BMJ Open Non-pharmacological interventions to achieve blood pressure control in African patients: a systematic review

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ABSTRACT

To cite: Cernota M, Kroeber ES, Demeke T, *et al.* Nonpharmacological interventions to achieve blood pressure control in African patients: a systematic review. *BMJ Open* 2022;**12**:e048079. doi:10.1136/ bmjopen-2020-048079

Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/ bmjopen-2020-048079).

Received 04 January 2021 Accepted 26 January 2022



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Correspondence to Dr Eric Sven Kroeber; eric.kroeber@posteo.de **Objectives** This systematic review aims to evaluate the evidence of non-pharmacological strategies to improve blood pressure (BP) control in patients with hypertension from African countries.

Design We performed a systematic review and searched Medline, Central, CINAHL and study registers until June 2020 for randomised studies on interventions to decrease BP of patients with hypertension in African countries. We assessed the study quality using the Cochrane risk of bias tool and narratively synthesised studies on nonpharmacological hypertension interventions.

Setting We included studies conducted in African countries.

Participants Adult African patients with a hypertension diagnosis.

Interventions Studies on non-pharmacological interventions aiming to improve BP control and treatment adherence.

Outcomes Main outcomes were BP and treatment adherence.

Results We identified 5564 references, included 23 with altogether 18153 participants from six African countries. The studies investigated educational strategies to improve adherence (11 studies) and treatment by healthcare professionals (5 studies), individualised treatment strategies (2 studies), strategies on lifestyle including physical activity (4 studies) and modified nutrition (1 study). Nearly all studies on educational strategies stated improved adherence, but only three studies showed a clinically relevant improvement of BP control. All studies on individualised strategies and lifestyle changes resulted in clinically relevant effects on BP. Due to the type of interventions studied, risk of bias in domain blinding of staff/participants was frequent (83%). Though incomplete outcome data in 61% of the studies are critical, the general study quality was reasonable.

Conclusions The identified studies offer diverse low-cost interventions including educative and taskshifting strategies, individualised treatment and lifestyle modifications to improve BP control. Especially trialled physical activity interventions show clinically relevant BP changes. All strategies were trialled in African countries and may be used for recommendations in evidence-based guidelines on hypertension in African settings. **PROSPERO registration number** CRD42018075062.

Strengths and limitations of this study

- This systematic review summarises evidence on a wide range of different non-pharmacological interventions, adding a comprehensive overview to the literature that can support physicians and healthcare policymakers in the African setting.
- Most of the included studies were conducted in urban areas of few Western and Southern African countries leading to a lack of generalisability to other African regions and showing a need of future research in rural areas.
- A main limitation of this systematic review occurs through deviations from the protocol. Due to the amount of search results for the initially planned more general scope on cardiovascular diseases, we decided to focus on hypertension.
- Nevertheless, this review was limited to studies with the highest level of evidence to investigate the benefits and harms of non-pharmacological interventions on blood pressure control in African patients with hypertension.
- This review adds to the scope of a recently published systematic review on the efficacy of common pharmacological treatment for patients with hypertension in sub-Saharan Africa.

BACKGROUND

Hypertension is a major public health problem and affects the lives of about 1.13 billion people.¹ The highest blood pressure (BP) levels shifted from high to low-income countries in South Asia and sub-Saharan Africa $(SSA)^2$ with a prevalence of 57% in older adults in African countries.^{3 4} The estimated number of adults with raised BP in SSA rose from 30 million in 1975 to over 100 million in 2016 due to population growth, ageing and westernisation of lifestyle.² Hypertension is a leading risk factor of cardiovascular disease (CVD), chronic kidney disease and diabetes.¹ Studies show that black people suffer from more severe forms of hypertension associated with more frequent treatment failure and more severe and earlier target organ damage, all resulting in higher morbidity and mortality.^{5 6} Hypertension is a major contributor to devastating health events like stroke or heart failure,^{7–9} which can be catastrophic to both individuals and healthcare systems in which resources are scarce.

Tackling and reducing the burden of premature mortality due to non-communicable diseases (NCDs) through prevention and treatment has been a designated goal within the United Nations (UN) 2030 Agenda.¹⁰ The Pan-African Society of Cardiology developed an algorithm including recommendations on screening, diagnosis and treatment to achieve 25% hypertension control in Africa by 2025 with a treatment target value of less than 140/90mm Hg. Screening programmes are proposed to be carried out in healthcare facilities as well as public places like markets and churches. The treatment starts with lifestyle modifications, is intensified through a monotherapy and a subsequent combination of two or three medications in higher stages and resistant forms of hypertension. In some cases, the assessment of secondary causes by specialists is recommended.⁹

However, the awareness of hypertension remains relatively low in many parts of Africa, hindering adequate screening, treatment and control to lower the long-term risks.^{11–13} Extensive counselling and education of patients and healthcare providers on the importance of adherence to medications and lifestyle modifications is necessary in order to improve hypertension control.¹⁴ ¹⁵ Especially patients with multiple medications benefit from the support of their healthcare providers to understand the treatment's purpose.¹⁶

Evidence is needed detailing regional differences in hypertension incidences, risk factors, and, as subject of this review, treatment strategies in different, transitioning populations on the African continent. Seeley *et al* recently published a systematic review on the efficacy of common pharmacological treatment for patients with hypertension in SSA.¹⁷ These interventions do not include treatment strategies like lifestyle modifications (eg, nutritional modifications, physical activity) or educational strategies, which can be summarised as non-pharmacological interventions.¹⁸ The main aim of this systematic review is to summarise the best available evidence on the effectiveness of non-pharmacological strategies on BP control in African patients with hypertension.

METHODS

A protocol of this systematic review was prospectively registered on PROSPERO (CRD42018075062) following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline¹⁹. We initially planned to include randomised controlled trials (RCTs) on all CVDs. Due to the high number and heterogeneity of eligible studies, we decided to focus this review on patients with hypertension as one of the main risk factors for other CVDs. We aim to describe all non-pharmacological

Table 1 Inc	lusion and exclusion criteria
Design	RCTs conducted in African countries, in international studies with at least 50% African countries
Population	African adult patients in secondary and tertiary prevention, diagnosis and treatment of hypertension Exclusion of patients with gestational diabetes, pre-eclampsia or eclampsia
Intervention	All non-pharmacological strategies to improve adequate diagnoses, prevention and treatment of hypertension
Control	 No intervention Standard care Another intervention
Outcome	Blood pressure (SBP, DBP, MAP) and adherence to recommendations (medications and lifestyle changes) within longest follow-up
Publication	Full-text publications according to CONSORT in English or German
CONSORT, Co	onsolidated Standards of Reporting Trials; DBP,

CONSORT, Consolidated Standards of Reporting Trials; DBP, diastolic blood pressure; MAP, mean arterial pressure; RCTs, randomised controlled trials; SBP, systolic blood pressure.

hypertension interventions in detail in order to broaden the scope of the existing evidence.

Patient and public involvement

The conception of this systematic review was discussed in detail with members and students at the Addis Ababa School of Public Health in order to consider the priorities in the African context. Consensus was to gather evidence on hypertension treatment as a measure of tackling the burden of NCDs which is part of the UN 2030 Agenda.¹⁰ No patients were involved.

Inclusion and exclusion criteria

We included full-text publications on RCTs²⁰ including cross-over RCTs and cluster RCTs on non-pharmacological interventions with adult patients with hypertension in African countries and reported results on BP. The study aims were improvement of prevention, diagnoses and treatment of hypertension in African countries. Studies on primary prevention were excluded due to the high variety of possible participants and interventions. International multicentre studies were included if more than 50% of centres were set in African countries. For detailed inclusion criteria, see table 1.

Literature search and study selection

Two electronic databases (Medline Ovid, Central) and registers of ongoing and completed studies (International Clinical Trials Registry Platform) were searched to identify all relevant studies (see online supplemental file 1). We added a search in CINAHL to cover nursing interventions. The main keywords of the search strategy included hypertension, high blood pressure, blood pressure control, Africa, a list of all African countries and randomized controlled trials. The first searches in 2017 included all CVDs, while updated strategies were limited to hypertension. The last search was conducted in June 2020. All searches were done without time frame constrictions. The study selection process was described in a flow chart according to the PRISMA statement.¹⁹ We exported articles retrieved from the literature search into a reference manager software (EndNote²¹). Duplicate references were identified in case of congruence of authors, title, year, and journal and deleted.

Titles, abstracts and full texts of potentially eligible articles were independently screened by three authors (MC, ESK and SU). Disagreements were resolved through consensus.

Interventions

This systematic review compares non-pharmacological interventions to improve adequate diagnoses, prevention and treatment of patients with hypertension with standard care, no intervention or another, less intensive or frequent intervention (table 1). Non-pharmacological interventions are considered non-medication treatment strategies such as educational programmes for patients or health professionals, individualised treatment, physical activity or nutrition-modification strategies.¹⁸

Outcomes

The main goal of non-pharmacological interventions for patients with hypertension is to improve BP control through the implementation of recommended lifestyle changes, attendance to follow-up visits and interventions promoting adherence to take hypertensive medications. We therefore report results on BP and adherence (table 1).

Data extraction and management

One author (MC or SU) extracted and a second author (SU or ESK) checked all information on study design and setting, participants, interventions and main results by using an assessment form in Excel. The form was especially designed for this systematic review and piloted for the first five studies.

We extracted information on the publication (study name consisting of the name of first author and year of the first publication of final results, registration and additional publications), study characteristics (design, country and region in which the study was conducted, duration, preplanned outcomes), participants (with inclusion/exclusion criteria, randomised sample size, prevention level, grade of hypertension, mean age, baseline BP), a short description of the intervention and control groups, and the main results on BP and adherence within the longest follow-up periods. The grade of hypertension was described as mild (grade 1, 140–159/90–99 mm Hg), moderate (grade 2, 160–179/100–109 mm Hg) or severe (grade 3, $\geq 180/\geq 110$ mm Hg).¹⁵ If BP was reported in

standing and supine position, we extracted results for supine position.

All effect sizes were reported with their corresponding CIs. They were calculated either on the basis of mean and SD for metric outcomes or by comparing the frequencies of better adherence or BP control. Positive mean differences (MDs) describe a positive treatment effect on BP with lower mean values or higher decrease in the intervention group. Relative risks (RRs), HRs and ORs compare the frequency of good adherence or BP control. Effect measures greater than 1 describe a better adherence or BP control in the intervention group.

Quality assessment and risk of bias

Risk of bias was evaluated for all studies based on the Cochrane risk of bias tool.²² Two investigators (MC or ESK and SU) independently assessed the risk of bias in seven domains (sequence generation, allocation concealment, blinding of personal and participants, blinding of outcome assessors, incomplete outcome data, selective outcome reporting and other sources of bias). Risk of bias due to selective outcome reporting was judged as low, when the study protocol was available and results on all preplanned outcomes were reported. Incomplete outcome data were judged as high, when more than 10% of randomised participants dropped out. Other sources of bias were reported to be high in cases of missing sample size calculation, no definition of the primary endpoint or no reporting of baseline values.

Data synthesis

The main aim of this review is a narrative synthesis of studies with their participants, different types of interventions and resulting outcomes. We added a figure visualising the effect sizes on BP of different types of interventions in forest plots using RevMan.²³ Due to the high clinical heterogeneity between included studies with their different settings, interventions, control groups and lengths of follow-up, we did not pool any results.

Treatment effects were described as statistically significant or clinically relevant. Statistically significant results on BP with MD over 5 mm Hg were defined as clinically relevant.

RESULTS

We identified a total of 5564 references from electronic databases and 18 references from the International Clinical Trials Registry Platform. Three hundred forty articles were potentially eligible and full texts were assessed for the inclusion and exclusion criteria. Of those, 298 articles were excluded including 13 articles on studies to treat heart failure, 7 articles on coronary heart diseases and 76 articles on pharmacotherapy for hypertension (see list of excluded studies in the online supplemental material 1). Twenty-three studies (reported in 42 articles)²⁴⁻⁶⁶ on non-pharmacological strategies to treat patients with hypertension matched the inclusion criteria and were

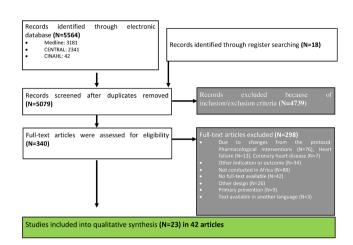


Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow chart describing the process of study selection.

included in this systematic review (figure 1 and list of included studies in the online supplemental material 2). The characteristics and main results of these studies were summarised in table 2.

Study characteristics

We identified 15 studies with two or more independent parallel groups and individual randomisation of patients and eight cluster RCTs with randomisation of different observation units, such as independent villages, healthcare facilities or different geographical regions (table 2). Most of the included studies were conducted in Nigeria (11 studies) and South Africa (8 studies), others in Ghana, Kenya, Cameroon and Egypt. One of the studies^{25 25} recruited patients in three countries (South Africa, Nigeria and Kenya). Nine studies (39%) were at least partly conducted in rurally located healthcare facilities (figure 2).^{24 27 32 34-36 52 56 64} The included studies were published between 1991 and 2019. Only three of the studies, all conducted in South Africa, were published before 2010.^{31 60 61}

Participants

The total sample size ranged from 30 to 4722 participants with a total number of 18153 participants (table 2). Eighteen studies (78%) randomised more than 100 participants. The mean age was between 45 and 63 years. Most studies (n=19) included more women. Two studies to enhance physical activity included women (Khalid *et al*)⁶³ or men (Lamina)³⁷ only. Mean systolic BP (SBP) at baseline was between 128 and 175 mm Hg, mean diastolic BP (DBP) between 76 and 117 mm Hg. Most studies included patients in secondary prevention with mild to moderate hypertension. Three studies^{56 58 66} included patients with hypertension post-stroke.

Intervention

Studies investigated educational strategies to improve adherence of patients and treatment by healthcare professionals (16 studies), to individualise treatment (2 studies), and to change lifestyle via enhanced physical activity (4 studies) or modified nutrition (1 study) (table 2).

Educational strategies to improve adherence

Sixteen studies (17090 participants), with follow-up periods from 2weeks in a short-term feasibility study (Wahab *et al*)⁶⁶ up to 18 months (Goudge *et al*),³⁴ were published between 1991 and 2019.

The main aim of 11 studies was the improvement of patients' knowledge on hypertension and adherence to self-monitoring of BP, recommendations on medication, lifestyle changes and regular attendance at healthcare facilities.²⁴ ²⁷⁻²⁹ ³⁶ ⁵⁶ ⁵⁸ ⁶⁰ ⁶¹ ⁶⁴ ⁶⁶ Five studies investigated strategies to improve adequate treatment of patients with hypertension by clinicians, nurses and healthcare workers.³² ³⁴ ³⁵ ⁵² ⁶²

Eight studies²⁷ ²⁸ ³⁶ ⁵⁶ ⁵⁸ ⁶⁰ ⁶¹ ⁶⁴ investigated the efficacy of adherence promotion via counselling and phone or letter-based interventions. Seven studies²⁴ ²⁹ ³² ³⁴ ³⁵ ⁵² ⁶⁶ investigated the efficacy of interventions on the basis of training measures with subsequent task-shifting to nurses or health workers for home visits and patient education. One study (Steyn *et al*)⁶² tested a multifaced intervention to implement national South African guidelines into primary care of patients with hypertension or diabetes. Another two studies investigated the efficacy of financial incentives as an additional health insurance coverage (Gyamfi *et al*)³⁵ or free treatment (Labhardt *et al*),³⁶ respectively.

Nearly all studies stated improved medication adherence.^{24 28 29 36 60 61} implementation of lifestyle recommendations (Ayodapo and Olukokun, Mendis *et al*), 2752 linkage to care, 365264 or knowledge and practical skills of healthcare professionals (Fairall et al, Gyamfi et al).^{32 35} In only three studies,^{27–29} these improvements resulted in modest benefits on BP (table 2 and figure 3A-C). In the study by Ayodapo and Olukokun,²⁷ counselling had a positive impact on lifestyle behaviour and resulted in a clinically relevant decrease of mean arterial BP (-9.8 mm Hg; 95% CI –11.5 to –8.1). Bobrow *et al*²⁸ assessed the effect of automated treatment adherence support delivered via mobile phone short messages. Bolarinwa *et al*²⁹ trialled home-based follow-up care with education and counselling of patients and modifications of environmental characteristics. Both studies achieved a 12% higher BP control with SBP <140 mm Hg and DBP <90 mm Hg in participants of the intervention compared with the control groups (RR: 1.12; 95% CI 1.01 to 1.23 and 1.12; 95% CI 1.00 to 1.25) (figure 3).

Individualised treatment strategies

Two studies (286 participants) with follow-up periods of 3 and 12 months were published in 2011 and 2017 (Akintunde *et al*, Okeahialam *et al*).^{25 55} Both investigated strategies on the efficacy of an individualised therapy. Therapy individualisation based on the patients' renin/

6									Open ac	cess
		Results on adherence and BP	IG vs CG; treatment effect (95% CI)		Excellent adherence (missed ≤2 pills per month): worse in IG: 72.5% vs 79.0%; OR a, 0.524 (0.30 to 0.75) BP control: no difference 65.0% vs 66.3%; RR 0.98 (0.87 to 1.11)	Met recommendations on: physical activity: better in IG: 22.4% vs 6.2% ; RR 3.60 (1.85 to 7.00) futi and vegetable consumption: better in IG: 71.4% vs 66% ; RR 1.74 (1.41 to 2.15) alcohol consumption: better in IG: 100% vs 87.6% ; RR 1.14 (1.08 alcohol consumption: better in IG: 100% vs 87.6% ; RR 1.14 (1.08 posking: no difference: 83.9% vs 78.5% ; RR 1.05 (0.95 to 1.17) smoking: no difference: 83.9% vs 78.5% ; RR 1.05 (0.95 to 1.17) BP: MAP: lower in IG: 94.6±8.1 vs 106.2±7.6mm Hg; MD –9.8 (–11.5 to –8.1)	Adherence (days with medication \geq 80%); higher with IG: 59.7% vs 62.8% vs 49.4%; RR 1.12 (1.01 to 1.23) (G2 vs CG: OR a 1.66 (1.39 to 2.49) (G1 vs CG: OR a 1.66 (1.39 to 2.46) BP: slightly lower with IG1 SBP: 132.7±17.5 vs 132.1±16.6 vs 134.3±17.3 mm Hg (G2 vs CG: MD a -1.6 mm Hg (-4.4 to -0.04) (G2 vs CG: MD a -2.2 mm Hg (-4.4 to -0.04) BP control: slightly better with (G: 65% vs 65% vs 58% (G1 vs CG: OR a 1.42 (1.03 to 1.95) (G2 vs CG: OR a 1.41 (1.02 to 1.95) (G2 vs CG: OR a 1.41 (1.02 to 1.95) (G2 vs CG: OR a 1.41 (1.02 to 1.95) (G2 vs CG: OR a 1.41 (1.02 to 1.95) (G2 vs CG: OR a 1.41 (1.02 to 1.95) (G2 vs CG: OR a 1.41 (1.02 to 1.95) (G2 vs CG: OR a 1.41 (1.02 to 1.95) (G2 vs CG) (G2 vs CG) (G2 vs CG) (G3 vs CG) (G4 vs C	Medical <u>adherence</u> : better with IG: low: 4% vs 16.6%, medium: 17.5% vs 34.7%, high: 78.5% vs 48.7% <u>BP control</u> : better with IG: 85.9% vs 76.7%; RR 1.12 (1.00 to 1.25)	Adherence: retention rate: 60% vs 65% vs 29%; lower risk of loss to follow-up from the programme and better adherence in IG IG2 vs CG: HR $_{\rm s}^{\circ}$ 0.38 (0.24 to 0.61) (IG1 vs CG: HR $_{\rm s}^{\circ}$ 0.38 (0.24 to 0.61) 35% vs 10% vs 10% vs 10% IG2 vs CG. MD $_{\rm s}^{\circ}$ 25% (14% to 42%) IG2 vs CG. MD $_{\rm s}^{\circ}$ 25% (13% to 37%) IG2 vs CG: MD $_{\rm s}^{\circ}$ 25% (13% to 37%) IG1 vs CG: MD $_{\rm s}^{\circ}$ 25% (13% to 37%) IG1 vs CG: MD $_{\rm s}^{\circ}$ 25% (13% to 70%) in IG1 vs CG: MD $_{\rm s}^{\circ}$ 25% (13% to 70%) in IG1 vs CG: MD $_{\rm s}^{\circ}$ 25% (13% to 70%) in IG1 vs CG: MD $_{\rm s}^{\circ}$ 25% (13% to 70%) in IG1 vs CG: MD $_{\rm s}^{\circ}$ 25% (13% to 70%) in IG1 vs CG: MD $_{\rm s}^{\circ}$ 25% (13% to 70%) in IG1 vs CG: MD $_{\rm s}^{\circ}$ 25% (13% to 70%) in IG1 vs CG: MD $_{\rm s}^{\circ}$ 25% (13% to 70%) in IG1 vs CG: MD $_{\rm s}^{\circ}$ 25% (13% to 70%) in IG1 vs CG: MD $_{\rm s}^{\circ}$ 25% (13% to 70%) in IG1 vs CG: MD $_{\rm s}^{\circ}$ 25% (13% to 70%) in IG1 vs CG: MD $_{\rm s}^{\circ}$ 25% (13% to 70%) in IG1 vs CG: MD $_{\rm s}^{\circ}$ 25% (13% to 70%) in IG1 vs CG: MD $_{\rm s}^{\circ}$ 25% (13% to 70%) in IG1 vs CG: MD $_{\rm s}^{\circ}$ 25% (13% to 70%) in IG1 vs CG: MD $_{\rm s}^{\circ}$ 25% (13% to 70%) in IG1 vs CG: MD $_{\rm s}^{\circ}$ 25% (13% to 70%) in IG1 vs CG: MD $_{\rm s}^{\circ}$ 25% (13% to 70%) in IG1 vs CG: MD $_{\rm s}^{\circ}$ 10% to 70\%) in IG1 vs CG: MD $_{\rm s}^{\circ}$ 10% to 70\%) in IG1 vs CG: MD $_{\rm s}^{\circ}$ 10% to 70\%) in IG1 vs CG: MD $_{\rm s}^{\circ}$ 10% to 70\%) in IG1 vs CG: MD $_{\rm s}^{\circ}$ 10% to 70\%) in IG1 vs CG: MD $_{\rm s}^{\circ}$ 10% to 70\%) in IG1 vs CG: MD $_{\rm s}^{\circ}$ 10% to 70\%) in IG1 vs CG: MD $_{\rm s}^{\circ}$ 10% to 70\%) in IG1 vs CG: MD $_{\rm s}^{\circ}$ 10% to 70\%) in IG1 vs CG: MD $_{\rm s}^{\circ}$ 10% to 70\%) in IG1 vs CG: MD $_{\rm s}^{\circ}$ 10% to 70\%) in IG1 vs CG: MD $_{\rm s}^{\circ}$ 10% to 70\%) in IG1 vs CG: MD $_{\rm s}^{\circ}$ 10% to 70\%) in IG1 vs CG: MD $_{\rm s}^{\circ}$ 10% to 70\%) in IG1 vs CG: MD $_{\rm s}^{\circ}$ 10% to 70\%) in IG1 vs CG: MD $_{\rm s}^{\circ}$ 10% to 70\%) in IG1 vs CG: MD $_{\rm s}^{\circ}$ 10% to 70\%) in IG1 vs CG: MD $_{\rm s}^{\circ}$ 10% to 70\%) in IG1 vs CG: MD $_{\rm s}^{\circ}$ 10% to 70\%) in IG1 v	Continued
			Follow-up (months)		ω	ო	2	2	<u>6</u>	
		Intervention (IG) vs control (CG) group	Description		Home visits by nurses and clinic management (community based, nurse- led treatment programme with physician backup; facilitation of clinic visits and health education; use of diuretics and a beta blocker as needed) vs clinic management	Counselling on lifestyle behaviours (physical activity, fruit and vegetable consumption, alcohol consumption, smoking) over 30–45 min, reminders (telephone calls/SMS) vs usual care	Mobile phone text messages on behaviour change techniques (IG2: interactive with information and possibility to response vs IG1: only information on hypertension, motivation to take medications and reminders) vs usual care	Task-shifting (driven by trained and professionally competent nurses) home-based follow-up care (BP and BMI monitoring, medical advice and counselling at home) vs usual care	Reminder letters in case of missing follow- up (IG2) vs financial incentive (1 month free treatment for regular attenders) (IG1) vs usual care in nurse-led facilities	
			Hypertension; SBP/ DBP (mm Hg)		Mild to moderate 167.4±19.2/91.8±12.3	MAP: 106.4±8.3	Mild to moderate 135.4±17.5/83.4±12.1	140.0±22.9/86.9±11.9	Mild to moderate 175.8/100.7	
		pants	Age (years)/ females		62.7±10.0/66%	60.9±10.0/51%	54.3±11.5/72%	61.1±10.8/77%	59.9±12.5/64%	
		Participants	Ē	1 RCTs)	668	322	1372	299	187	
	Study characteristics		Country	Educational strategies for patients (11 RCTs)	Nigeria (mixed)	Nigeria (mixed)	South Africa (urban)	Nigeria (urban)	Cameroon (rural)	
	Table 2 Stud		Name (design)	Educational strat	Adeyemo <i>et al</i> ²⁴ (RCT)	Ayodapo and Olukokun ²⁷ (RCT)	Bobrow <i>et al²⁸</i> (PACTR2014 11000724141) (RCT)	Bolarinwa <i>et al</i> ²⁹ (PACTR2016 06001671335) (RCT)	Labhardt et al [%] (cluster RCT)	

Table 2 Continued	nued						
		Participants	oants		Intervention (IG) vs control (CG) group		Results on adherence and BP
Name (design)	Country	Ē	Age (years)/ females	Hypertension; SBP/ DBP (mm Hg)	Description	Follow-up (months)	IG vs CG; treatment effect (95% CI)
Owolabi et a ^{pis} (NCT01900756) (RCT)	Nigeria (mixed)	400*	57.2±11.7/37%	All stroke (n=400); 138.3±23.6/83.0±15.2 stroke and uncontrolled hypertension (SBP/DBP >140/90mm Hg) (n=168) 158.7±21.7/92.5±15.6	Chronic care model components of delivery system redesign (increased follow-up visits, pre-appointment phone texts), self-management support (patient report card, post-clinic follow-up phone texts, waiting room educational video) and clinical information systems (patient report card as part of medical chart, hospital registry) vs standardised usual care (risk factor identification and control) and phone contact information	12	<u>BP:</u> No difference for all patients after stroke: SBP: 136.5±22.3 vs 136.2±21.2 mm Hg Patients with uncontrolled hypertension: SBP: 145.1±22.6 vs 148.5±22.8 mm Hg
Sarfo <i>et al⁶⁸</i> (NCT02568137) (cluster RCT)	Ghana (urban)	*09	55±13/35%	Stroke and uncontrolled hypertension; 143.8±26.7/90.5±15.7	Nurse-led, multilevel approach with m- Health technology for monitoring and reporting BP measurement and tailored motivational text messages vs usual care	თ	<u>Adherence</u> : modified MMA score: no difference: 13 ± 1.5 vs 13 ± 1.7 <u>BP</u> . BP control: no difference: 47% vs 40% ; OR ₃ : 1.24 (0.83 to 1.84) SBP <140 mm Hg: better in IG: 73% vs 43% DBP <90 mm Hg: better in CG: 47% vs 77%
Saunders <i>et al^{eo}</i> (RCT)	South Africa (urban)	224	65% between 40 and 50/73%	Mild to moderate; n.r. 116.6	Reminder letters and home visits by fieldworkers and patient-retained records for self-monitoring of medication compliance and BP control vs usual care (appointment system and health education)	۵	Adherence (treatment received) over 6 months: higher for newly treated (135.5±48.9 vs 95.0±60.0 days) and infrequent attenders (168.4±16.4 vs 116.7±56.9 days) of 180 days >80% of treatment: better for newly treated (59% vs 29%; p<0.001) and infrequent attenders (87% vs 42%; p<0.001) $\frac{1}{21}$ mered patients (87% vs 42%; p<0.001) $\frac{1}{21}$ mm Hg (0.5 to 13.7), no difference for infrequent attenders: 97.5 vs 94.7 mm Hg; MD: -2.8 mm Hg (-6.9 to 1.3))
Stewart <i>et al</i> ⁶¹ (RCT)	South Africa (urban)	83	Late middle- aged/n.r.	All hypertensives; 146.4±18.5/93.5±11.1	Telephonic intervention (educational and home-based exercise programme+support of a healthcare practitioner and a family member) vs control group (educational and home- based exercise programme only)	Q	Adherence: better with IG: 62.8%±34.5% vs 39.3±42.8%; p=0.007 BP: no difference: SBP: 142±16 vs 144±20 mm Hg; MD: -2 mm Hg (-10.3 to 6.3) DBP: 92±12 vs 91±10 mm Hg, change: MD: 1 mm Hg (-4.0 to 6.0)
Vedanthan <i>et al⁶⁴</i> (NCT01844596) (cluster RCT)	Kenya (rural)	1460	54.2±16.4/58%	All hypertensives; 159.4±19.5/89.7±12	Tailored behavioural communication (smartphone (IG2) or paper-based (IG1)) vs usual care	<u>0</u>	$\begin{array}{l} \label{eq:construct} \best results with IG2, worse with IG1: IG2 vs CG: OR_{a}: 1.21 (0.70 to 2.01) \\ IG1 vs CG: OR_{a}: 0.64 (0.43 to 0.91) \\ IG1 vs CG: OR_{a}: 0.64 (0.43 to 0.91) \\ IG2 vs IG1: OR_{a}: 1.95 (1.23 to 3.01) \underline{BP}: no difference \\ 13.1205 vs Su vs 150.2421 6 vs 150.04229 mm Hg, change: \\ -13.14205 vs - 84424 0 vs - 9.7425.1 mm Hg \\ IG2 vs CG: MD_{a}: -2.13 mm Hg (-4.89 to 0.42) \\ IG1 vs CG: MD_{a}: -2.13 mm Hg (-4.89 to 0.42) \\ IG2 vs IG1: MD_{a}: -2.07 mm Hg (-5.14 to 1.12) \\ IG2 vs IG1: MD_{a}: -2.07 mm Hg (-5.14 to 1.12) \\ IG2 vs IG1: MD_{a}: -2.07 mm Hg (-5.14 to 1.12) \\ IG2 vs IG1: MD_{a}: -2.07 mm Hg (-5.14 to 1.12) \\ IG2 vs IG1: MD_{a}: -2.07 mm Hg (-5.14 to 1.12) \\ IG2 vs IG1: MD_{a}: -2.07 mm Hg (-5.14 to 1.12) \\ IG2 vs IG1: MD_{a}: -2.07 mm Hg (-5.14 to 1.12) \\ IG2 vs IG1: MD_{a}: -2.07 mm Hg (-5.14 to 1.12) \\ IG2 vs IG1: MD_{a}: -2.07 mm Hg (-5.14 to 1.12) \\ IG2 vs IG1: MD_{a}: -2.07 mm Hg (-5.14 to 1.12) \\ IG2 vs IG1: MD_{a}: -2.07 mm Hg (-5.14 to 1.12) \\ IG2 vs IG1: MD_{a}: -2.07 mm Hg (-5.14 to 1.12) \\ IG2 vs IG1: MD_{a}: -2.07 mm Hg (-5.14 to 1.12) \\ IG2 vs IG1: MD_{a}: -2.07 mm Hg (-5.14 to 1.12) \\ IG2 vs IG1: MD_{a}: -2.07 mm Hg (-5.14 to 1.12) \\ IG2 vs IG1: MD_{a}: -2.07 mm Hg (-5.14 to 1.12) \\ IG2 vs IG1: ND_{a}: -2.07 mm Hg (-5.14 to 1.12) \\ IG2 vs IG1: ND_{a}: -2.07 mm Hg (-5.14 to 1.12) \\ IG2 vs IG1: OR_{a}: 0.97 (0.63 to 1.24) \\ IG2 vs IG1: OR_{a}: 0.97 (0.63 to 1.24) \\ IG2 vs IG1: OR_{a}: 0.97 (0.63 to 1.24) \\ IG2 vs IG1: OR_{a}: 0.97 (0.63 to 1.24) \\ IG2 vs IG1: OR_{a}: 0.97 (0.63 to 1.24) \\ IG2 vs IG1: OR_{a}: 0.97 (0.63 to 1.24) \\ IG2 vs IG1: OR_{a}: 0.97 (0.63 to 1.24) \\ IG2 vs IG1: OR_{a}: 0.97 (0.63 to 1.24) \\ IG2 vs IG1: OR_{a}: 0.97 (0.63 to 1.24) \\ IG2 vs IG1: OR_{a}: 0.97 (0.63 to 1.24) \\ IG2 vs IG1: OR_{a}: 0.97 (0.63 to 1.24) \\ IG3 vs IG1: OR_{a}: 0.97 (0.63 to 1.24) \\ IG3 vs IG1: OR_{a}: 0.97 (0.63 to 1.24) \\ IG3 vs IG1: OR_{a}: 0.97 (0.63 to 1.24) \\ IG3 vs IG1: OR_{a}: 0.97 (0.63 to 1.24) \\ IG3 vs IG1: OR_{a}: 0.97 (0.63 to 1.24) \\ IG3 vs IG1: OR_{a}:$
							Continued

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		Participants	pants		Intervention (IG) vs control (CG) group		Results on adherence and BP
Name (design)	Country	۲	Age (years)/ females	Hypertension; SBP/ DBP (mm Hg)	Description	Follow-up (months)	IG vs CG; treatment effect (95% CI)
Wahab <i>et af⁶⁶</i> (RCT)	Nigeria (urban)	35*	58.1±10.5/34%	All patients with stroke; 138.3±24.2/85.0±12.4	Feasibility of a nurse-led Intervention (education and skill building, BP monitor with review, phone calls) vs usual care	0.5	<u>Adherence:</u> no difference, but improvement in both groups: MMA score: 7.32±0.33 vs 7.03±1.36 BP: no difference SBP: 137.5±23.0 vs 133.1±18.2 mm Hg; MD: 4.40 mm Hg (–9.4 to 18.2) DBP: 84.1±9.7 vs 84.2±13.1 mm Hg; MD –0.1 mm Hg (–7.7 to 7.5)
Educational strategies for healthcare professionals (5 RCTs)	ies for healthcare	profest	sionals (5 RCTs)				
Fairall <i>et af³²</i> (ISRCTN20283604) (cluster RCT)	South Africa (rural)	4393	52 (IQR 43- 62)/73%	Mild to moderate 139±23.6 90±13.2	Education of nurses on NCD care (nurse training in educational outreach sessions with a primary care programme to expand their role in NCD care, authorisation to prescribe an expanded range of drugs on NCDs) vs usual training	4	<u>Adherence:</u> no difference <u>BP:</u> BP controlled: no difference: 33% vs 32%; RR 1.01 (0.2 to 1.8)
Goudge <i>et al^{a4}</i> (ISRCTN12128227) (cluster RCT)	South Africa (rural)	4722	56.6±19.4/56%	Hypertension: 46.6%, of them: 53.4%, on treatment and controlled: 8.6%, on treatment and uncontrolled: 9%, not on treatment: 29%	Support of nurses by health workers (eg, assistance with booking appointments, retrieve and fill patient files, health education, measurements in the vital signs queue, prepacking of medications, reminders to appointment for patients) to provide chronic disease care vs usual care	8	No hypertension: 50.9% vs 52.9% <u>Adherence and BP: no</u> difference on treatment and controlled: 11.3% vs 11.2% on treatment and uncontrolled: 13.0% vs 13.2% not on treatment: 24.9% vs 22.7% undiagnosed: 24.1% vs 22.2% taking medication: 24.3% vs 24.4%
Gyamfi <i>et al⁸⁵</i> (NCT01802372) (cluster RCT)	Ghana (mixed)	757	58.0±12.4/60%	Mild to moderate 155.9±12.1/89.6±10.8	Training of nurses in task-shifting for hypertension control-health insurance coverage vs health coverage	12	BP: improvement in both groups, but no difference between groups. SBP: 137.1±27.5 vs 138.4±27.3 mm Hg; change: -19.5±18.0 vs -16.6±17.9 mm Hg; MD: -2.9 mm Hg (-6.9 to 1.0) DBP: 79.8±22.9 vs 81.8±22.8 mm Hg; change -9,3±11.5 vs 8.7±18.7 mm Hg; MD -0.6 mm Hg (-2.9 to 1.7) BP control: 55.2% vs 49.9% (MD 5.2% (-1.8% to 12.4%))
Mendis <i>et af⁶²</i> (cluster RCT)	Nigeria (mixed)	1188	55±4.7/58%	Mild to moderate 153.2±12.4/94±9.7	Education of healthcare workers and patients with a simple cardiovascular risk management package vs usual care	сі Ч	Adherence: higher with IG Attended visits: 90.1% vs 74.5% quit smoking: 100% vs 74.4% (p=0.023) Increased fruit consumption: 93.4% vs 18.8% (p<0.0001) Increased vegetable consumption: 14.2% vs 7.0% (p=0.0002) BP: higher decrease in IG SBP: -11.0 ± 15.4 vs -6.6 ± 20.6 mm Hg; MD -4.4 mm Hg (-6.7 to -2.1) DBP: -5.4 ± 10.0 vs -2.0 ± 13.2 mm Hg; MD -3.4 mm Hg (-4.9 to -1.9)
Steyn <i>et al⁶²</i> (PACTR2013 03000493351) (cluster RCT)	South Africa (urban)	920	60.3±11.1/79%	All hypertensives 151.2±26.7/87.1±12.4	Multifaced intervention to implement national guidelines (structured record of national guidelines and visits to train clinicians) vs usual care (passive dissemination) at primary care level	12	BP: no difference SBP: 161±28.9 vs 158.2±29.5 mm Hg; MD 2.8 mm Hg (–1.2 to 6.8) DBP: 88.1±13 vs 87.1±12.6 mm Hg; MD 1.00 mm Hg (–0.73 to 2.73) controlled BP: 23.1% vs 26%
Individualised treatment (3 RCTs)	nent (3 RCTs)						

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Table 2 Continued	nued						
		Participants	oants		Intervention (IG) vs control (CG) group		Results on adherence and BP
Name (design)	Country	Ē	Age (years)/ females	Hypertension; SBP/ DBP (mm Hg)	Fc Description (m	Follow-up (months)	IG vs CG; treatment effect (95% CI)
Akintunde <i>et al²⁵</i> (ISRCTN69440037) (RCT) (RCT) (Akintunde, 2017 #4980} (ISRCTN69440037)	Nigeria, Kenya, South Africa (urban)	105	56.6±14.3/53%	Uncontrolled 170.9±19.2/85.6±21.8	Physiologically individualised care (guided 12 by their physiological phenotype, based on plasma renin and aldosterone) vs usual care	12	<u>BP:</u> lower in IG SBP: 139.4±17.4 vs 152.6±12.3mm Hg; MD –13.2mm Hg (–19.4 to –7.0) DBP: 84.0±11.0 vs 89.6±7.0mm Hg; MD –5.6mm Hg (–9.4 to –1.8) BP control: 50.0% vs 11.1% (p=0.0001)
Okeahialam <i>et al</i> ⁶⁵ (RCT)	Nigeria (urban)	181	49.7±14.2/61%	Mild to moderate 150.3±14.8/93.7±9.6	Chronotherapy: drug intake in the night (22:00) vs drug intake in the morning (10:00)	ო	<u>BP</u> : higher decrease in IG SBP: −18.1±17.9 vs −14.1±14.7mm Hg; MD −4.0mm Hg (−9.0 to 1.0) DBP: −15.6±12.2 vs −8.7±10.2mm Hg; MD −6.9mm Hg (−10.4 to −3.4)
Physical activity (4 RCTs)	RCTs)						
Aweto et al ²⁶ (RCT)	Nigeria (urban)	50	45±12.3/58%	Mild to moderate 138.7±10.9/79.9±9.3	Dance movement therapy (50 min) vs educational sessions, both 2×/week over 4 weeks		BP: lower in IG SBP: 119.9±8.3 vs 135.5±11.6mm Hg; MD –15.6mm Hg (–22.4 to –8.8) DBP: 70.9±7.2 vs 74.1±7.7mm Hg; MD –3.2mm Hg (–8.1 to 1.7)
Lamina ³⁷ (RCT)	Nigeria (urban)	485	58.5±6.8/0%	Mild to moderate, stable 165.4±13.2/98.1±4.6	Training programmes on bicycle ergometer, 3x/week, 45–60min: interval training (IG2) vs continuous training (IG1) vs usual care over 8 weeks	N	<u>BP</u> : lower in IG SBP: 150.4±16.7 vs 154.4±12.6 vs 163.5±14.9mm Hg; MD −11.1mm Hg (−14.8 to −7.4) DBP: 95±5 vs 94.4±8.8 vs 96.1±2.7 mm Hg; MD −1.4mm Hg (−2.6 to −0.2)
Maruf <i>et al</i> ⁶¹ (ISRCTN81952488) (RCT)	Nigeria (urban)	120	52.8±8.4 (range 38–65)/71%	Mild to moderate, 155.7±11.4/93±10	Aerobic dance training (3×/week, 45min) s vs usual care over 12weeks	ო	<u>BP:</u> lower in IG SBP: 135.3±5.6 vs 142.4±4.7 mm Hg; MD: −7.1 mm Hg (−9.3 to −4.9) DBP: 82.2±3.4 vs 83.3±2.8 mm Hg; MD: −1.7 mm Hg (−3.0 to −0.4)
Khalid <i>et al⁶³</i> (RCT)	Egypt (urban)	30	52.8±2.4, 40– 50/100%	Postmenopausal hypertensives 151±6.2/94.5±4.2	Moderate aerobic exercise training (40 min, 3x/week) by walking on a treadmill vs usual care over 8 weeks	5	<u>BP:</u> lower in IG SBP: 124±5.6 vs 145±6.7 mm Hg; MD: −21.0 mm Hg (−25.8 to −16.2) DBP: 85±5.4 vs 95±3.7 mm Hg: MD: −10.0 mm Hg (−13.7 to −6.3)
Modified nutrition (1 RCT)	1 RCT)						
Charlton <i>et a</i> ⁸¹ (RCT)	South Africa (urban)	6	61.1±7/84%	Mild to moderate 134.6±15.7/81.1±8.1	Food-based dietary strategy (modified food, salt replacement, +500 mL of maas (fermented milk) vs control (same quantities of the targeted foods of standard commercial composition, 500 mL/day artificially sweetened cool drink)	2	<u>BP:</u> lower in IG SBP: 132.5±15.8 vs 127.5±15.8 mm Hg; MD _a : –6.2 mm Hg (–11.4 to –0.9) DBP: 82.2±9.5 vs 79.2±11.4 mm Hg; MD _a : –0.6 mm Hg (–3.0 to 1.8)
*Tertiary prevention. BMI, body mass index; communicable disease	; BP, blood pressure; L ;; n.r, not reported; OR	DBP, diast ^{a,} adjuste	olic blood pressure; MA d OR; RCT, randomised	P, mean arterial pressure; MD I controlled trial; RR, relative ri	, mean difference; MD _a , adjusted mean difference; Mi isk; SBP, systolic blood pressure; SMS, short messag	AMA, Morisk) ige service.	^{-T} ertiary prevention. BMI, body mass index; BP, blood pressure; DAP, mean arterial pressure; MD, mean difference; MD _a , adjusted mean difference; MMA, Morisky medication adherence; n, number of randomised participants; NCD, non- communicable disease; n.r, not reported; OR _a ¹ adjusted OR; RCT, randomised controlled trial; RR, relative risk; SBP, systolic blood pressure; SMS, short message service.

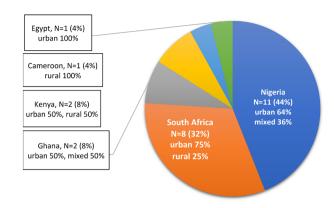


Figure 2 Spatial distribution of countries in which randomised studies were conducted.

aldosterone profile (Akintunde *et al*)²⁵ resulted in more appropriate prescriptions and a relevant decrease of SBP (MD: -13.2 mm Hg; 95% CI -19.4 to -7.0) and DBP (MD: -5.6; 95% CI -9.4 to -1.8) in patients with uncontrolled hypertension. The second study (Okeahialam *et al*)⁵⁵ showed a higher reduction of DBP in patients using their anti-hypertensives at night compared with a morning intake (MD: -6.9 mm Hg; 95% CI -10.4 to -3.4) but stated no change in SBP (table 2).

A: Results on systolic blood pressure (SBP)

	Inter	ventio	n	Co	ontrol		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Random, 95% CI	IV, Random, 95% CI
1.1.1 SBP at end of f	ollow-up							
Owolabi 2019	145.1	22.6	84	148.5	22.8	74	-3.40 [-10.50, 3.70]	+
Stewart 2005	142	16	38	144	20	36	-2.00 [-10.28, 6.28]	
Bobrow 2016	132.4	17.1	800	134.3	17.3	396	-1.90 [-3.98, 0.18]	-+-
Gyamfi 2017	137.1	27.5	323	138.4	27.3	319	-1.30 [-5.54, 2.94]	-+
Fairall 2016	134	23	1927	135	21.7	2014	-1.00 [-2.40, 0.40]	++
Vedanthan 2019	149.8	21.2	751	150	22.9	355	-0.20 [-3.02, 2.62]	-+
Steyn 2013	161	28.9	429	158.2	29.5	408	2.80 [-1.16, 6.76]	++
Wahab 2017	137.5	23.1	17	133.1	18.2	18	4.40 [-9.43, 18.23]	
1.1.2 SBP change to	the end (of follo	w-up					
Mendis 2010	-11	15.4	530	-6.6	20.6	447	-4.40 [-6.72, -2.08]	
Gyamfi 2017	-19.5	18	323	-16.6	17.9	319	-2.90 [-5.68, -0.12]	-+-
vedanthan 2019	-10.8	23.3	751	-9.7	25.1	355	-1.10 [-4.20, 2.00]	-+-
Owolabi 2019	-11.71	2.4	84	-11.18	2.84	74	-0.53 [-1.36, 0.30]	+
Fairall 2016	1.2	21.8	1925	-1.1	21.7	2044	2.30 [0.95, 3.65]	+
								-20 -10 0 10 20

B: Results on diastolic blood pressure (DBP)

	Inte	rventi	on	C	ontrol		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Random, 95% CI	IV, Random, 95% CI
1.2.1 DBP at end of f	ollow-up							
Gyamfi 2017	79.8	22.9	323	81.8	22.8	319	-2.00 [-5.54, 1.54]	-+-
Wahab 2017	84.1	9.7	17	84.2	13.1	18	-0.10 [-7.71, 7.51]	
Vedanthan 2019	91.2	13.4	751	91	25.1	355	0.20 [-2.58, 2.98]	+
Stewart 2005	92	12	38	91	10	36	1.00 [-4.02, 6.02]	i
Fairall 2016	88	13.2	1927	87	12.7	2014	1.00 [0.19, 1.81]	+
Steyn 2013	88.1	13	429	87.1	12.6	408	1.00 [-0.73, 2.73]	+-
1.2.2 DBP change to	the end	of foll	ow-up					
Mendis 2010	-5.4	10	530	-2	13.2	447	-3.40 [-4.89, -1.91]	+
Gyamfi 2017	-9.3	11.5	323	-8.7	18.7	319	-0.60 [-3.00, 1.80]	-+-
Vedanthan 2019	1	14	751	0.1	14.7	355	0.90 [-0.93, 2.73]	+-
Fairall 2016	0	13.5	1925	-1.8	13.4	2044	1.80 [0.96, 2.64]	+
								-20 -10 0 10 20 Favours intervention Favours control

C: Results on Blood pressure (BP) control

	Interver	ntion	Cont	lor	Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	M-H, Random, 95% CI	M-H, Random, 95% Cl
Adeyerno 2013	182	280	175	264	0.98 [0.87, 1.11]	-+
Goudge 2018	125	1109	160	1430	1.01 [0.81, 1.26]	
Fairall 2016	139	426	128	399	1.02 [0.83, 1.24]	_
Bobrow 2016	520	800	230	396	1.12 [1.01, 1.23]	—
Bolarinwa 2019	128	149	115	150	1.12 [1.00, 1.25]	
Sarfo 2019	14	30	12	30	1.17 [0.65, 2.09]	
						0.5 0.7 1 1.5 2
						Favours control Favours intervention

Figure 3 Results of educational strategies to improve adherence (3a Results on systolic blood pressure; 3b Results on diastolic blood pressure; 3c Results on blood pressure control)

A: Results on systolic blood pressure (SBP)

	Inte	rventi	on	с	ontrol		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Random, 95% CI	IV, Random, 95% CI
SBP at end of fe	ollow-up	,						
Khalid 2013	124	5.6	12	145	6.7	13	-21.00 [-25.83, -16.17]	← ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓
Aweto 2012	119.9	8.3	23	135.5	11.6	15	-15.60 [-22.38, -8.82]	
Lamina 2010	152.4	14.6	152	163.5	14.9	105	-11.10 [-14.78, -7.42]	_ —
Maruf 2016	135.3	5.6	45	142.4	4.7	43	-7.10 [-9.26, -4.94]	+
B: Results on dia	stolic	bloo	od pr	essur	e (D	BP)		-20 -10 0 10 20 Favours intervention Favours control
	Inte	ervent	ion	c	ontro	4	Mean Difference	Mean Difference

	Inter	venti	on	C	ontro	d	Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Random, 95% CI	IV, Random, 95% CI
DBP at end of f	ollow-up							
Khalid 2013	85	5.4	12	95	3.7	13	-10.00 [-13.66, -6.34]	
Aweto 2012	70.9	7.2	23	74.1	7.7	15	-3.20 [-8.08, 1.68]	-++
Maruf 2016	82.2	3.4	45	83.9	2.8	43	-1.70 [-3.00, -0.40]	+
Lamina 2010	94.7	6.9	152	96.1	2.7	105	-1.40 [-2.61, -0.19]	+
								-20 -10 0 10 20
								Favours intervention Favours control

Figure 4 Results of strategies to enhance physical activity (4a Results on systolic blood pressure; 4b Results on diastolic blood pressure).

Strategies with physical activity

Four studies²⁶³⁷⁵¹⁶³ (685 participants), published between 2010 and 2016, investigated the BP-lowering effect of different aerobic training strategies over 4–12 weeks. Enhanced physical activities were performed two or three times a week and included dance training (Aweto *et al*, Maruf *et al*)²⁶⁵¹ and exercise training on an ergometer (Lamina)³⁷ or treadmill (Khalid *et al*).⁶³

All studies stated a clinically relevant benefit with mean reductions of SBP between 21 and 7.1 mm Hg and DBP between 10 and 1.4 mm Hg (figure 4). The highest BP decrease was achieved in a study on the effect of moderate aerobic exercise training by walking on a treadmill in postmenopausal women with hypertension (Khalid *et al*)⁶³ (MD: -21 mm Hg; 95% CI -25.8 to -16.2).

Modified nutrition strategies

Charlton *et al*^{β 1} tested a food-based dietary strategy (reduced salt consumption) in 92 patients with mild to moderate hypertension from a low socioeconomic background, stating a clinically relevant decrease in SBP after 2 months (MD: -6.2 mm Hg; 95% CI -11.4 to -0.9), but no effect on DBP (table 2).

Potential biases

The greatest restriction of study quality was a high risk of bias in the blinding of staff and study participants in 19 studies. Especially educational strategies were not examined in double-blinded studies, however three of these studies^{34 56 58} reported a quality assurance against detection bias with blinded measurement of BP. Two studies on physical activity enhancement in comparison with usual care (Lamina, Maruf *et al*)^{37 51} were described as double blinded without reporting further details. Only the study on modified nutrition (Charlton *et al*)³¹ adequately reported detailed methods to ensure blinding of participants and fieldworkers. Another frequent problem was incomplete outcome data in 14 studies with loss to follow-up of over 10% of randomised participants or per-protocol analyses. Selective reporting was checked in all 13 studies with a published protocol. Of those, five studies^{29 35 36 51 56} did not report all preplanned outcomes.

Problems concerning randomisation were identified in three studies with a non-random component in sequence generation or allocation concealment.^{25 37 52} Other sources of bias include missing sample size calculations, reporting of intermediate results only and relevant differences at baseline in nine studies (table 3, figure 5).^{24–26 29 51 55 63 64 66}

DISCUSSION

This systematic review describes interventions and treatment effects of 23 studies with a total of 18153 participants with hypertension from six African countries. Most of the studies investigated successful low-cost concepts to improve BP control through improved adherence to medical treatment and lifestyle changes.

While lower-income and middle-income countries' CVD mortality remained unchanged over the last decades, high-income countries have reduced the CVD mortality by more than 50% since 1990,⁶⁷ largely by using country-specific guidelines, evidence-based policy interventions to reduce risk factor levels, strengthening the health system at the primary care level and improving acute care with attention to early initiation of treatment. However, policies to reduce population-wide risk factors of hypertension have not been widely adopted in low-income and middle-income countries.⁶⁸

Pharmacotherapy with the well-established antihypertensive medications is the mainstay of hypertension management.^{15 69} Nevertheless, treatment recommendations on adherence to medication and changed lifestyle habits are often only incompletely applied in practice.^{70–72} Patients are frequently unwilling to take drugs due to possible side effects. They may benefit from adequate knowledge as well as a higher motivation to take their prescribed medications and to implement sustainable lifestyle changes.^{73–75} Despite the frequent lack of acute symptoms, uncontrolled BP may result in severe longterm outcome and increased mortality. The risk increases in cases of inadequate treatment and low patient adherence as well as inconsistent follow-up on BP control.⁴ Therefore, all strategies with the aim to increase knowledge, awareness and adherence are essential to lowering BP levels and improving the prognoses of patients.⁶⁹⁷⁶ Due to the short-term follow-up, no study reported longterm outcomes on mortality, and we interpreted available results on BP changes and treatment adherence.

Several strategies to improve health-related behaviour concerning hypertension with convincing results were examined. We identified eight studies that investigated the efficacy of phone or letter-based interventions (eg, via short message service) to improve knowledge on hypertension, with adherence support or reminder letters for follow-up.^{27 28 36 56 58 60 61 64} All these studies showed strong effects of the intervention concerning self-reported behavioural changes, but only two of these studies showed improved BP during follow-up (Ayodapo and Olukokun, Bobrow *et al*).^{27 28} Three studies^{29 35 52} reported improved adherence and two of those a decreased BP level through

nurse-led interventions (Bolarinwa *et al*, Mendis *et al*).²⁹⁵² These studies demonstrated the efficacy of task-shifting interventions in a low-resource setting. Furthermore, low-cost interventions suited to the environment, including financial incentives for adherent patients with minimal additional resources, can significantly improve the adherence of patients (Labhardt *et al*)³⁶ and thus potentially influence BP control.

Even though cost-effective interventions are globally available, there are major gaps in their implementation, particularly in limited-resource settings.⁶⁸ Two large multilevel studies that combined phone or letter-based interventions with task-shifting to nurses or health workers were not successful in achieving a relevant improvement in adherence and BP control (Fairall et al, Goudge et al).^{32 34} On the other hand, no harm was observed after the expansion of the nurses' roles (Fairall et al).³² Thus, the intervention might be a practical and acceptable tool to expand the scope of non-physician clinicians into primary care of patients with common NCDs. There is a generally good access to essential medications in four countries where the included studies have been conducted (South Africa, Egypt, Kenya and Ghana). The access is not as widespread in Cameroon and Nigeria.⁷⁷ Nevertheless, one study conducted in rural parts of South Africa between 2014 and 2015 (Goudge *et al*)³⁴ reported insufficient or unavailable equipment and medication shortage. Moreover, increasing numbers of patients with NCD require an adequate number of nursing personnel as well as healthcare facilities. Similar factors contributed to the poor results of the implementation of national guidelines in resource-scarce primary healthcare settings in South Africa.⁶² which did not show improved outcomes in patients with hypertension and diabetes. In studies with follow-up-periods of less than 1 year, the time frame might have been too short to reach a clinically relevant BP control through improved knowledge and awareness, since lifestyle changes are oftentimes challenging and should be applied over a long time.^{24 61 66} Generally, the results of the systematic review are consistent with existing evidence on the importance of long-acting patient-centred interventions. Unfortunately, these interventions do not reach all patients and often, a full benefit of medical treatment on clinically important outcomes cannot be achieved.⁷⁸

Most studies in this review included participants in secondary prevention with mild to moderate hypertension. In contrast, observational studies and conclusions from a systematic review on pharmacological treatment generally concerned participants with higher grades of hypertension.^{5 7 79} Interventions for patients with severe or uncontrolled hypertension and potentially target-organ damage are under-represented. Interventions for high-risk patients are especially necessary due to the high frequency of late first diagnosis⁷ and high prevalence of severe forms of hypertension at an early age in African patients.⁶ A multicentre study on patients with uncontrolled hypertension in clinics in Nigeria, Kenya

Table 3 Risk of	of bias assessm	ient		-			
	-		Blinding of				
Study	Sequence generation	Allocation concealment	Personnel/ participants	Outcome assessors	Incomplete outcome data	Selective reporting	Other sources
Educational st	rategies						
Adeyemo et al ²⁴			8		8		8
Ayodapo and Olukokun ²⁷	<mark>⊕</mark>		<mark>©</mark>	<mark>8</mark>		<mark></mark>	<mark>⇔</mark>
Bobrow et al ²⁸	\bigcirc		8	<mark>⇔</mark>	8		
Bolarinwa et al ²⁹	\bigcirc		8	<mark>©</mark>	<mark>©</mark>	8	<mark>©</mark>
Fairall et al ³²	☺		8	<mark>⇔</mark>			\odot
Goudge et al ³⁴	\bigcirc		<mark>©</mark>	<mark>8</mark>	<mark>©</mark>		
Gyamfi <i>et al³⁵</i>	\bigcirc		8		8	<mark>©</mark>	\bigcirc
Labhardt et al ³⁶			B	8	<mark>©</mark>	8	
Mendis <i>et al⁵²</i>	<mark>©</mark>	8	8	8	8		\bigcirc
Owolabi <i>et al⁵⁶</i>	\bigcirc	<mark>@</mark>	<mark>©</mark>			<mark>©</mark>	
Sarfo <i>et al⁵⁸</i>			8				\bigcirc
Saunders et al ⁶⁰	<mark>⊕</mark>	<mark></mark>	<mark>©</mark>	<mark>8</mark>		<mark></mark>	
Stewart <i>et al</i> 61	<mark>@</mark>	<mark></mark>	8	8	8		
Steyn <i>et al⁶²</i>	\bigcirc		<mark>©</mark>	<mark>©</mark>			
Vedanthan et al ⁶⁴	<mark>⊕</mark>		8	8	8		8
Wahab <i>et al⁶⁶</i>	\bigcirc	\odot	<mark>©</mark>	8			8
Standardised 1	treatment						
Akintunde et al ²⁵	8	<mark></mark>	<mark>⇔</mark>	<mark>⇔</mark>	<mark>8</mark>		<mark>©</mark>
Okeahialam et al ⁵⁵	\bigcirc		8		8		8
Physical activi	ty						
Aweto <i>et al</i> ²⁶	<mark>@</mark>	<mark></mark>	8	<mark>©</mark>	<mark>©</mark>	<mark></mark>	8
Lamina ³⁷	<mark>©</mark>	<mark>@</mark>			<mark>©</mark>		
Maruf et al ⁵¹	\bigcirc		<mark></mark>			8	8
Khalid et al ⁶³			8	<mark>©</mark>	<mark>©</mark>		<mark>©</mark>
Modified nutri	tion						
Charlton <i>et al</i> ³¹							\odot
😳: low; 😐: und	clear; 😕: high risk	of bias.					

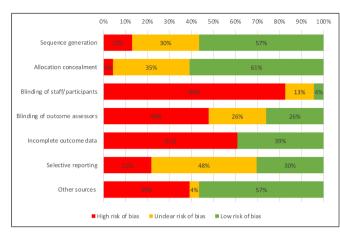


Figure 5 Summary of risk of bias.

and South Africa stated the efficacy of an individualised therapy based on phenotyping with plasma renin and aldosterone to improve BP control (Akintunde *et al*).²⁵ The researchers suggest testing this approach in African Americans and patients of any race with therapy-resistant hypertension. Three studies^{56 58 66} investigated the implementation of multilevel approaches including educational, telephone-based, nurse-led, self-management supporting interventions, as well as BP monitoring for stroke survivors. These studies were not successful in sufficiently improving BP control, possibly due to short follow-up periods.

Regarding the different grades of hypertension, low-risk patients with grade 1 hypertension benefit from lifestyle modifications including regular physical activity, sodium restriction, weight reduction, smoking cessation, moderation of alcohol consumption and other dietary changes. These are recommended as initial strategies to reduce BP levels in order to prevent or delay the use of pharmacotherapy.^{14 15} Nevertheless, even for patients with higher grades of hypertension, lifestyle modifications remain important in addition to pharmacotherapy.¹⁴ ¹⁵ ⁶⁹ ⁸⁰ The clinically accepted relevant BP-lowering effect of mediumintensity to high-intensity physical activity as a single or additive treatment for hypertension⁸¹ was demonstrated in four of the included studies.^{26 37 51 63} Only one study from South Africa investigated the effect of a modified nutrition strategy (reduction of salt intake) and stated a clinically relevant effect on SBP (Charlton *et al*).³¹ To the authors' knowledge, no randomised study investigated the efficacy of other recommended lifestyle interventions, like smoking cessation or weight reduction, in patients with hypertension in an African country.

Strengths and limitations of this review

We were able to generate evidence on a wide range of different non-pharmacological interventions, adding a comprehensive overview to the literature that can support physicians and healthcare policymakers in the African setting.

A main limitation occurs through deviations from the protocol. We planned a comprehensive summary of all

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RCTs to prevent, diagnose and treat patients with CVDs in African countries. Due to a high number of eligible studies in the first systematic search, we decided to focus on published studies on hypertension. We therefore had to change the preplanned outcomes and instead focus on BP and additionally describe results on medication adherence and lifestyle changes. The preplanned outcomes mortality, New York Heart Association (NYHA) classification and hospital admission were dropped. Due to the recently published systematic review by Seeley *et al*,¹⁷ this publication describes non-pharmacological strategies. The complete results, including pharmacological interventions, were summarised in a doctoral thesis paper.⁸²

Nevertheless, this review was limited to studies with the highest level of evidence to investigate the benefits and harms of non-pharmacological interventions for hypertension. The randomised allocation ensures the comparability of participants across intervention groups. However, the unfeasibility of double blinding might restrict the internal validity of results.

The external validity might be limited by our restriction to studies published in the English language and the disproportionally high number of studies conducted in urban areas in some Western and Southern African countries. According to the UN, there are currently 54 African countries. RCTs have been conducted in only six of those countries. Inhabitants of these countries (approximately 480 million) represent only a fraction of the African population of about 1.34 billion.⁸³ Especially Central and Northern Africa were under-represented. There are high levels of diversity within and between African populations. Subpopulations with genetic variants are living in geographically distant areas with specific local lifestyle or environmental conditions, which may be associated with a susceptibility to specific NCDs.⁸⁴ Therefore, it is uncertain whether our results can be extrapolated to patients living in other areas than those studied. A significant amount of the African population lives in rural areas while the majority of studies were conducted in urban settings. However, it is crucial to make health service available as close as possible to the population in order to achieve the most comprehensive care. Thus, research on nonpharmacological interventions such as educational strategies to improve adherence and lifestyle modification should be expanded across all parts of Africa. Research must be conducted especially in rural areas to ensure a higher generalisability, quality of services and resulting improvement of the African people's health.

CONCLUSION

This systematic review shows that even though hypertension is a critical health problem, there are still few randomised studies on non-pharmacological treatment of hypertension conducted on the African continent. Available studies do not represent all Africans since they were conducted in only six countries, many in urban settings only. It is advisable to plan and implement studies on patients with hypertension and healthcare professionals in rural areas as well as Northern and Central African countries.

An improvement in the prognosis of patients with high BP in Africa requires the implementation of practical and effective solutions to diagnose, treat and control hypertension in specific settings.⁹ The identified studies describe diverse approaches tested in African countries that may be used to generate local African evidencebased guidelines on hypertension treatment. Especially trialled physical activity interventions and individualised treatment strategies show clinically relevant BP changes. Educational strategies for patients and medical personnel show mixed results and offer a comprehensive insight into trialled approaches as well as a basis for future research opportunities. This review summarises miscellaneous low-cost interventions including task-shifting, education individualised treatment and lifestyle modifications to improve BP control.

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Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval No ethics approval and consent to participate was necessary.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as supplemental information.

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Search strategies

Medline (Ovid): Search on CVDs

Nr.	Searches (24th July 2017)	Results
Indicat	ion	
1.	exp heart diseases/	
2.	exp vascular diseases/	
3.	cerebrovascular disorders/	
4.	exp brain ischemia/	
5.	exp carotid artery diseases/	
6.	exp dementia, vascular/	
7.	exp intracranial arterial diseases/	
8.	exp intracranial embolism/ and thrombosis/	
9.	exp intracranial hemorrhages/	
10.	exp stroke/	
11.	exp hyperlipidemias/	
12.	Exp hypercholesteremia/	
13.	exp Myocardial Ischemia/	
14.	angina.tw	
15.	(heart adj3 disease\$).tw.	
16.	(coronary adj3 disease\$).tw.	
17.	(peripheral adj3 disease\$).tw.	
18.	(cerebrovascular disease).tw	
19.	Renal artery stenosis.tw	
20.	(Aortic aneurism or Aneurysm\$).tw	
21.	myocardial infarct\$.tw.	
22.	exp Myocardial Revascularization/	
23.	(coronary adj3 bypass\$).tw.	
24.	(coronary adj3 angioplast\$).tw.	
25.	(heart adj3 infarct\$).tw.	
26.	postmyocardial infarct\$.tw.	
27.	cardiovascular diseases/	
28.	Hypertens\$.tw	
29.	(high adj2 blood pressure).tw	
30.	(blood pressure control).tw	
31.	Hypertensive heart disease.tw.	
32.	Cardiomyopath\$.tw.	
33.	Heart failure.tw.	

Nr.	Searches (24th July 2017)	Results
34.	(Pulmonary heart disease).tw	
35.	Cardiac dysrhythmia*.tw.	
36.	Inflammatory heart disease.tw.	
37.	Endocarditis.tw.	
38.	Cardiomegaly.tw	
39.	Valvular heart disease.tw.	
40.	Rheumatic heart disease.tw	
41.	Myocarditis.tw	
42.	Arrhythmi\$.tw	
43.	Vasculitis.tw	
44.	or/1-43	2 498 192
Africa a	nd African countries	
45.	Africa.tw	
46.	Exp Africa/	
47.	Algeria\$.tw or exp Algeria/	
48.	Angol\$.tw or exp Angola/	
49.	Benin\$.tw or exp Benin/	
50.	Botswan\$.tw or exp Botswana/	
51.	Burkina Faso.tw or exp Burkina Faso/	
52.	Burund\$.tw or exp Burundi/	
53.	Cameroon\$.tw or exp Cameroon/	
54.	Cape Verde.tw or exp Cape Verde/	
55.	Central African Republic\$.tw or exp Central African Republic/	
56.	Chad\$.tw or exp Chad/	
57.	Comoros\$.tw or exp Comoros/	
58.	Cote d'Ivoire.tw or exp Cote d'Ivoire/	
59.	Democratic Republic of Congo.tw or exp Democratic Republic of Congo	
60.	Djibout\$.tw or exp Djibouti/	
61.	Egypt\$.tw or exp Egypt/	
62.	Equatorial Guinea\$.tw or exp Equatorial Guinea/	
63.	Eritrea\$.tw or exp Eritrea/	
64.	Ethiop\$.tw or exp Ethiopia/	
65.	Gabon\$.tw or exp Gabon/	
66.	Gambia\$.tw or exp Gambia/	
67.	Ghana\$.tw or exp Ghana/	
68.	Guinea\$.tw or exp Guinea/	
69.	Guinea-Bissau.tw or exp Guinea-Bissau/	
05.	1	1

Nr.	Searches (24th July 2017)	Results
70.	Kenya\$.tw or exp Kenya/	
71.	Lesoth\$.tw or exp Lesotho/	
72.	Liberia\$.tw or exp Liberia/	
73.	Libya\$.tw or exp Libya/	
74.	Madagascar\$.tw or exp Madagascar/	
75.	Malawi\$.tw or exp Malawi/	
76.	Mali.tw or exp Mali/	
77.	Mauritania\$.tw or exp Mauritania/	
78.	Mauritius\$.tw or exp Mauritius/	
79.	Morocc\$.tw or exp Morocco/	
80.	Mozambique\$.tw or exp Mozambique/	
81.	Namibia\$.tw or exp Namibia/	
82.	Niger.tw or exp Niger/	
83.	Nigeria\$.tw or exp Nigeria/	
84.	Rwanda\$.tw or exp Rwanda/	
-	(Sao Tome and Principe).tw	
85.	Senegal\$.tw or exp Senegal/	
86.	Seychell\$.tw	
87.	Sierra Leone.tw or exp Sierra Leone/	
88.	Somalia\$.tw or exp Somalia/	
89.	South Africa\$.tw or exp South Africa.de	
90.	South Sudan.tw or exp South Sudan/	
91.	Sudan\$.tw or exp Sudan/	
92.	Swaziland\$.tw or exp Swaziland/	
93.	Tanzania\$.tw or exp Tanzania/	
94.	Togo\$.tw or exp Togo/	
95.	Tunisia\$.tw or exp Tunisia/	
96.	Uganda\$.tw or exp Uganda/	
97.	Zambia\$.tw or exp Zambia/	
98.	Zimbabwe\$.tw or exp Zimbabwe/	
99.	Somaliland\$.tw or exp Somaliland/	
100.	#1.tw	
101.		
102.	or/45-101	436 084
103.	44 and 102	19 017
	design randomized controlled trial.pt.	
104.	controlled clinical trial.pt.	
105.		

Nr.	Searches (24th July 2017)	Results
106.	randomized.ab.	
107.	placebo.ab.	
108.	randomly.ab.	
109.	trial.ab.	
110.	groups.ab.	
111.	or/104-110	2 535 560
112.	exp animals/ not humans.sh.	
113.	111 not 112	2 133 129
114.	103 and 113	2643

Medline (Ovid): Update on hypertension

Nr.	Searches (23th June 2020)	Results		
Indica	Indication			
1.	Exp hypertension			
2.	Hypertens\$.ti,ab			
3.	(high adj2 blood pressure).ti,ab			
4.	(blood pressure control).ti,ab			
5.	or/1-4	464 555		
Africa	and African countries			
6.	Africa.tw			
7.	Exp Africa/			
8.	Algeria\$.tw or exp Algeria/			
9.	Angol\$.tw or exp Angola/			
10.	Benin\$.tw or exp Benin/			
11.	Botswan\$.tw or exp Botswana/			
12.	Burkina Faso.tw or exp Burkina Faso/			
13.	Burund\$.tw or exp Burundi/			
14.	Cameroon\$.tw or exp Cameroon/			
15.	Cape Verde.tw or exp Cape Verde/			
16.	Central African Republic\$.tw or exp Central African Republic/			
17.	Chad\$.tw or exp Chad/			
18.	Comoros\$.tw or exp Comoros/			
19.	Cote d'Ivoire.tw or exp Cote d'Ivoire/			
20.	Democratic Republic of Congo.tw or exp Democratic Republic of Congo			
21.	Djibout\$.tw or exp Djibouti/			

Nr.	Searches (23th June 2020)	Results
22.	Egypt\$.tw or exp Egypt/	
23.	Equatorial Guinea\$.tw or exp Equatorial Guinea/	
24.	Eritrea\$.tw or exp Eritrea/	
25.	Ethiop\$.tw or exp Ethiopia/	
26.	Gabon\$.tw or exp Gabon/	
27.	Gambia\$.tw or exp Gambia/	
28.	Ghana\$.tw or exp Ghana/	
29.	Guinea\$.tw or exp Guinea/	
30.	Guinea-Bissau.tw or exp Guinea-Bissau/	
30. 31.	Kenya\$.tw or exp Kenya/	
31. 32.	Lesoth\$.tw or exp Lesotho/	
-	Liberia\$.tw or exp Liberia/	
33.	Libya\$.tw or exp Libya/	
34.	Madagascar\$.tw or exp Madagascar/	
35.	Malawi\$.tw or exp Malawi/	
36.	Mali.tw or exp Mali/	
37.	Mauritania\$.tw or exp Mauritania/	
38.	Mauritius\$.tw or exp Mauritius/	
39.	Morocc\$.tw or exp Morocco/	
40.	Mozambique\$.tw or exp Mozambique/	
41.	Namibia\$.tw or exp Namibia/	
42.	Niger.tw or exp Niger/	
43.	Nigeria\$.tw or exp Nigeria/	
44.	Rwanda\$.tw or exp Rwanda/	
45.		
46.	(Sao Tome and Principe).tw	
47.	Senegal\$.tw or exp Senegal/	
48.	Seychell\$.tw	
49.	Sierra Leone.tw or exp Sierra Leone/	
50.	Somalia\$.tw or exp Somalia/	
51.	South Africa\$.tw or exp South Africa.de	
52.	South Sudan.tw or exp South Sudan/	
53.	Sudan\$.tw or exp Sudan/	
54.	Swaziland\$.tw or exp Swaziland/	
55.	Tanzania\$.tw or exp Tanzania/	
56.	Togo\$.tw or exp Togo/	
57.	Tunisia\$.tw or exp Tunisia/	
58.	Uganda\$.tw or exp Uganda/	

Nr.	Searches (23th June 2020)	Results	
59.	Zambia\$.tw or exp Zambia/		
60.	Zimbabwe\$.tw or exp Zimbabwe/		
61.	Somaliland\$.tw or exp Somaliland/		
62.	Sahrawi Arab Democratic Republic.tw.		
63.	or/6-62	530 370	
Study o	Study design		
64.	randomized controlled trial.pt.		
65.	controlled clinical trial.pt.		
66.	(randomized or randomised or randomly).ti,ab		
67.	placebo.ab.		
68.	trial.ab.		
69.	groups.ab.		
70.	or/64-69	2 757 989	
71.	5 and 63 and 70	3036	
72.	exp animals/ not humans.sh.		
73.	71 not 72		
74.	73 not (comment or editorial).pt	2964	
75.	Limit 74 to yr= "2017-Current"	538	

CENTRAL: Search on CVDs

Nr.	Searches (14th August 2017)	Results
1	Africa, explode all trees	
2	Algeria* or Angol* or Benin* or Botswan*	
3	(Burkina Faso) or Burund* or Cameroon* or (Cape Verde) or (Central African Republic)	
4	Chad* or Comoros* or Cote d'Ivoire or Congo*	
5	Djibout* or Egypt* or (Equatorial Guinea*) or Eritrea*	
6	Ethiop* or Gabon* or Gambia* or Ghana* or Guinea* or Guinea-Bissau	
7	Kenya* or Lesoth* or Liberia* or Libya* or Madagascar* or Malawi*	
8	Mali* or Mauritania* or Mauritius* or Morocc* or Mozambique* or Namibia* or Niger*	
9	Nigeria* or Rwanda* or (Sao Tome and Principe) or Senegal* or Seychell*	
10	Sierra Leone or Somalia* or (South Africa) or (South Sudan*) or Sudan* or Swasiland	
11	Tanzania [*] or Togo [*] or Tunisia [*] or Uganda [*] or Zambia [*] or Zimbabwe [*] or Somaliland or (Sahrawi Arab Democratic Republic)	
12	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11	39 610
13	MeSH descriptor Cardiovascular Diseases, this term only	
14	MeSH descriptor Heart Diseases explode all trees	
15	MeSH descriptor Vascular Diseases explode all trees	
16	MeSH descriptor Cerebrovascular Disorders, this term only	
17	MeSH descriptor Brain Ischemia explode all trees	
18	MeSH descriptor Carotid Artery Diseases explode all trees	
19	MeSH descriptor Dementia, Vascular explode all trees	
20	MeSH descriptor Intracranial Arterial Diseases explode all trees	
21	MeSH descriptor Intracranial Embolism and Thrombosis explode all trees	
22	MeSH descriptor Intracranial Hemorrhages explode all trees	
23	MeSH descriptor Stroke explode all trees	
24	MeSH descriptor Hyperlipidemias explode all trees (4197)	
25	(coronar* or heart or peripheral* or cerebrovascular* or myocardial) near 3 (disease or infarct*)	
26	myocardi* near 3 (infarct* or revascular* or ischaem* or ischem*)	
27	vascular* near 3 (peripheral* or disease* or complication*))	
28	hypertensi* or (high near 2 blood pressure)	
29	(heart near 2 failure) or stroke	
30	Endocarditis or myocarditis or Cardiomegaly or arrythmi*	
31	#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	101 472
32	#12 and #31	4139
32	Trials	2008

CENTRAL, Update on hypertension

Nr.	Searches (23th June 2020)	Results
1	Africa, explode all trees	
2	Algeria* or Angol* or Benin* or Botswan*	
3	(Burkina Faso) or Burund* or Cameroon* or (Cape Verde) or (Central African Republic)	
4	Chad* or Comoros* or Cote d'Ivoire or Congo*	
5	Djibout* or Egypt* or (Equatorial Guinea*) or Eritrea*	
6	Ethiop* or Gabon* or Gambia* or Ghana* or Guinea* or Guinea-Bissau	
7	Kenya* or Lesoth* or Liberia* or Libya* or Madagascar* or Malawi*	
8	Mali* or Mauritania* or Mauritius* or Morocc* or Mozambique* or Namibia* or	
	Niger*	
9	Nigeria* or Rwanda* or (Sao Tome and Principe) or Senegal* or Seychell*	

Nr.	Searches (23th June 2020)	Results
10	Sierra Leone or Somalia* or (South Africa) or (South Sudan*) or Sudan* or Swasiland	
11	Tanzania* or Togo* or Tunisia* or Uganda* or Zambia* or Zimbabwe* or Somaliland or (Sahrawi Arab Democratic Republic)	
12	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11	60 623
13	MeSH descriptor: [Hypertension] explode all trees	
14	hypertensi* or (high near 2 blood pressure)	
15	#13 or #14	67 954
16	#12 and #15	2929
	Trials, 2017-Current	333

CINAHL, Search on 23.06.2020

(Africa\$ or Africa\$ or Algeria\$ or Angol\$ or Benin\$ or Botswan\$ or (Burkina Faso) or Burund\$ or Cameroon\$ or (Cape Verde) or (Central African Republic) or Chad\$ or Comoros\$ or Cote d'Ivoire or Congo\$ Djibout\$ or Egypt\$ or (Equatorial Guinea\$) or Eritrea\$ or Ethiop\$ or Gabon\$ or Gambia\$ or Ghana\$ or Guinea\$ or Guinea Bissau or Kenya\$ or Lesoth\$ or Liberia\$ or Libya\$ or Madagascar\$ or Malawi\$ or Mali\$ or Mauritania\$ or Mauritius\$ or Morocc\$ or Mozambique\$ or Namibia\$ or Niger\$ or Nigeria\$ or Rwanda\$ or (Sao Tome and Principe) or Senegal\$ or Seychell\$ or Sierra Leone or Somalia\$ or (South Africa) or (South Sudan\$) or Sudan\$ or Swasiland or Tanzania\$ or Togo\$ or Tunisia\$ or Uganda\$ or Zambia\$ or Zimbabwe\$ or Somaliland or (Sahrawi Arab Democratic Republic)) in Abstract

AND

hypertension or high blood pressure or elevated blood pressure or htn or hypertensive in Abstract AND

randomized or rct or randomised in Abstract AND In English AND Peer-reviewed And Humans **Total: 42 results**

International Clinical Trials Registry Platform (<u>http://apps.who.int/trialsearch/AdvSearch.aspx</u>), Search on 22 October 2019

hypertension or (blood pressure control) or (high blood pressure) in the condition,

Recruitment status: all

Countries of recruitment:

- Africa or African in the title: 90 trials
- Algeria or Angola or Behin or Burkina Faso or Botswana or Burundi or Cameroon or Central Africa Republic or Chad or Congo or Cabo Verde or Cite D'Ivoire: 13 trials
- Democratic Republic of Congo or Djibouti or Egypt or Equatorial Guinea or Eritrea or Ethiopia or Gabon or Gambia or Ghana or Guinea or Guinea-Bissau or Kenya: 78 trials
- Lesotho or Liberia or Libya or Madagascar or Malawi or Mali or Mauritius or Morocco or Mozambique: 14 trials
- Namibia or Niger or Nigeria or Rwanda or Sao Tome and Principe or Senegal or Seychelles or Sierra Leone or Somalia or Sudan or South Sudan or Swaziland: 23 trials
- Togo or Tunezia or United Republic of Tanzania or Uganda or Zambia or Zimbabwe: 25 trials

Total: 18 results

Heart failure (N=13)

1. Adigun AQ, Ajayi OE, Sofowora GG, Ajayi AA (1998) Vasodilator therapy of hypertensive acute left ventricular failure: comparison of captopril-prazosin with hydralazine-isosorbide dinitrate. International Journal of Cardiology, 67(1):81-6.

2. Ajayi AA, Balogun MO, Oyewo EA, Ladipo GO (1989) Enalapril in African patients with congestive cardiac failure. British Journal of Clinical Pharmacology, 27(3):400-3.

3. Ajayi AA, Sofowora GG, Adigun AQ, Asiyanbola B (2003) Adjunctive sympathoplegic therapy to ACE inhibition in Blacks with congestive heart failure: a comparison of alpha-1 with beta-1 blockade on exercise tolerance and cardiac sympathovagal reflex activity. Ethnicity & Disease, 13(1):71-9.

4. Ajiboye OA, Anigbogu CN, Ajuluchukwu JN, Jaja SI (2013) Therapeutic Effects of Exercise Training On Selected Cardio-Pulmonary Parameters and Body Composition of Nigerians with Chronic Heart Failure (A Preliminary Study). Nigerian Quarterly Journal of Hospital Medicine, 23(4):295-301.

5. Ajiboye OA, Anigbogu CN, Ajuluchukwu JN, Jaja SI (2015) Exercise training improves functional walking capacity and activity level of Nigerians with chronic biventricular heart failure. Hong Kong Physiotherapy Journal 33(1): 42-9.

6. Ibrahim MH, Elmahdy MA (2014) Improvement of exercise performance and ventilator efficiency in patients with chronic heart failure after sildenafil use for 8 weeks. Egyptian Journal of Chest Diseases and Tuberculosis 63(2): 477-81.

7. Mahgoub AA, El-Medany AH, Abdulatif AS (2002) A comparison between the effects of diltiazem and isosorbide dinitrate on digoxin pharmacodynamics and kinetics in the treatment of patients with chronic ischemic heart failure. Saudi Medical Journal, 23(6):725-31.

8. Mansour S, Youssef A, Rayan M, Ayman Saleh M (2011) Efficacy of ivabradine in idiopathic dilated cardiomyopathy patients with chronic heart failure. Egyptian Heart Journal63(2):79-85.

9. Marcus RH, Raw K, Patel J, Mitha A, Sareli P (1990) Comparison of intravenous amrinone and dobutamine in congestive heart failure due to idiopathic dilated cardiomyopathy. American journal of cardiology 66(15):1107-12.

10. Nouira S, Boukef R, Bouida W, Kerkeni W, Beltaief K, Boubaker H, et al. (2011) Noninvasive pressure support ventilation and CPAP in cardiogenic pulmonary edema: a multicenter randomized study in the emergency department. Intensive care medicine, 37(2):249-56.

11. Sliwa K, Damasceno A, Davison BA, Mayosi BM, Sani MU, Ogah O, et al. (2016) Bitreatment with hydralazine/nitrates vs. placebo in Africans admitted with acute Heart Failure (BA-HEF). European Journal of Heart Failure, 18(10):1248-58.

12. Sliwa K, Norton GR, Kone N, Candy G, Kachope J, Woodiwiss AJ, et al. (2004) Impact of initiating carvedilol before angiotensin-converting enzyme inhibitor therapy on cardiac function in newly diagnosed heart failure. Journal of the American College of Cardiology, 44(9):1825-30.

13. Wisenbaugh T, Katz I, Davis J, Essop R, Skoularigis J, Middlemost S, et al. (1993) Longterm (3-month) effects of a new beta-blocker (nebivolol) on cardiac performance in dilated cardiomyopathy. Journal of the American College of Cardiology, 21(5):1094-100.

Coronary heart disease (N=7)

1. Adel M, Mansour S, Sabri NA, Badary OA, Ayman Saleh M (2016) A clinical study evaluating the effect of ivabradine on inflammation in patients with non ST-segment elevation acute coronary syndromes. International Journal of Pharmaceutical Sciences and Research, 7(4):1441-9.

2. Ahmed RM, Mohamed el HA, Ashraf M, Maithili S, Nabil F, Rami R, et al. (2013) Effect of remote ischemic preconditioning on serum troponin T level following elective percutaneous coronary intervention. Catheterization & Cardiovascular Interventions, 82(5):E647-53.

3. Coetzee A, Roussouw G, Macgregor L (1996) Failure of allopurinol to improve left ventricular stroke work after cardiopulmonary bypass surgery. Journal of cardiothoracic and vascular anesthesia, 10(5):627-33.

4. Hamza MA, Galal A, Suweilam S, Ismail M (2014) Local intracoronary eptifibatide versus mechanical aspiration in patients with acute ST-elevation myocardial infarction. International journal of vascular medicine. Available from: http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/189/CN-00995189/frame.html

5. Harilall Y, Adam JK, Biccard BM, Reddi A (2014) The effect of optimising cerebral tissue oxygen saturation on markers of neurological injury during coronary artery bypass graft surgery. Heart, Lung & Circulation, 23(1):68-74.

6. Nassar YS, Laimud M, Afify M, Shawky MA (2014) Platelet aggregation inhibition by Eptifibatide versus high dose Tirofiban during primary percutaneous interventions. Egyptian Heart Journal, 66(3): 241-50.

7. Shehata M, Fayez G, Nassar A (2015) Intensive Statin Therapy in NSTE-ACS Patients Undergoing PCI: Clinical and Biochemical Effects. Texas Heart Institute Journal, 42(6):528-36.

Pharmacotherapy for hypertension (N=76)

1. Abengowe CU (1985) A double-blind comparison of acebutolol (Sectral) and propranolol (Inderal) in the treatment of hypertension in black Nigerian patients. Journal of International Medical Research. 13(2):116-21

2. Abson CP, Levy LM, Eyherabide G (1981) Once-daily atenolol in hypertensive Zimbabwean blacks. A double-blind trial using two different doses. South African Medical Journal Suid-Afrikaanse Tydskrif Vir Geneeskunde 60(2):47-8.

3. Ahaneku JE, Agbedana OE, Taylor OG (1995) Relationship between body mass index (BMI) and changes in plasma total and HDL-cholesterol levels during treatment of hypertension in African patients. Acta Medica Okayama. 49(5):267.

4. Ajayi AA, Oyewo EA, Ladipo GO, Akinsola A (1989) Enalapril and hydrochlorothiazide in hypertensive Africans. European Journal of Clinical Pharmacology. 36(3):229-34.

5. Ajayi AA, Akintomide AO (1995) The efficacy and tolerability of amlodipine and hydrochlorothiazide in Nigerians with essential hypertension. Journal of the National Medical Association. 87(7):485-8.

6. Bosman AR, Goldberg B, McKechnie JK, Offermeier J, Oosthuizen OJ (1977) South African multicentre study of metoprolol and propranolol in essential hypertension. South African Medical Journal Suid-Afrikaanse Tydskrif Vir Geneeskunde. 51(3):57-61.

7. Cilliers AJ (1979) Atenolol as primary therapy in previously untreated hypertensives and as an adjuvant to other therapy. A South African Multicentre Study. South African Medical Journal Suid-Afrikaanse Tydskrif Vir Geneeskunde. 55(9):321-4.

8. Daniels AR, Opie LH (1987) Monotherapy with the calcium channel antagonist nisoldipine for systemic hypertension and comparison with diuretic drugs. American journal of cardiology 60(8): 703-7.

9. Dean G, Louw S, Hersch C, Kirsten HO, Brereton DN, Finnemore L, et al. (1971) A double-blind trial in hypertension comparing Baycaron (FBA 1500), hydrochlorothiazide and placebo. South African Medical Journal Suid-Afrikaanse Tydskrif Vir Geneeskunde. 45(12):323.

10. Djoumessi RN, Noubiap JJ, Kaze FF, et al. (2016) Effect of low-dose spironolactone on resistant hypertension in type 2 diabetes mellitus: a randomized controlled trial in a sub- Saharan African population. BMC Res Notes. 9:187.

11. Fadayomi MO, Akinroye KK, Ajao RO, Awosika LA (1986) Monotherapy with nifedipine for essential hypertension in adult blacks. Journal of Cardiovascular Pharmacology. 8(3):466-9.

12. Farag, SM, Rabea HM, Mahmoud HB (2018) Effect of Amlodipine/Valsartan Versus Nebivolol/Valsartan Fixed Dose Combinations on Peripheral and Central Blood Pressure. High Blood Pressure & Cardiovascular Prevention. 25:407-13.

13. Goodman C, Rosendorff C, Coull A (1985) Comparison of the antihypertensive effect of enalapril and propranolol in black South Africans. South African Medical Journal Suid-Afrikaanse Tydskrif Vir Geneeskunde. 67(17):672-6.

14. Habte B (1992) The efficacy of hydrochlorothiazide, timolol and enalapril in Ethiopians with essential hypertension. Ethiop Med J 30: 163–7.

15. Isles CG, Johnson AO, Milne FJ (1986) Slow release nifedipine and atenolol as initial treatment in blacks with malignant hypertension. British journal of clinical pharmacology 21(4): 377-83.

16. Iyalomhe GB, Omogbai EK, Isah AO, Iyalomhe OO, Dada FL, Iyalomhe SI (2013) Efficacy of initiating therapy with amlodipine and hydrochlorothiazide or their combination in hypertensive Nigerians. Clinical & Experimental Hypertension 35(8):620-7.

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