

RESEARCH ARTICLE

Implementation strategies to improve outcomes in patients with established cardiovascular disease in sub-Saharan Africa: A systematic review

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Abstract

Sub-Saharan Africa (SSA) is experiencing an epidemic of cardiovascular disease (CVD). Despite numerous evidence-based therapies and management guidelines for patients with acute or established CVD, significant gaps persist in their implementation in SSA. This systematic review aims to describe, synthesise and identify key gaps in the implementation strategies of evidence-based approaches that can improve clinical outcomes for patients with acute or established CVD in SSA. We searched four databases for studies that examined the implementation strategies of evidence-based interventions for patients with acute or established CVD in SSA. Studies that did not focus on interventions were excluded. The primary outcome was major adverse cardiovascular events including myocardial infarction, stroke, cardiovascular death or hospitalisation. Secondary outcomes included adherence to treatment, improvement in modifiable risk factors, symptom measures, treatment complications, and psychosocial metrics, particularly those related to quality of life. Nineteen studies met the inclusion criteria (nine evaluated patients with heart failure, three evaluated heart failure or ischaemic heart disease, three evaluated ischaemic heart disease, and four evaluated stroke). Of the 19 studies, 14 were targeted at healthcare recipients, two at healthcare workers and three at the healthcare organisation. The most common interventions evaluated were in the field of cardiac rehabilitation. Only three studies (two evaluating stroke and one heart failure) implemented an intervention in the acute setting with the rest evaluating strategies at discharge or in the ambulatory population. No studies evaluated implementation strategies in hospitalised patients with ischaemic heart disease. This study highlights significant gaps in the implementation of interventions in patients



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with established cardiovascular disease. Gaps were highlighted in the acute care setting, specifically related to cardiac pathologies and implementation strategies targeting pharmacotherapeutic optimisations. We also highlight a notable lack of studies focusing on effective implementation strategies in primary care facilities and lower-level hospital settings.

SYSTEMATIC REVIEW REGISTRATION

The protocol was registered in PROSPERO prior to the study implementation (ID: CRD42023465781). The protocol can be accessed at crd.york.ac.uk/PROSPERO/ display_record.php?RecordID=465781

Introduction

Sub-Saharan Africa (SSA) is experiencing an epidemic of cardiovascular disease (CVD) [1]. Stroke, heart failure and ischaemic heart disease, the predominant pathologies constituting CVD, now make up an increasing proportion of acute admissions to hospitals in SSA [2–4]. Despite being nearly a decade younger, short and long-term outcomes following acute cardiovascular events are worse across patients in SSA when compared to high-income countries [5–7]. Individuals with acute or established CVD (stroke, heart failure or ischaemic heart disease) suffer from poorer outcomes and significant economic impact making their effective management a public health priority [8–10]. The NCD Countdown 2030 Health Policy paper identifies the management of patients with acute or established cardiovascular disease as crucial interventions. These are prioritized to achieve the United Nations Sustainable Development Goal target 3.4, aiming to reduce premature mortality from non-communicable diseases by a third [11].

Management of acute and established CVD consists of both pharmacological and non-pharmacological (for example dietary changes, physical activity, lifestyle management and cardiac rehabilitation) approaches to mitigate future cardiovascular morbidity and mortality and maximise the function and quality of life of individuals [12,13]. Despite extensive evidence-based guidance for managing patients with acute or established CVD, significant gaps persist in their implementation in SSA. In particular, prescription of and adherence to proven treatments following cardiovascular events are suboptimal in SSA [5,6,14], and much lower than other regions of the world [15,16].

Although research evaluating strategies to improve implementation of evidence-based interventions for primary prevention of cardiovascular disease in SSA has been increasing, similar research for managing patients with established CVD remains limited [17–19]. This systematic review aims to describe, synthesise, and identify key gaps in the implementation strategies of evidence-based pharma-cological and non-pharmacological approaches that improve clinical outcomes for patients with acute or established CVD in SSA.



Methods

Data sources and search strategy

The study was reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (<u>S1 Checklist</u>) [20]. We searched MEDLINE, EMBASE, Global Health, and Google Scholar for studies that examined the implementation strategies of evidence-based approaches for patients with acute or established CVD in SSA. We manually searched bibliographic references of key papers. Our search strategy utilised the keywords: "cardiovascular disease", "prevention interventions", and "Sub-Saharan Africa". We included studies of any design, in any language, published from database inception up to the 31st of December 2023. The full search criteria are provided in <u>S1</u> <u>Text</u>. The protocol was registered in PROSPERO prior to the study implementation (ID: CRD42023465781).

Eligibility criteria

We included studies reporting on interventions for managing acute or established CVD among adults (>=18 years) in the SSA region. Cardiovascular disease was restricted to the following pathologies: stroke, heart failure or ischaemic heart disease. Clinical trials, non-randomised clinical studies, pre- and post-intervention studies, case-control studies, and cross-sectional studies were eligible for inclusion. We did not impose restrictions based on specific definitions or diagnostic criteria of cardiovascular diseases to ensure inclusion of studies that may not have explicitly detailed their criteria. Studies that did not evaluate implementation of interventions were excluded alongside those studies that solely evaluated interventions targeted at primary prevention of cardiovascular disease.

Outcome

The primary outcome was major adverse cardiovascular events, which included recurrent myocardial infarction, stroke, cardiovascular death, and hospitalisation due to heart failure or other cardiovascular causes. Given the expected heterogeneity of studies and diverse outcomes, secondary outcomes were also assessed. These included adherence to treatment, improvement in modifiable risk factors, hospitalizations, symptom measures, treatment complications, and psychosocial metrics, particularly those related to quality of life.

Study selection

Two reviewers (LAS & JAH) independently screened and assessed studies for eligibility based on the inclusion and exclusion criteria. Conflicts were resolved through consensus or consultation with a third reviewer (ASVS). Data, including study characteristics and baseline population details, were extracted by one investigator (LAS) and verified by another (JAH). All studies identified were imported to Rayyan [21], an internet-based program that facilitates collaboration between investigators during the screening and selection of studies to be finally included in the review. Duplicates were removed.

Evidence synthesis and risk of bias

A narrative synthesis was conducted to provide an overview of the findings from the included studies, focusing on the type and effectiveness of implementation strategies to improve outcomes in patients with CVD in SSA. We categorised the implementation strategies based on the target actor being the healthcare recipient, healthcare worker or the healthcare organisation as defined by the Cochrane Effective Practice and Organisation of Care Group [17,22].

We evaluated the reporting and methodological quality of the included studies using the Evidence project risk of bias tool [23]. We specifically chose this risk of bias tool as it encompassed both randomised and non-randomised intervention studies. This tool awards one point for each of the following eight items: (1) prospective cohort; (2) control or comparison group; (3) pre/post intervention data; (4) random assignment of participants to the intervention; (5) random selection of



subjects for assessment; (6) follow-up rate of 80% or more; (7) comparison groups equivalent on socio-demographic measures; and (8) comparison groups equivalent at baseline on outcome measures.

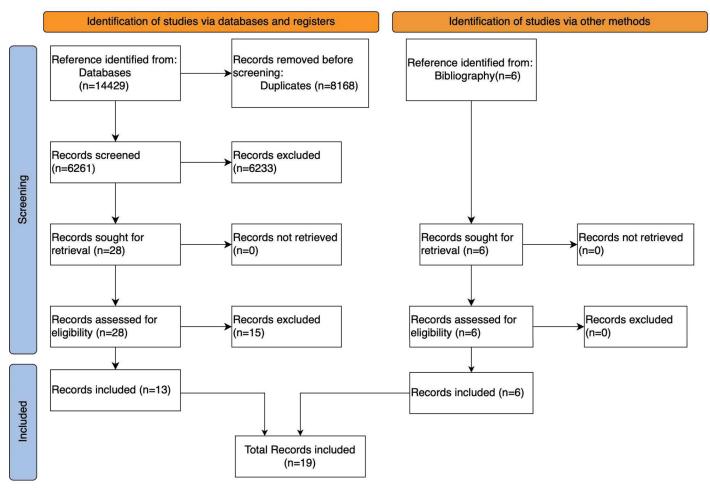
Results

Review of search results

The search yielded 14,435 results, and six additional studies were identified from bibliographic references giving a total of 14,435 studies reviewed. After screening, 34 studies were read in detail to assess eligibility. Of these, 19 met the inclusion criteria and were included in the final analysis (Fig 1 and S1 Table). This included six studies identified via the bibliographic search. We did not find any studies that required translation to English.

Characteristics of the studies included

Geographical distribution. Out of the 19 studies included, one study (5.3%) was international, encompassing three SSA countries (South Africa, Mozambique and Nigeria) [24]. The remaining studies were conducted in single countries as follows: five studies (26.3%) in South Africa [25–29], four (21%) in Nigeria [30–33], two (10.5%) in Ghana [34,35]





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and Ethiopia [<u>36,37</u>], one (5.3%) in Uganda [<u>38</u>], Sudan [<u>39</u>], Rwanda [<u>40</u>], Kenya [<u>41</u>] and Benin [<u>42</u>] (<u>Table 1</u> & <u>Fig 2</u>). Studies included in this review represented 10 (20%) of the 49 countries in the SSA region.

Study setting and population

All studies recruited participants from either hospital outpatient or inpatient medical facilities, with none conducted in community settings. Four studies (21.1%) included participants with stroke [26,30,34,38]; nine (47.4%) with heart failure [24,31-33,35-37,39,40]; three (15.8%) with ischaemic heart disease [25,27,28]; and three (15.8%) with ischaemic heart disease or heart failure [29,41,42] (Table 1). A total of 4,397 participants were included, with individual study sizes ranging from 18 to 1,078 participants. The mean age was reported in 14 studies and ranged from 43 to 69 years. The proportion by sex was reported across 15 studies and female sex ranged from 5.5% to 68.4%. Out of 19 studies, five (26.3%) were individual participant level randomised controlled trials [24,30-33], two were cluster randomised trials [34,37], three were non-randomised clinical studies [27,38,41], eight were pre-post intervention studies and one was a retrospective study [25,26,28,29,35,36,39,42].

Only three studies (one evaluating heart failure [24] and two evaluating stroke [26,38]) recruited participants in the acute setting with the remaining involving patients post discharge or community ambulatory patients. Eleven studies (57.9%) were conducted in either tertiary or teaching hospitals [31-39,41,42], one study (5.3%) was conducted across teaching and district-level hospitals [30] and four studies were conducted in rehabilitation centres [25,27-29]. Only one study (5.3%) was specifically conducted in a rural setting [40], and two studies (10.5%) did not report the healthcare facility level [24,26].

Study quality

The assessment of the quality of studies is summarised in <u>Table 2</u>. Of the 19 studies which were included, five were individual participant level randomised controlled trials [24,30-33]; two were cluster randomised trials [34,37]; three were non-randomised clinical studies [27,38,41]; eight were pre-post intervention studies [25,26,28,29,35,36,39,42]; and one was a retrospective study [40].

All but four studies scored 3–5 out of eight in the quality assessment. One study [40] scored 1 out of 8 and three studies [24,30,34] scored 7 out of 8. The three studies which scored 7 were all randomized controlled trials. Two of these studies [24,30,34] did not mask both the participants and investigators to treatment allocation. Five studies [25,26,28,29,39] did not report on attrition and one study [33] had follow-up rate of less than 80% (Table 2).

Types of studies

Across all three cardiovascular pathologies, implementation strategies were targeted at different levels. Of the 19 studies, 14 were targeted at healthcare recipients [25,27-29,31-37,39,41,42], two at healthcare workers [24,40] and three at the healthcare organisation [26,30,38] (Table 3). Most of the heart failure and ischaemic heart studies evaluated interventions targeted at healthcare recipients. Conversely of the four stroke studies, three [26,30,38] evaluated an intervention targeted at the healthcare organisation. Fourteen of the 19 studies evaluated non-pharmacological interventions [25-34,37,38,41,42] with the remaining five implementing an intervention with a pharmacological component [24,35,36,39,40]. All studies evaluating an intervention with a pharmacological component were targeted at populations with heart failure (Table 3).

Five studies, all evaluating heart failure care, tested the role of task sharing with nurse- or pharmacy-led care delivery $[\underline{35}-\underline{37},\underline{39},\underline{40}]$. Two studies, both evaluating stroke, tested the role of mobile health $[\underline{30},\underline{34}]$. Twelve studies evaluated care models $[\underline{24}-\underline{29},\underline{31}-\underline{33},\underline{38},\underline{41},\underline{42}]$. Of these, nine were specific to cardiac rehabilitation in the context of heart failure or ischaemic heart disease $[\underline{25},\underline{27}-\underline{29},\underline{31}-\underline{33},\underline{41},\underline{42}]$. The remaining three studies evaluated patients in the acute setting with



Table 1. Baseline characteristics of included studies.

Author, Year, Country	Design and setting	Population	Intervention	Comparator	Sam- ple size	Mean age (years)	Female (%)	Outcome measure(s)	Measure- ment time points	Effects of the intervention
Heart Failu	ire									
Anane et al, 2013 [<u>35];</u> Ghana	Pre-post inter- vention study; Teach- ing hospital	Adult discharged with HF	Pharmacist led counselling sessions involving education on medical risk manage- ment, health behaviour change, and medica- tion compliance.	No	583	NR	NR	Functional improve- ment; all-cause mor- tality and all cause re- hospitalization	6 months	New York Heart Asso- ciation class improved before and after intervention.
Eberly et al, 2019 [<u>40];</u> Rwanda	Retro- spective cohort; Rural district level hospital	Adult discharged with HF	Nurses-led delivery care model for heart failure management with monthly supervi- sion from cardiologist.	NR	719	NR	72	All-cause mortality	5 years	Improvement in 5-year mortality over time: 38.8% in the first 5-year period (2006–2011) and 27.1% in the second 5-year period (2012–2017)
Wondesen A et al, 2022 [<u>36</u>]; Ethiopia	Pre-post inter- vention study; Tertiary care hospital	Ambula- tory adults with HF	Pharmacist and nurse led care providing infor- mation and educational material on self-care, physical activity, and medication adherence. Pharmacists identified and resolved drug therapy problems.	No	412	45	54	a) Drug therapy prob- lem (adverse drug reactions, unneces- sary drug therapy, need for additional drug therapy, dosage review); b) Medication adherence; and c) Treatment satisfaction	6 months	Reduced drug therapy prob- lems, improved medication adherence, and increased treatment satisfaction.
Ahmed et al., 2021 [<u>39];</u> Sudan	Pre-post inter- vention study; Tertiary care hospital	Ambula- tory adults with HF	Pharmacist led management of heart failure including initiation, up titration, and changes between drug classes.	No	110	56	43	Achievement of target doses for heart failure pharmacotherapy	6 months	Improvement in the propor- tion of patients achieving target doses of guide- line directed medical therapy and improve- ment in LVEF.
Dessie et al., 2021 [<u>37];</u> Ethiopia	Cluster random- ized control trial; Tertiary care hospital	Ambula- tory adults with HF	Nurse led heart failure self-care educational program comprising of intensive four-day training followed by one-day sessions offered every four months.	Yes, Control group received usual care	219	NR	48 (inter- vention) and 68 (control)	Hear failure self-care adherence measured	Baseline, 4, 8 and 12 months	Higher self-care adherence scores observed in the inter- vention group after two and three rounds of educational sessions.
Mebazaa et al., 2022 [24]; Mozam- bique, Nigeria, South Africa	Ran- domised con- trolled trial; Setting not reported	Adults with acute HF not on optimal medical therapy.	Risk stratification and post-discharge care based of optimisa- tion of heart failure therapies and in vitro diagnostics	Yes, Control group received usual care	1078	63	39	Heart failure read- mission or all cause death	180 days	Reduction in heart failure readmission or all cause death (15.2% vs. 23.3%, RRR 0.66 [95%CI 0.5 to 0.86], p=0.0021)

(Continued)



Table 1. (Continued)

Author, Year, Country	Design and setting	Population	Intervention	Comparator	Sam- ple size	Mean age (years)	Female (%)	Outcome measure(s)	Measure- ment time points	Effects of the intervention
Ajiboye et al, 2015 [<u>33];</u> Nigeria	Ran- domized con- trolled trial; Teach- ing hospital	Ambulatory adults with HF	Supervised exercise training including a combination of aerobic and resistance exer- cises, performed three times a week for 12 weeks.	Yes, Control group received usual care	51	54	NR	Functional improvement	12 weeks	Improvement in functional status, haemodynam- ics and body mass index in the intervention group compared to the control group
Awotidebe et al., 2016 [<u>31];</u> Nigeria	Ran- domized con- trolled trial; Teach- ing hospital	Ambula- tory adults with HF	Supervised cardiac rehabilitation exer- cises that included both aerobic and resistance exercises that increased in intensity weekly.	Yes, Control group randomly assigned to usual phar- macological care	70	69 (inter- vention) and 64 (control)	49 (inter- vention) and 60 control	Functional improvement	8 weeks	Improvements in functional sta- tus using activ- ity of daily living questionnaire in the inter- vention group compared to the control group
Ajiboye et al., 2013 [<u>32];</u> Nigeria	Ran- domized con- trolled trial; Teaching hospital	Ambula- tory adults with HF	Supervised cardiac rehabilitation including a combination of aerobic and resistance exercises	Yes, Control group received edu- cation and counselling sessions but not exercise training	38	54	47	Haemodynamics	12 weeks	Improvement in haemody- namics and respiratory parameters
	re/ Ischae	mic heart dis			1	1	1	1		1
Ngeno et al., 2022 [<u>41];</u> Kenya	Nonran- domised clinical study; Teach- ing hospital	Ambula- tory adults with HF including those with cardiac ischaemia	Non randomly enrolled to institution-based supervised cardiac rehabilitation, home based cardiac rehabil- itation or an observa- tion group.	Yes, enrolled to observation arm/control group	100	51	28	Protocol adherence along with functional improvement	1 month	Higher protocol adherence observed in the institution-based rehabilitation group. All three arms showed improvement in functional status.
Digenio A.G et al., 1996 [29]; South Africa	Pre-post inter- vention study; Reha- bilitation Centre	Patients discharged following an acute myocardial infarction and docu- mented left ventricular impairment	Medically supervised exercise training programme	No	28	64	NR	Haemodynamics, left ventricular function and effort tolerance	6 months	Improvement in exercise capacity. No change in left ventricular function at rest or during exercise.
Kpadonou et al, 2013 [42]; Benin	Pre-post inter- vention study; Teach- ing hospital	Ambulatory patients diagnosed with HF, coronary disease, or hyperten- sion.	Institution based supervised exercise training	No	27	46 (Cor- onary dis- ease); 43 (HF); 43 (Hyper- tension)	26	Haemodynamics	10 weeks	Improvement in haemody- namics



Table 1. (Continued)

Author, Year, Country	Design and setting	Population	Intervention	Comparator	Sam- ple size	Mean age (years)	Female (%)	Outcome measure(s)	Measure- ment time points	Effects of the intervention
lschaemic	heart dise	ase								
van Rooy & Y Coopoo, 2017 [25]; South Africa	Pre-post inter- vention study; Reha- bilitation Centre	Ambu- latory patients who had undergone coronary artery bypass grafting	Supervised Indi- vidualized exercise programmes and provision of lifestyle manual	No	18	NR	6	Cardiovascular disease risk; change in lifestyle habits, nutrition knowledge and physical activity profile	12 weeks	The interven- tion reduced all evaluated indices of cardiovascular disease risk and increased physical activ- ity levels
Morris et al., 1993 [<u>28];</u> South Africa	Pre-post inter- vention study; Reha- bilitation Centre	Ambu- latory patients with ischaemic heart disease	Cardiac rehabili- tation programme consisting of aerobic exercise sessions and advice on lifestyle modification.	No	108	57	12	Change in lipid profile and exercise capacity	6 months	Improvement in exercise capacity and lipid profile fol- lowing cardiac rehabilitation
Joughin et al., 1999 [27]; South Africa	Non ran- domised clinical study; Reha- bilitation Centre	Ambu- latory patients with coro- nary heart disease	Endurance training including combination of walking and jogging on a measured out- door circuit or cycling on a stationary ergom- eter. Compliers allo- cated to intervention group were compared to non- compliers/ dropouts allocated to control group	Yes, Patient dropping out of cardiac rehabil- itation assigned to control group.	111	57 (inter- ven- tion); 59 (control)	9 (inter- ven- tion); 6 (control)	Haemodynamics and exertional tolerance	6month and 18month after inter- vention	Improvement in haemodynam- ics and exer- cise capacity.
Stroke										
Nakibuuka et al., 2016 [<u>38];</u> Uganda	Non ran- domised clinical study; Tertiary care hospital	Hospi- talised patients with stroke	Stroke care bundle including rapid initial stroke screening; brain imaging; bedside swallow evaluation; aspirin administration; physiological monitor- ing and management; and early rehabilitation	Yes, control group received usual care	254	NR	NR	Mortality and func- tional improvement	30 days post stroke	No improve- ment in mortality rates or functional outcomes following implementation of stroke care bundle.
Sarfo et al., 2019 [<u>34</u>]; Ghana	Cluster random- ized con- trolled trial; Teach- ing hospital	Ambu- latory patients with recent stroke and uncon- trolled hyperten- sion	Mobile health nurse guided intensive home blood pressure monitoring with the use of bluetooth blood pressure device and smartphone.	Yes, Ran- domized control selection, unmasked, control received text message on healthy lifestyle behaviour but not medication adherence	60	54 (inter- ven- tion); 56 (control)	40 (inter- ven- tion); 30 (control)	Blood pressure control	9 months	Study showed feasibility and signal of improvement in blood pressure control.

(Continued)



Table 1. (Continued)

Author, Year, Country	Design and setting	Population	Intervention	Comparator	Sam- ple size	Mean age (years)	Female (%)	Outcome measure(s)	Measure- ment time points	Effects of the intervention
Owolabi et al., 2019 [<u>30];</u> Nigeria	Ran- domized con- trolled trial; Teach- ing and district hospitals	Ambu- latory patients with recent stroke within the last year.	Chronic care model components of care delivery system rede- sign (follow-up visits and pre-appointment phone texts); self- management support; and clinical information systems (e.g., hospital registry).	Yes, Controls received usual care with name and contact information of a phone contact	400	57	37	Blood pressure control	12 months	No significant difference in systolic blood pressure reduction between the two groups.
De Villiers et al., 2009 [26]; South Africa	Pre-post inter- vention study; Hospital setting	Hospi- talised patients with a clinical diagnosis of stroke	Stroke unit imple- mentation delivering multidisciplinary stroke care includ- ing a) stroke treat- ment guidelines and b) twice weekly stroke ward rounds with allied health professionals	No	195	59	60	a) Length of hospital stay; b) in-hospital mortality; c) transfer to referral hospital; d) number of patients who had CT brain scans performed	3 months pre- and post- inter- vention	Decrease in-hospital mortality (33% to 16%) and increase in hospital stay from 5 to 7 days; increase in referral to inpatient rehabilitation (5% to 19%). No increase in number of CT brain scans and number of refer- rals to tertiary facility

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two evaluating care models in stroke [26,38]; one in heart failure [24] and one evaluating multidisciplinary medical models in stroke [30]. These studies are discussed in detail, by cardiovascular pathology, below.

Heart failure

Twelve studies recruited patients with heart failure. Among these, nine studies (75%) specifically recruited patients with heart failure [24,31-33,35-37,39,40] and three studies included patients with heart failure or ischaemic heart disease [29,41,42]. Only one study [24] targeted care delivery of acute heart failure, with the remaining designed to improve care for recently discharged or ambulatory patients with heart failure. Ten of the 12 studies (83%) targeted an intervention at the healthcare recipient [29,31-33,35-37,39,41,42], two targeted the healthcare worker [24,40] and none targeted the healthcare organisation. Of the healthcare recipient targeted interventions, three addressed medication compliance and up-titration in chronic heart failure pharmacotherapy [35,36,39]. These included pharmacy and nurse-led interventions to target appropriate up-titration and ensure compliance of guideline directed medical therapy in ambulatory patients [35,36,39]. These studies showed either improved adherence or treatment satisfaction alongside an increase in the proportion of patients receiving goal directed medical therapy. One of these studies provided medical counselling to hospitalised patients with heart failure in Ghana, showing better clinical outcomes at 6 month follow up [35].

Implementation of supervised cardiac rehabilitation care models was the focus of six studies [29,31–33,41,42] with five implementing institution-based exercise programmes [29,31–33,42] and one study from Kenya [41] comparing home-based with institution-based cardiac rehabilitation. All six studies reported improvements across a variety of physiological



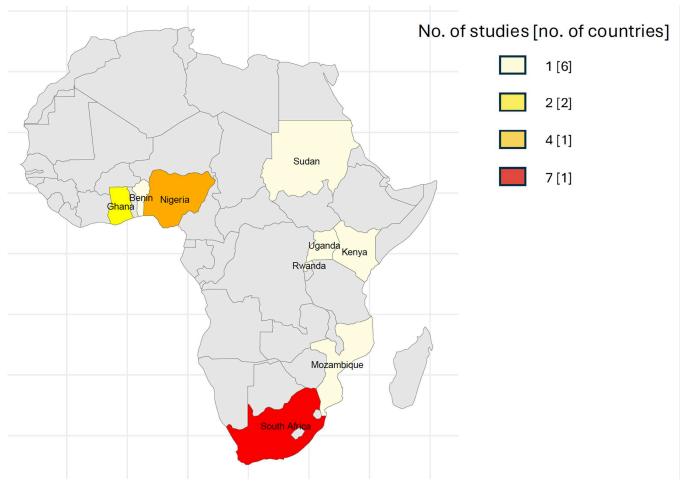


Fig 2. Cartogram highlighting countries contributing studies to this systematic review. The colours illustrate the numerical scale for the number of studies. The colour box in the legend summarises the number of studies with the number in the squared brackets summarising the number of countries. Figure created in R Version 4.4.0 using the rnaturalearth package. Source of base map is from natural earth available at <u>http://www.naturalearthdata.</u> com/about/terms-of-use/ (accessed 8th April 2025).

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measures. Educational interventions were also prominent, with three of the interventions targeted at healthcare recipients, providing education about heart failure and support health-promoting behaviours [<u>35–37</u>].

STRONG-HF, a large multinational randomised controlled trial recruited heart failure patients in South Africa, Mozambique, and Nigeria. The study implemented a care model which incorporated an intensive follow-up regimen post discharge for patients who had been admitted with acute heart failure [24]. The regimen was based on risk-stratification using circulating biomarkers of cardiac remodelling, and showed a significant improvement in a composite of all-cause mortality and heart failure rehospitalization.

Stroke

Studies recruiting patients with stroke evaluated implementation strategies in both the inpatient [26,38] and outpatient hospital settings [30,34]. In the inpatient setting, two studies implemented structured stroke care. De Villiers *et al.* established a multi-disciplinary stroke unit within the medical ward engaging allied healthcare professionals and



Table 2. Quality assessment of included studies.

Reference and country	Design	cohort	control or com- parison group	pre/post inter- vention data	random assignment of partici- pants to the intervention	random selection of partici- pants for assessment	follow up rate of>80%	compari- son groups equivalent on sociode- mographic	comparison groups equiva- lent at baseline on outcome measures	Score
Nakibuuka et al. 2016 [<u>38]</u> ; Uganda	Nonran- domised clinical study	yes	yes	na	no	yes	yes	yes	na	5
Ahmed et al. 2021 [39]; Sudan	Pre-post intervention study	yes	no	yes	no	no	nr	na	na	2
Wondesen A et al 2022 [<u>36];</u> Ethiopia	Pre-post intervention study	yes	no	yes	yes	yes	yes	yes	na	6
Dessie et al 2021 [37]; Ethiopia	Cluster randomised control trial	yes	yes	yes	yes	no	yes	no	yes	6
Sarfo et al 2019 [<u>34];</u> Ghana	Cluster randomised control trial	yes	yes	yes	yes	no	yes	yes	yes	7
Anane et al 2013 [<u>35</u>]; Ghana	Pre-post intervention study	yes	no	yes	no	no	yes	na	na	3
Ngeno et al 2022 [41]; Kenya	Nonran- domised clinical study	yes	yes	no	no	no	yes	no	no	3
Eberly et al 2019 [40]; Rwanda	Retro- spective review of intervention	yes	na	no	na	no	na	nr	nr	1
Ajiboye et al 2015 [<u>33];</u> Nigeria	Ran- domised controlled trial	yes	yes	no	yes	no	no	yes	yes	5
Owolabi et al 2019 [30]; Nigeria	Ran- domised controlled trial	yes	yes	yes	yes	no	yes	yes	yes	7
de Villiers et al 2009 [<u>26];</u> South Africa	Pre-post intervention study	yes	no	yes	no	no	nr	no	nr	2
Van Rooy & Y Coopoo 2017 [25]; South Africa	Pre-post intervention study	yes	no	yes	no	no	nr	na	na	2
Awotidebe et al. 2016 [<u>31];</u> Nigeria	Ran- domised controlled trial	yes	yes	no	yes	no	yes	no	yes	5
Ajiboye et al 2013 [32]; Nigeria	Ran- domised controlled trial	yes	yes	no	yes	no	yes	yes	yes	6

(Continued)



Table 2. (Continued)

Reference and country	Design	cohort	control or com- parison group	pre/post inter- vention data	random assignment of partici- pants to the intervention	random selection of partici- pants for assessment	follow up rate of>80%	compari- son groups equivalent on sociode- mographic	comparison groups equiva- lent at baseline on outcome measures	Score
Kpadonou et al 2013 [42]; Benin	Pre-post intervention study	yes	no	yes	no	no	yes	na	na	2
Joughin et al 1999 [27]; South Africa	Non ran- domised clinical study	yes	yes	yes	no	no	yes	no	no	4
Digenio et al 1996 [29]; South Africa	Pre-post intervention study	yes	no	yes	no	no	nr	na	na	2
Morris et al 1993 [28]; South Africa	Pre-post intervention study	yes	no	yes	no	no	nr	na	na	2
Mebazaa et al 2022 [24]; Mozambique, Nigeria, South Africa	Ran- domised controlled trial	yes	yes	yes	yes	no	yes	yes	yes	7

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creating protocols to enhance stroke care [26]. This approach reduced inpatient mortality and increased referrals to rehabilitation centres. Conversely, Nakibuuka *et al.* implemented a stroke care bundle at a tertiary hospital in Uganda for acute stroke patients [38]. A formal acute stroke care pathway was implemented which included haemodynamic and glycaemic monitoring; brain imaging; and administration of pharmacotherapy. Funds were made available to implement the care pathway. Importantly, the acute care pathway was implemented for a period of 72 hours, followed by usual care. However, the study did not show any improvement in patient mortality following implementation. This may reflect differences in patient characteristics including greater stroke severity in patients enrolled during the intervention phase.

In the outpatient setting, two studies attempted to improve blood pressure control in stroke survivors [30,34]. The PINGS trials [34] implemented nurse-guided intensive home blood pressure monitoring facilitated by a smartphone application, while the THRIVES trial [30] employed text-message reminders, tailored disease self-management report cards, and educational videos. Both these interventions showed feasibility. The THRIVES trial did not demonstrate a significant improvement in blood pressure control, whilst the PINGS feasibility study did show a signal towards improved blood pressure control.

Ischaemic heart disease

Three studies [25,27,28] solely evaluated patients with ischaemic heart disease. All studies looked at cardiac rehabilitation care models and originated from South Africa, showing an improvement in haemodynamics and parameters of exertional tolerance. Our systematic review did not find any studies evaluating care models for patients with ischaemic heart disease in the acute setting including those presenting with acute coronary syndrome.

Discussion

Our systematic review summarises the body of literature evaluating implementation strategies of evidence-based interventions for management of patients with CVD in SSA. We identified 19, of which five were individual participant level



Author, Year, Country	Intervention type	Intervention strategy target
Heart Failure		
Anane et al, 2013 [<u>35</u>]; Ghana	Pharmacological and non-pharmacological	Healthcare recipients
Eberly et al, 2019 [40]; Rwanda	Pharmacological and non-pharmacological	Healthcare recipients and workers
Wondesen A et al, 2022 [36]; Ethiopia	Pharmacological and non-pharmacological	Healthcare recipients
Ahmed et al., 2021 [<u>39</u>]; Sudan	Pharmacological and non-pharmacological	Healthcare recipients
Dessie et al., 2021 [<u>37</u>]; Ethiopia	Non-pharmacological	Healthcare recipients
Mebazaa et al., 2022 [24]; Mozambique, Nigeria, South Africa	Pharmacological	Healthcare workers
Ajiboye et al, 2015 [33]; Nigeria	Non-pharmacological	Healthcare recipients
Awotidebe et al., 2016 [31]; Nigeria	Non-pharmacological	Healthcare recipients
Ajiboye et al., 2013 [32]; Nigeria	Non-pharmacological	Healthcare recipients
Heart failure/ Ischaemic heart disease		
Ngeno et al., 2022 [41]; Kenya	Non-pharmacological	Healthcare recipients
Digenio A.G et al., 1996 [29]; South Africa	Non-pharmacological	Healthcare recipients
Kpadonou et al, 2013 [42]; Benin	Non-pharmacological	Healthcare recipients
Ischaemic heart disease		
van Rooy & Y Coopoo, 2017 [25]; South Africa	Non-pharmacological	Healthcare recipients
Morris et al., 1993 [28]; South Africa	Non-pharmacological	Healthcare recipients
Joughin et al., 1999 [27]; South Africa	Non-pharmacological	Healthcare recipients
Stroke		
Nakibuuka et al., 2016 [38]; Uganda	Non-pharmacological	Healthcare organisation
Sarfo et al., 2019 [34]; Ghana	Non-pharmacological	Healthcare recipients
Owolabi et al., 2019 [30]; Nigeria	Non-pharmacological	Healthcare organisation
De Villiers et al., 2009 [26]; South Africa	Non-pharmacological	Healthcare organisation

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randomised controlled trials [24,30-33]; two were cluster randomised trials [34,37]; three were non-randomised clinical studies [27,38,41]; eight were pre-post intervention studies [25,26,28,29,35,36,39,42]; and one was a retrospective study [40]. Of the seven randomised trials, four evaluated cardiac rehabilitation care models in the context of heart failure, showing improvements in exertional tolerance or cardiac haemodynamics [31-33,37]. Mebazaa et al showed a significant reduction in hospitalisation and mortality, following randomisation to biomarker-guided post discharge care [24]. The remaining two randomised trials [30,34] were in patients with stroke using text messages to improve blood pressure control. Both showed feasibility with one study showing a signal towards better blood pressure control. Of the eight prepost intervention studies, four were based on cardiac rehabilitation in patients with heart failure or ischemic heart disease [25,28,29,42]. Similar to randomised trials [31-33,37], the majority of these showed improvement in exertional tolerance or haemodynamics. Two pre-post intervention studies were pharmacist led, showing improved medical adherence and target drug dose achievement [36,39].

Several important observations emerge from our review. First, most studies did not focus on patients in the acute or peri-discharge period. This is important, as the highest risk of morbidity and mortality is experienced by patients during this period, either as inpatients or shortly after discharge [43]. Second, studies specifically targeting implementation strategies of pharmacotherapy, diagnostic tools, multi-disciplinary teams or risk stratification approaches in the acute



setting were scarce; we found only one study for acute heart failure and two for stroke. We found none evaluating patients with acute coronary syndrome. Third, only three studies [26,30,40] recruited patients from non-teaching or non-tertiary care settings. This finding has particular relevance to the region, given that nearly 6 out 10 people in SSA do not reside in urban regions [44]. The applicability of study findings from urban settings to rural ones will further be hindered given differences in health infrastructure, healthcare provider expertise and availability of CVD care at lower-level healthcare facilities. Fourth, the studies that we identified only covered 10 of the 49 countries in the SSA. This limits generalizability of our study findings to the SSA region and further demonstrate substantial evidence gaps in CVD care implementation in the region. Finally, it was encouraging to observe that many studies did evaluate the implementation of cardiovascular rehabilitation programmes, an area that is generally given less importance.

Despite SSA bearing a significant and increasing global burden of CVD, its populations remain underrepresented in both evidence generation and implementation. The prognosis following acute cardiac pathologies in SSA remains unacceptably poor, with a quarter of all adult hospitalizations in certain countries being cardiovascular-related. Despite being a decade younger on average compared to high-income countries, cardiac patients in SSA experience up to 3-fold higher short-term case fatality rates (30% vs. 9%) [9,45]. Annually, low and middle-income countries witness an estimated 16 million excess deaths, with over a third attributed to CVD. Approximately 4.5 million of these deaths occur in the African region, predominantly due to inadequate secondary care health systems [46]. These deficiencies contribute as significantly to excess deaths as immature primary care systems in Africa. The high mortality, at least in part, may be exacerbated by poor links between different levels of care. Furthermore, despite the high burden of CVD and poor outcomes, research funding for the discipline has been disproportionately low.

Provision of appropriate pharmacotherapy across SSA patients with established CVD remains poor. Across SSA, only 1 in 10 patients with established CVD use aspirin [16], and less than 50% of heart failure patients receive appropriate management in Kenya [47]. Low uptake of appropriate pharmacotherapeutic and non-pharmacotherapeutic approaches across patients in SSA with established CVD is likely to be due to inadequacies across several implementation strategic domains [48]. These implementation strategies specifically tackle the 'how to' component for delivering optimal clinical care with recent guidance published on defining and operationalising these strategies [17,18]. These guidelines should be considered by implementation researchers and stakeholders aiming to improve care in patients with acute or established CVD in SSA.

The lack of published literature, especially in the acute cardiovascular care setting, may reflect the current funding priorities in global cardiovascular health. For example, from 2017-2024, UK funding bodies, like the NIHR, allocated over £370 million in healthcare research, with less than 1% (~£2 million) directed towards management of patients with acute or established CVD compared to £40 million for primary cardiovascular care [49]. The mismatch between disease burden due to established cardiovascular disease and research funding underscores the importance of further research in the area. Efforts now need to concentrate on the optimal approaches in implementing evidence-based therapy for the three core cardiovascular pathologies. These efforts need to be contextualised to the settings, considering the differing health-care infrastructure both within and between countries across the African continent.

Several limitations of our work should be considered. The literature search was confined to four databases and excluded grey literature, potentially omitting relevant unpublished studies. Furthermore, our focus was restricted to specific cardiovascular pathologies, namely stroke, heart failure and ischaemic heart disease. Whilst these pathologies constitute most of CVD, our review does not shed any light on gaps in the implementation strategies of other prevalent CVD such as peripheral vascular disease.

Recommendations

Our review highlights several areas where the findings from implementation studies may improve outcomes in patients with acute or established CVD and point towards areas of further research. There is relatively strong evidence for



implementation of cardiac rehabilitation programmes, particularly in the context of heart failure and ischaemic heart disease. Implementation of these programmes, if contextualised to rural settings, can improve functional and clinical outcomes. Our evidence synthesis highlights that the implementation of acute care bundles has mainly been tested in the field of stroke medicine. Urgent evidence is now needed in the acute cardiovascular setting, particularly in the context of diagnosing and treating acute heart failure and acute coronary syndrome.

Conclusion

This evidence synthesis highlights significant gaps in the implementation strategies for managing acute or established CVD in SSA. Particular gaps were highlighted in the acute care setting, specifically related to acute coronary syndrome and implementation strategies targeting pharmacotherapeutic optimizations. We also highlight a notable lack of studies focusing on effective implementation strategies in primary care facilities and lower-level hospital settings.

Supporting information

S1 Checklist. PRISMA checklist for the systematic review. (DOCX)

S1 Table. Details of the search criteria stratified by database. (XLSX)

S1 Text. List of hits from the initial abstract and title screening alongside list of full papers reviewed and selected for the systematic review.

(DOCX)

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