiple drug regimens to treat hypertension was lower in low-income countries compared the higher-, upper middle- or the lower middle-income countries [10].

The prevalence of uncontrolled hypertension has declined significantly in studies published after 2015 compared to those published before 2015 probably because of adherence to the changing guidelines promoting tighter blood pressure control for people with comorbidities. However, despite the observed decline, the prevalence of uncontrolled hypertension among people with comorbidities is very high and needs further research to understand the interventions that can reduce the uncontrolled hypertension rate so it can be adapted in other countries.

Our findings have the potential to inform public health strategies to reduce the burden of uncontrolled hypertension in SSA. Addressing the barriers identified is essential in achieving optimal blood pressure levels. The World Health Organization's global target on hypertension control action plan recommends integrated care programmes for the management of hypertension and comorbidities, a recommendation supported by the results of the current study [1].

Strengths and Limitations

Strengths of our systematic review and meta-analysis include the use of a published comprehensive protocol [23] to identify all available evidence without language restriction, reporting in accordance with PRISMA guidelines, search using multiple electronic databases, searching grey literature, contacting experts in the field for additional data sources to reduce study selection bias, and heterogeneity test by subgroup analyses and sensitivity analyses.

This study should however, be interpreted in the context of the following limitations. First, it is important to note that control of hypertension among those on treatment was not the main outcome of most of the included studies. Secondly, the prevalence of UHTN in some comorbidities such as atrial fibrillation and chronic kidney disease were reported in single studies probably because these conditions are understudied in SSA thus limiting the generalizeability of such findings. Fourth, most of the studies included in the meta-analysis were hospital based studies (60%) that used non-random sampling procedures (80%). Therefore, population based studies are warranted. Lastly, we found substantial heterogeneity between the studies and conducted meta-regression analysis, which did not explain the heterogeneity. The lack of uniformity and variance in the blood pressure cut-off points for the different comorbidities may have resulted in this heterogeneity.

Conclusion

In conclusion, the prevalence of uncontrolled hypertension is high in people with comorbid conditions in sub-Saharan Africa, particularly among people with diabetes. These findings strengthen the case for action to implement integrated care in the control of hypertension more effectively in African

populations and other low-and-middle-income countries. Such efforts include improved access to blood pressure testing among people with cormbodities, strategies to improve adherence, reviewing treatment guidelines and training of healthcare workers in managing people with hypertension comorbidities, and monitoring blood pressure control among all patients on treatment.

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Disclosures

None.

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Data availability

All data relevant to the study are included in the article or uploaded as supplementary information.

No additional data available.

Ethics Approval

No ethics approval was sought for this study. This study only used published material.

Contributors

SFM conceived the study. SFM, OAU, MKM, GA, ASM, and PG designed the search strategy. SFM and ASM conducted the searches, retrieved articles, screened abstract and title, and the full text of potentially relevant articles. SFM wrote the first draft of the manuscript. All authors critically revised the manuscript and contributed to subsequent iterations.

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Figure 1: Study selection flow diagram

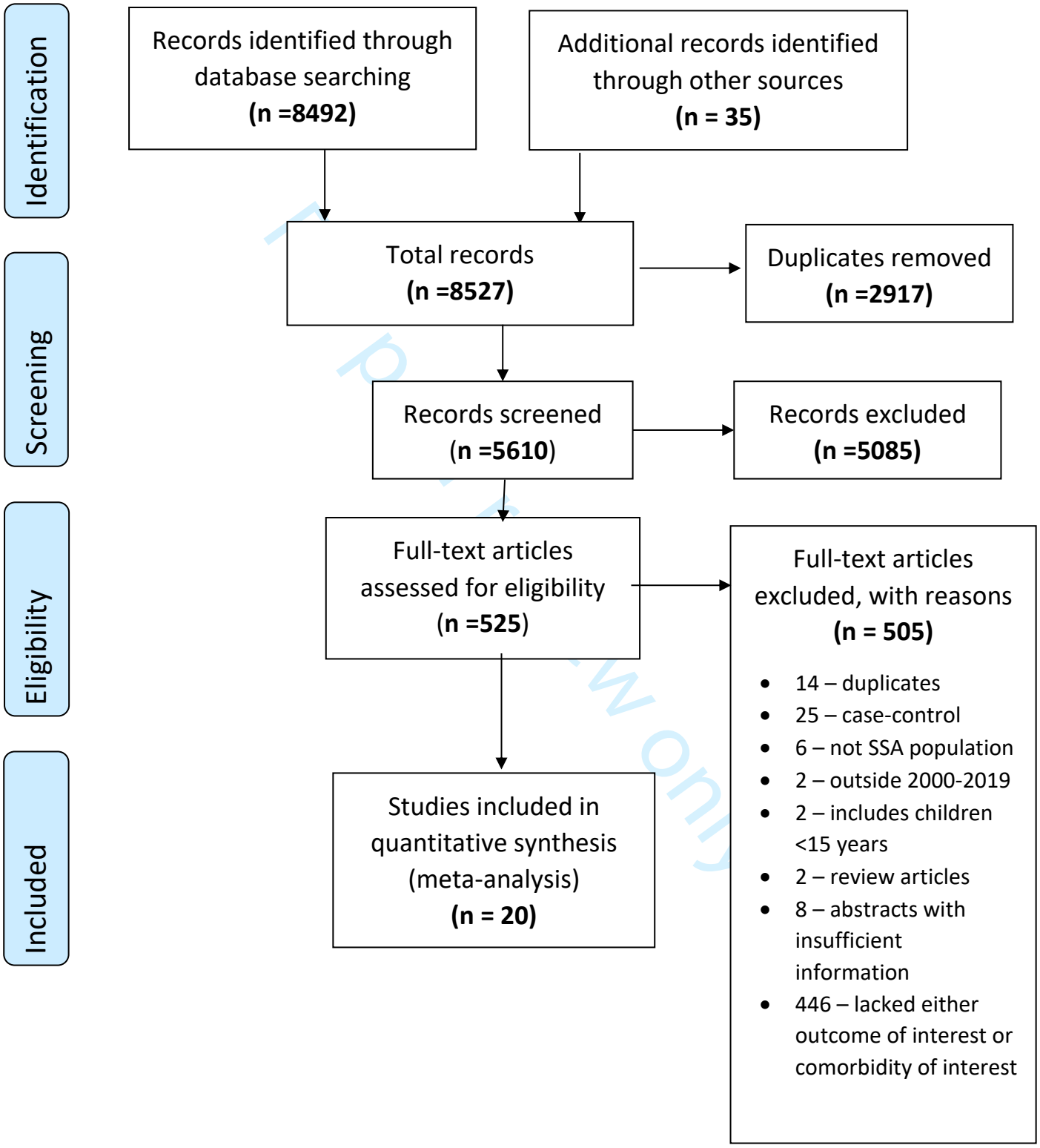


Figure 2: Funnel plot of the prevalence of uncontrolled hypertension in people with comorbidities in sub-Saharan Africa

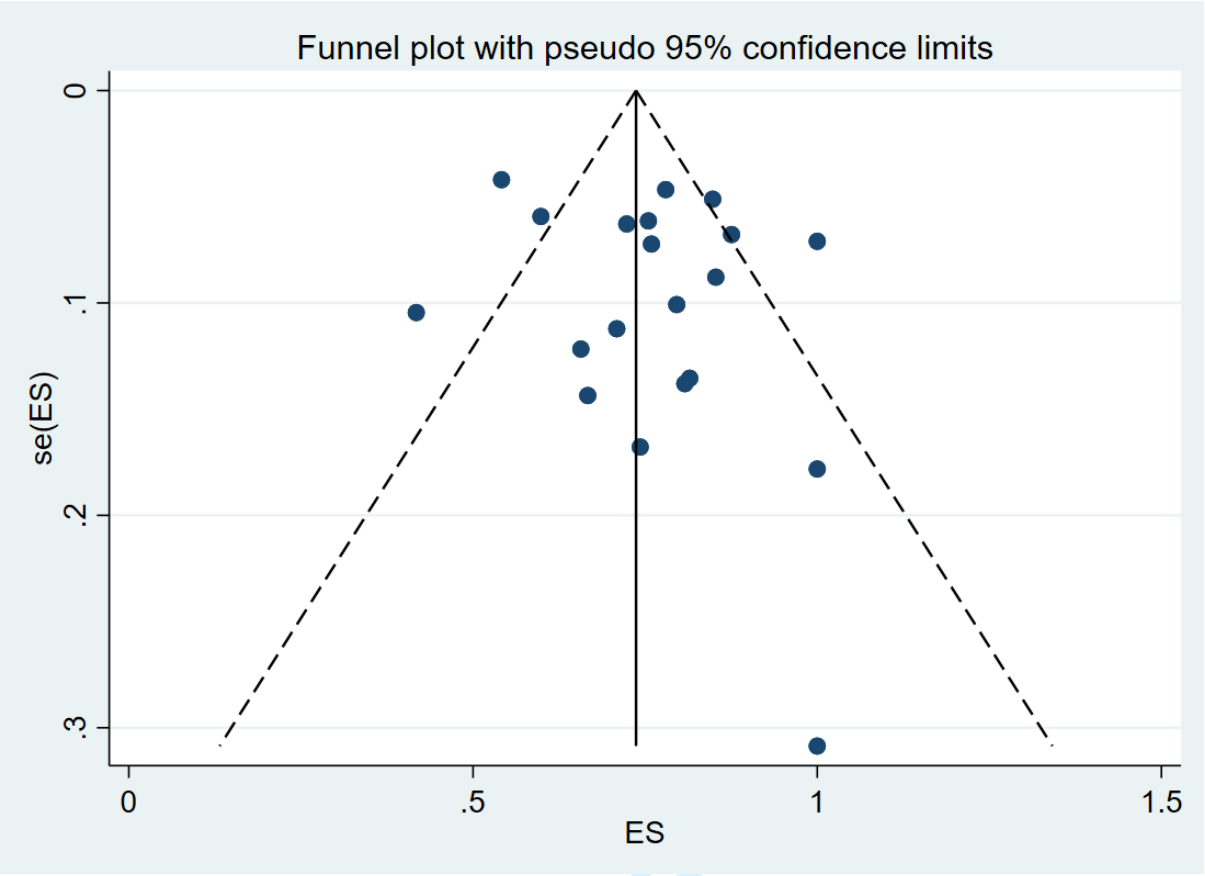


Figure 3: Pooled prevalence of uncontrolled hypertension in people with comorbidities in sub-Saharan Africa, by comorbidities

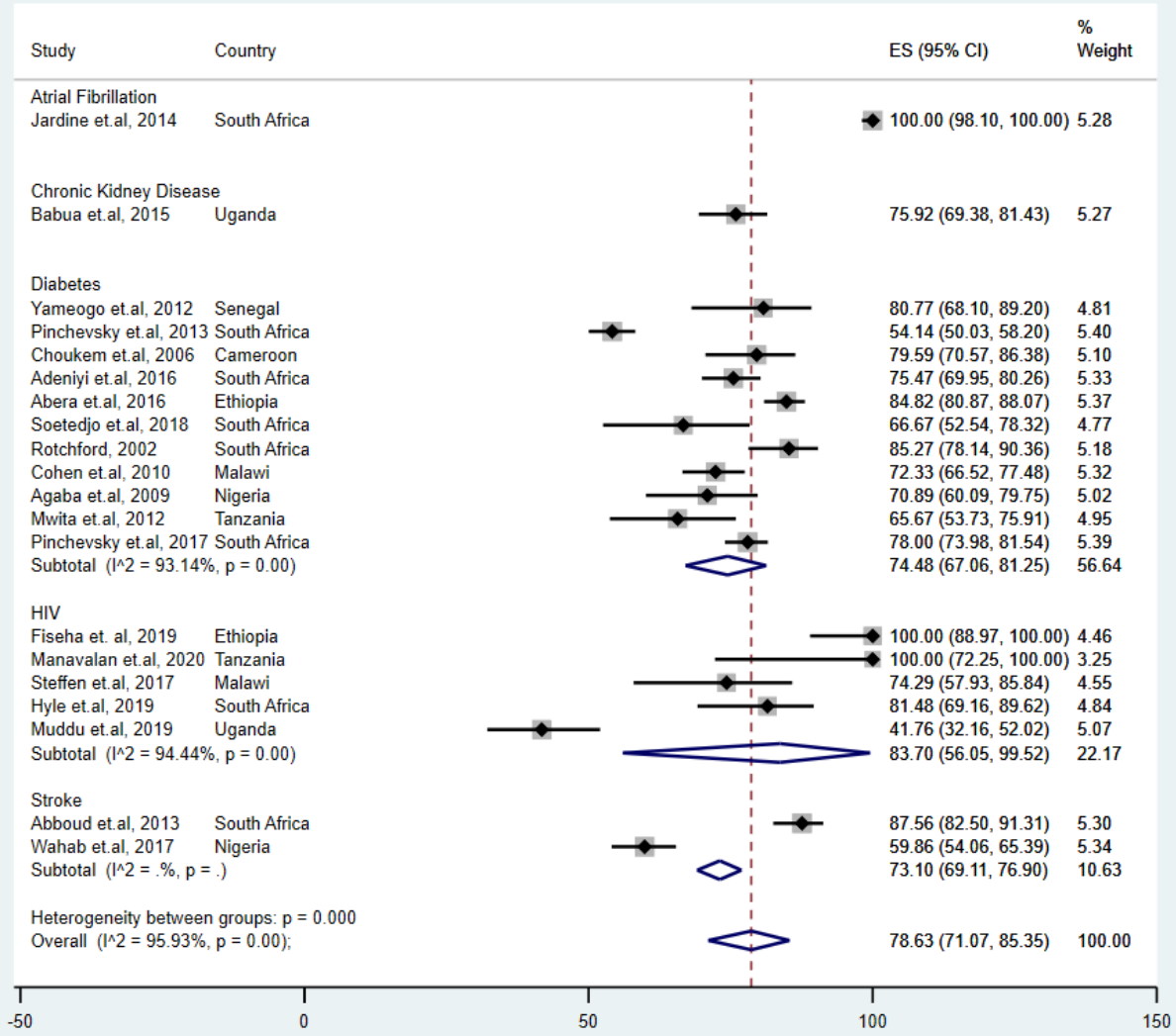
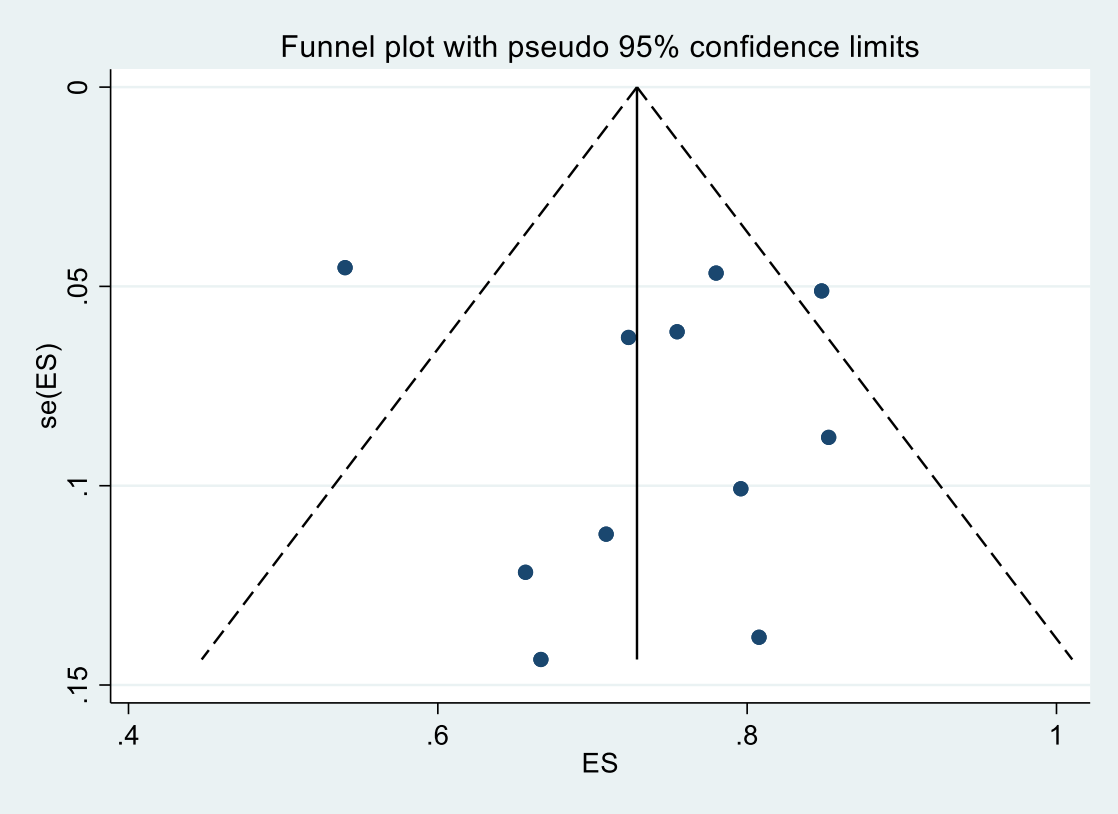


Figure 4: Funnel plot of the prevalence of uncontrolled hypertension in people with diabetes in sub-Saharan Africa



Supplementary file S1 – Search strategy

Medline - search

1. exp Hypertension/ or hypertension.mp.
2. exp Hypertension/ or uncontrolled hypertension.mp.
3. exp Hypertension/ or uncontrolled blood pressure.mp.
4. high blood pressure.mp. or exp Hypertension/
5. 1 or 2 or 3 or 4
6. type 2 diabetes mellitus.mp. or exp Diabetes Mellitus, Type 2/
7. type 2 diabetes.mp. or exp Diabetes Mellitus, Type 2/
8. exp Diabetes Mellitus, Type 2/ or type II diabetes.mp.
9. dyslipidemia.mp. or exp Dyslipidemias/
10. exp Dyslipidemias/ or dyslipidimia.mp.
11. exp Dyslipidemias/ or dyslipidaemia.mp.
12. Hypercholesterolemia.mp. or exp Hypercholesterolemia/
13. Hypercholesterolaemia.mp. or exp Hypercholesterolemia/
14. Hypercholesterolimia.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
15. hypertriglyceridemia.mp. or exp Hypertriglyceridemia/
16. exp Hypertriglyceridemia/ or hypertriglyceridaemia.mp.
17. hypertriglyceridimia.mp.
18. hyperlipidemia.mp. or exp Hyperlipidemias/
19. exp Hyperlipidemias/ or hyperlipidaemia.mp.
20. hyperlipidimia.mp.
21. obesity.mp. or exp Obesity/
22. chronic kidney disease.mp. or exp Renal Insufficiency, Chronic/
23. stroke.mp. or exp Stroke/
24. transient ischemic attack.mp. or exp Ischemic Attack, Transient/
25. Stroke/ or exp Ischemic Attack, Transient/ or transient ischaemic attack.mp.
26. coronary heart disease.mp. or exp Coronary Disease/
27. Heart failure.mp. or exp Heart Failure/
28. peripheral vascular disease.mp. or exp Peripheral Vascular Diseases/
29. atrial fibrillation.mp. or exp Atrial Fibrillation/
30. depression.mp. or exp Depression/
31. HIV/ or HIV.mp.
32. human immunodeficiency virus.mp. or exp HIV/
33. 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32
34. (Angola or Benin or Botswana or "Burkina Faso" or "Upper Volta" or Burundi or Urundi or Cameroon or Cameroons or "Cape Verde" or "Central African Republic" or Chad or Comoros or "Comoro Islands" or Comores or Mayotte or Congo or Zaire or "Cote d'Ivoire" or "Ivory Coast" or ("Democratic Republic of the Congo" or Djibouti or "French Somaliland" or Eritrea or Ethiopia or Gabon or "Gabonese Republic" or Gambia or Ghana or "Gold Coast" or Guinea or Kenya or Lesotho or Basutoland or Liberia) or (Madagascar or "Malagasy Republic" or Malawi or Nyasaland or Mali or Mauritania or Mauritius or Mozambique or Namibia or Niger or Nigeria) or (Rwanda or "Sao Tome" or Seychelles or Senegal or "Sierra Leone" or Somalia or "South Africa" or Sudan or Swaziland or Tanzania or Togo or "Togolese Republic" or Uganda or Zambia or Zimbabwe or Rhodesia)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
35. sub-Saharan africa.mp. or exp "Africa South of the Sahara"/
36. subsaharan africa.mp. or exp "Africa South of the Sahara"/
37. 34 or 35 or 36
38. 5 and 33 and 37
39. limit 38 to (humans and yr="2000 - 2021")

Embase - search

1. hypertension.mp. or exp hypertension/
2. exp hypertension/ or uncontrolled hypertension.mp. or exp antihypertensive agent/
3. exp antihypertensive agent/ or exp hypertension/ or uncontrolled blood pressure.mp.
4. high blood pressure.mp. or exp hypertension/
5. 1 or 2 or 3 or 4
6. type 2 diabetes mellitus.mp. or exp non insulin dependent diabetes mellitus/
7. type 2 diabetes.mp. or exp non insulin dependent diabetes mellitus/
8. type II diabetes.mp. or exp non insulin dependent diabetes mellitus/
9. dyslipidemia.mp. or exp dyslipidemia/
10. dyslipidimia.mp.
11. dyslipidaemia.mp. or exp dyslipidemia/
12. exp hypercholesterolemia/ or Hypercholesterolemia.mp.
13. Hypercholesterolaemia.mp. or exp hypercholesterolemia/
14. Hypercholesterolimia.mp.
15. hypertriglyceridemia.mp. or exp hypertriglyceridemia/
16. hypertriglyceridaemia.mp. or exp hypertriglyceridemia/
17. hypertriglyceridimia.mp. or exp hypertriglyceridemia/
18. hyperlipidemia.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
19. hyperlipidaemia.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
20. hyperlipidimia.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
21. obesity.mp. or exp obesity/
22. chronic kidney disease.mp. or exp chronic kidney failure/
23. stroke.mp. or exp cerebrovascular accident/
24. transient ischemic attack.mp. or exp transient ischemic attack/
25. transient ischaemic attack.mp. or exp transient ischemic attack/
26. coronary heart disease.mp. or exp ischemic heart disease/
27. Heart failure.mp. or exp heart failure/
28. peripheral vascular disease.mp. or exp peripheral vascular disease/
29. atrial fibrillation.mp. or exp atrial fibrillation/
30. exp depression/ or depression.mp.
31. HIV.mp. or exp Human immunodeficiency virus/
32. 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31
33. (Angola or Benin or Botswana or "Burkina Faso" or "Upper Volta" or Burundi or Urundi or Cameroon or Cameroons or "Cape Verde" or "Central African Republic" or Chad or Comoros or "Comoro Islands" or Comores or Mayotte or Congo or Zaire or "Cote d'Ivoire" or "Ivory Coast" or ("Democratic Republic of the Congo" or Djibouti or "French Somaliland" or Eritrea or Ethiopia or Gabon or "Gabonese Republic" or Gambia or Ghana or "Gold Coast" or Guinea or Kenya or Lesotho or Basutoland or Liberia) or (Madagascar or "Malagasy Republic" or Malawi or Nyasaland or Mali or Mauritania or Mauritius or Mozambique or Namibia or Niger or Nigeria) or (Rwanda or "Sao Tome" or Seychelles or Senegal or "Sierra Leone" or Somalia or "South Africa" or Sudan or Swaziland or Tanzania or Togo or "Togolese Republic" or Uganda or Zambia or Zimbabwe or Rhodesia)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
34. sub-Saharan africa.mp. or exp "Africa south of the Sahara"/
35. subsaharan africa.mp. or exp "Africa south of the Sahara"/

36. 33 or 34 or 35
37. 5 and 32 and 36
38. limit 37 to (human and yr="2000 - 2021")

Web of Science - search

# 38	**2,114**	#37 AND #33 AND #5 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 37	**421,085**	#36 OR #35 OR #34 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 36	**301**	TS=(subsaharan Africa) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 35	**33,673**	TS=(sub-Saharan Africa) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 34	**407,520**	TS=(Angola OR Benin OR Botswana OR "Burkina Faso" OR "Upper Volta" OR Burundi OR Urundi OR Cameroon OR Cameroons OR "Cape Verde" OR "Central African Republic" OR Chad OR Comoros OR "Comoro Islands" OR Comores OR Mayotte OR Congo OR Zaire OR "Cote d'Ivoire" OR "Ivory Coast" OR "Democratic Republic of the Congo" OR Djibouti OR "French Somaliland" OR Eritrea OR Ethiopia OR Gabon OR "Gabonese Republic" OR Gambia OR Ghana OR "Gold Coast" OR Guinea OR Kenya OR Lesotho OR Basutoland OR Liberia OR Madagascar OR "Malagasy Republic" OR Malawi OR Nyasaland OR Mali OR Mauritania OR Mauritius OR Mozambique OR Namibia OR Niger OR Nigeria OR Rwanda OR "Sao Tome" OR Seychelles OR Senegal OR "Sierra Leone" OR Somalia OR "South Africa" OR Sudan OR Swaziland OR Tanzania OR Togo OR "Togolese Republic" OR Uganda OR Zambia OR Zimbabwe OR Rhodesia) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 33	**1,764,519**	#32 OR #31 OR #30 OR #29 OR #28 OR #27 OR #26 OR #25 OR #24 OR #23 OR #22 OR #21 OR #20 OR #19 OR #18 OR #17 OR #16 OR #15 OR #14 OR #13 OR #12 OR #11 OR #10 OR #9 OR #8 OR #7 OR #6 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 32	**85,771**	TS=(Human immunodeficiency virus) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 31	**272,497**	TS=(HIV) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 30	**369,094**	TS=(depression)	Edit

		Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI *Timespan=2000-2019*	
# 29	**80,988**	TS=(atrial fibrillation) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 28	**20,886**	TS=(peripheral vascular disease) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 27	**226,090**	TS=(heart failure) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 26	**144,037**	TS=(coronary heart disease) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 25	**1,959**	TS=(transient ischaemic attack) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 24	**11,095**	TS=(transient ischemic attack) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 23	**278,508**	TS=(stroke) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 22	**75,433**	TS=(chronic kidney disease) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 21	**280,562**	TS=(obesity) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 20	**5**	TS=(hyperlipidimia) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 19	**2,534**	TS=(hyperlipidaemia) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 18	**21,065**	TS=(hyperlipidemia) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 17	**2**	TS=(hypertriglyceridimia) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit

# 16	1,000	TS=(hypertriglyceridaemia) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 15	8,591	TS=(hypertriglyceridemia) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 14	0	TS=(hypercholesterolimia) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 13	3,188	TS=(hypercholesterolaemia) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 12	27,232	TS=(hypercholesterolemia) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 11	4,539	TS=(dyslipidaemia) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 10	6	TS=(dyslipidimia) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 9	25,588	TS=(dyslipidemia) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 8	16,630	TS=(type II diabetes) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 7	173,805	TS=(type 2 diabetes) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 6	94,317	TS=(Type 2 diabetes mellitus) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 5	375,418	#4 OR #3 OR #2 OR #1 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 4	113,713	TS=(high blood pressure) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 3	3,503	TS=(uncontrolled blood pressure) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit

# 2	**4,063**	TS=(uncontrolled hypertension) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	Edit
# 1	**307,652**	**TOPIC:** (hypertension) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=2000-2019*	

Table S1: List of 11 conditions included as comorbidity

	Conditions
1	Diabetes
2	Hypercholesterolemia/dyslipidemia/hyperlipidemia/hypertriglyceridemia
3	Obesity
4	Chronic kidney disease
5	Stroke and or transient Ischemic attack
6	Coronary heart disease
7	Heart failure
8	Peripheral vascular disease
9	Atrial fibrillation
10	Depression
11	HIV

Table S2: Assessment of Risk of Bias (RoB)

	External validity	Yes/No		Internal validity	Yes/No
1	Was the target population representative of the population in relation to relevant variables?		5	Were data collected directly from the subjects (as opposed to a proxy)?	
2	Was the sampling frame a true or close representation of the target population?		6	Was an acceptable case definition used in the study?	
3	Was some form of random selection used to select the sample, OR was a census undertaken?		7	Was the study instrument that measured the parameter of interest shown to have validity and reliability?	
4	Was the likelihood of nonresponse bias minimal in the study?		8	Was the same mode of data collection used for all subjects?	
			9	Were the numerator(s) and denominator(s) for the parameter of interest appropriate?	
10	Summary item on the overall risk of study bias				

Adapted from Hoy D, Brooks P, Woolf A, Blyth F, March L, Bain C, et al. Assessing risk of bias in prevalence studies: modification of an existing tool and evidence of interrater agreement. Journal of clinical epidemiology. 2012;65(9):934-9.

Table S3: Characteristics of studies in the prevalence of uncontrolled hypertension in sub-Saharan Africa

Year of publication (n = 20)	2002-2020
Period of inclusion (n = 20)	2000-2021
Mean age, years (n = 20)	56.8(±0.12)
% of males (n = 20)	41.8(±0.27)
Comorbidities	**N studies**
Diabetes	11
HIV	5
Stroke	2
Atrial fibrillation	1
Chronic Kidney Disease (CKD)	1
sub-Saharan African regions	
Eastern Africa	6
Western Africa	3
Central Africa	1
Central Africa	10
Study design	
Cross sectional	19
Not reported	1
Sampling	
Consecutive	16
Random	2
Not reported	2
Timing of data collection	
Retrospectively	5
Prospectively	14
Not reported	1
Data sources	
Medical records	5
Participants	11
from both medical records and participants	3
Not reported	1
Study site	
Hospital	12
Health Center	8
Gross National Income (GNI)	
Below sub-Saharan Africa average	9
Above sub-Saharan Africa average	11

Table 4: **Meta-regression analysis for the variation of the prevalence of uncontrolled hypertension in people with comorbidity in SSA**

Variables (reference)	Univariate analysis				Multivariate analysis	
	N studies	P value	Odds ratio (95% CI)	R^2, %	P-value	Odds ratio (95% CI)
Year of publication (after 2015)	20	0.595	0.96 (0.83; 1.11)	0.00		
More females	20	0.172	0.09 (-0.04; 0.23)	11.35		
Risk of bias (low)	20			18.41		
Moderate		0.923	0.99 (0.76; 1.29)			
High		**0.080**	1.22 (0.97; 1.53)			
Sample size (small studies)	20			0		
Large studies		0.563	1.04 (0.90; 1.21)			
SSA regions (Eastern)	20			0.00		
Western		0.636	0.95 (0.74; 1.21)			
Central		0.747	1.06 (0.73; 1.53)			
Southern		0.679	1.04 (0.87; 1.24)			
Comorbidities (atrial fibrilation)	20			3.50		
Chroninc kidney disease		0.222	0.78 (0.53; 1.16)			
Diabetes		0.082	0.77 (0.58; 1.03)			
HIV		0.097	0.75 (0.53; 1.06)			
Stroke		0.119	0.76 (0.54; 1.08)			
Setting (Health center)	20			0		
Hospital		0.958	1.00 (0.86; 1.17)			
Sampling (Consecutive)	18			0		
Random		0.536	0.94 (0.75; 1.16)			
BP target used (recommended comorbidity target not used)	20			21.34		
Recommended BP control used		0.111	0.90 (0.79; 1.03)			
GNI (Below SSA average)	20					
Above SSA average		0.821	1.02 (0.88; 1.18)	0		

BP=Blood pressure

Table S5: **Meta-regression analysis for the variation of the prevalence of uncontrolled hypertension in people with diabetes in SSA**

Variables (reference)	Univariate analysis				Multivariate analysis	
	N studies	P value	Coefficient (95% CI)	R^2, %	P value	Adjusted coefficient (95% CI)
Year of publication (after 2015)	11	0.274	0.0793 (-0.0748; 0.2334)	18.20		
More females	11	0.205	0.1157 (-0.0758; 0.3072)	16.26		
Risk of bias (low)	11			-15.57		
Moderate		0.858	-0.0278 (-0.3753; 0.3198)			
High		0.688	0.0711 (-0.3228; 0.4650)			
Sample size (small studies)	11			-11.04		
Large studies		0.89	.0115 (-0.1714; 0.1943)			
SSA regions (Eastern)	11			-18.36		
Western		0.815	-.0341 (-0.3664; 0.2982)			
Central		0.952	.0101 (-0.3755; 0.3956)			
Southern		0.500	-0.0709 (-0.3067; 0.1649)			
Setting (Health center)	11			-15.43		
Hospital		0.860	.0160 (-0.1825; 0.2144)			
Sampling (Consecutive)	10					
Random		**0.001**	-0.2366 (-0.3477 -0.1255)	100.00	**0.043**	-0.1880 (-0.3686; -0.0074)
BP target used (recommended diabetes BP target not used)	11			56.66	0.439	-0.0563 (-0.2188; 0.1062)
Recommended diabetes BP control target used		**0.054**	-0.1320 (-0.2671; 0.0030)			
GNI (Below SSA average)	11					
Above SSA average		0.401	-0.0633 (-0.2256; 0.0991)	3.10		
Mean age	11	0.296	0.0047 (-.0046; 0.0139)	-0.16		

BP=Blood pressure

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.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
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.	4
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.	4-5
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.	4-5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplement file 1
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).	5
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.	5
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5
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.	5-6
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	6
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.	6

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).	7
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	6
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.	7 and figure 1
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.	7-8
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).	10
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.	9-12 and figure 3
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	10-14
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	10
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	11-13
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).	14-16
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).	17
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	17
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.	17

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