# **BMJ Open** Tertiary prevention interventions for patients with stroke in African countries: a systematic review

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#### ABSTRACT

**To cite:** Adam L, Unverzagt S, Ngeh E, *et al.* Tertiary prevention interventions for patients with stroke in African countries: a systematic review. *BMJ Open* 2025;**15**:e080585. doi:10.1136/ bmjopen-2023-080585

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (https://doi.org/10.1136/ bmjopen-2023-080585).

Received 10 October 2023 Accepted 16 May 2025



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Lucas Adam; Lucas.adam@uk-halle.de **Objectives** To summarise the best available evidence on tertiary prevention interventions for patients with stroke conducted in African countries, identify the gaps in stroke prevention research and augment efforts to establish stroke rehabilitation guidelines in African countries. **Design** We performed a systematic review following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement on the basis of a published protocol.

**Data sources** We conducted a systematic search of nine electronic databases, including PubMed, the Cochrane Library and African Index Medicus, published until August 2023 and additionally contacted authors and screened reference lists.

**Eligibility criteria** We included randomised controlled trials (RCTs) and prospective cohort studies on African adult patients with a clinical diagnosis of stroke. The primary outcome was global disability, and secondary outcomes were neurologic function scales.

Data extraction and synthesis Two authors independently screened the search results, with data extracted by one author and verified by a second author. The data were narratively synthesised. A meta-analysis was done using a random-effects model for metric data using standardised mean differences. Risk of bias was assessed using the Cochrane Risk of Bias tool. **Results** Of 3305 publications, 25 studies met the inclusion criteria involving cumulatively 973 patients with subacute and chronic stroke. Two-thirds of the trials were conducted in Nigeria and Egypt. The interventions covered physiotherapeutic, electrophysiologic, psychotherapeutic and transitional care domains with mostly beneficial outcomes. All included studies were RCTs with some concerns about methodologic quality.

**Conclusion** This systematic review comprises heterogeneous effective interventions for tertiary stroke prevention mostly conducted in small productive research clusters. There is a growing body of research from African countries covering important fields of stroke rehabilitation, including local adaptations of the rehabilitation process and new knowledge concerning transcranial magnetic stimulation. There remains an urgent need to implement interventions aimed at overcoming barriers to stroke rehabilitation.

PROSPERO registration number CRD42020159125.

# STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ We only included randomised controlled trials with patients with stroke from African countries.
- ⇒ A systematic search was conducted in nine electronic databases, including African-specific databases.
- ⇒ A meta-analysis of global disability was performed for electrophysiologic interventions.
- ⇒ Due to the lack of radiologic equipment, stroke mimics may be included in the trials.
- ⇒ None of the studies fulfilled the requirements for an overall low risk-of-bias assessment.

# **INTRODUCTION**

Generally, stroke is the second most common cause of death<sup>1</sup> and the third most common cause of disability-adjusted life-years (DALYs) worldwide with a lifetime risk prevalence of approximately one in four adults.<sup>2-4</sup> Around 87% of all stroke-related deaths occur in lowincome and medium-income countries such as those in Africa.<sup>1–3</sup> Average annual incidence rates increased from 81.2 per 100000 in 2013<sup>5</sup> to 106.9 per 100000 in 2022.6 Stroke-related age-standardised DALYs decreased in African countries from 1990 to 2016 but increased in absolute numbers.<sup>27</sup> A review by Adeloye and colleagues stated there were 535000 new stroke cases and 2.09 million stroke survivors for 2013, suggesting an increase of 10.8% and 9.6% of incident stroke cases and stroke survivors, respectively.<sup>5</sup> Additionally, global health estimates data for 2000-2019 demonstrate consistent increase in prevalence but a reduction of crude death rates from 51.4 in the year 2000 to 39.0 per 100000 patients with stroke in the WHO African Region.<sup>8</sup>

Therefore, Africa is home to more stroke survivors and the numbers are likely to increase in prevalence. This process is driven by factors such as population growth, ageing, changes in lifestyle, epidemiologic transition in many rural regions<sup>5 9</sup> and relatively slow

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growth in healthcare that is failing to meet the growing burden and care demands.  $^{10\,11}$ 

Major factors associated with the risk of stroke are hypertension, smoking, unhealthy diet and a low level of physical activity.<sup>12</sup> Hypertension is the leading modifiable risk factor for stroke,<sup>13</sup> with regional incidences of up to 82.2% undiagnosed and untreated patients.<sup>14</sup> Furthermore, epidemiologic data suggest that haemorrhagic stroke in particular occurs approximately two decades earlier in younger, productive age groups in sub-Saharan Africa, compared with high-income countries (HICs).<sup>11</sup>

The need to improve stroke prevention at all levels (primary, secondary and tertiary) and care is becoming compelling, in accordance with the WHO Rehabilitation 2030 Initiative.<sup>15</sup> Despite advances in healthcare provision globally, African healthcare systems remain fragile with inadequate prevention programmes and lack of diagnostic and treatment capacity to meet the demands of patients with stroke.<sup>16 17</sup> Moreover, the capacity to provide rehabilitative care post-stroke is highly limited.<sup>15</sup> Challenges in the African settings include complex pathways to care, limited transport options, long waiting times, out-of-pocket payments and physical mobility issues.<sup>18-20</sup> This lack of access to quality healthcare services, particularly in rural areas, hinders timely and appropriate treatment of many patients with stroke, leading to poorer outcomes.<sup>21</sup><sup>22</sup> On the patient side, underutilisation of healthcare resources is common.<sup>15 23</sup>

Stroke survivors are enduring long-term effects of this acute health condition, often living with physical or cognitive limitations.<sup>24–26</sup> Tertiary prevention interventions aim to reduce the effects of the disease after stroke onset,<sup>27–28</sup> covering, for example, physiotherapeutic, psychotherapeutic, electrophysiologic and transitional care domains.<sup>24</sup> These interventions have been shown to have positive overall effects, including increase in patients' body functioning, DALYs and quality of life (QoL).<sup>24</sup>

To address the growing burden of stroke in Africa, it is necessary to increase awareness, prevention and management of the conditions and risk factors, as well as improve access to healthcare services and treatment options.<sup>20 29</sup> This includes the development of stroke care networks, infrastructure development and the training of healthcare professionals in stroke management.<sup>23</sup>

Well-developed clinical practice guidelines that are context specific are instrumental to optimise healthcare, including management of stroke and its associated risk factors.<sup>30</sup> Currently less than 10 out of 54 countries in Africa have stroke-specific clinical practice guidelines.<sup>31</sup> It is necessary to evaluate and synthesise the existing data generated in Africa to inform the effective management of stroke survivors. Thus, the aims of this systematic review are to summarise the best available evidence on tertiary prevention interventions for African patients with stroke and identify the gaps in stroke prevention research in Africa.

# METHODS

This systematic review was registered on PROSPERO (CRD42020159125). We published detailed methods in a protocol<sup>32</sup> following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guideline<sup>29</sup> (see online supplemental checklist S1).

# Inclusion and exclusion criteria

We included full-text publications of randomised controlled trials (RCTs) and confounder-adjusted observational studies that enrolled patients with stroke from African countries and reported results on the efficacy of tertiary interventions for studies that measured our predefined primary (global disability) or secondary (neurologic function scales) outcomes. We included randomised and non-randomised studies to provide a comprehensive overview of the existing high-quality research given the limited number of existing literature. Observational studies were restricted to prospective cohort studies with a control of most important potential confounders (eg, age, stroke severity, time after onset) to minimise biased treatment effects.<sup>33–35</sup> We differentiated between acute stroke ( $\leq$ 48 hours after stroke onset), subacute stroke (>48 to  $\leq$ 6 months after stroke onset) and chronic stroke (>6 months after stroke onset). Tertiary prevention interventions involve physiotherapy, electrophysiologic treatment, psychotherapeutic interventions, community rehabilitation and transitional care following the current American Heart Association (AHA) guideline  $(table 1).^{24}$ 

# Systematic search

We performed a systematic search in nine electronic bibliographic databases (MEDLINE, Embase, the Cochrane Library, the Cumulative Index to Nursing & Allied Health Literature, CAB Direct, Physiotherapy Evidence Database), including specialised African databases (African Journals Online, African Index Medicus) and in the International Clinical Trials Registry Platform until January 2022, with an update using MEDLINE in August 2023, according to our search strategy.<sup>32</sup> The search strings included Medical Subject Headings, keywords describing stroke (eg, cerebrovascular, cerebral or intracranial accidents, infarction, disease, haemorrhage or ischaemia), Africa, a list of all 55 African countries and keywords related to eligible study designs. A detailed search strategy is provided in online supplemental file 2. We additionally screened the reference lists of all included full-text papers, contacted specialists and asked all first authors of the included studies for similar ongoing studies. No language limits were applied.

# Study selection, data extraction and quality assessment

All references were imported to Rayyan,<sup>36</sup> which is a web and mobile app for systematic reviews. After exclusion of duplicates, a title and abstract screening was performed independently by two authors (LA, ESK). Then, a fulltext screening was independently performed by the same 1

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Table 1 Inc	lusion criteria	characteristics and results of second author (BYW) checked		
Design and setting Participants	<ul> <li>Randomised controlled trials and prospective cohort studies with adequate confounder adjustment initiated and conducted in African countries, multicentre studies with at least 50% sites in African countries</li> <li>African adult patients</li> <li>Clinical diagnosis of stroke, including</li> <li>Ischaemic stroke</li> <li>Intracerebral haemorrhage</li> <li>Acute stroke (&gt;48 hours after stroke onset), subacute stroke (&gt;48 months after stroke onset) and chronic stroke (&gt;6 months after stroke onset)</li> </ul>	Data synthesis We narratively synthesised studies comprehensively. analysis for electrophysic random-effects model on r differences (MDs) and sy negative SMD for the Bay Rankin scale was regarded treatment effects are repo 95% 95% CIs. We used SI		
Interventions	<ul> <li>Tertiary prevention interventions</li> <li>Rehabilitation interventions (eg, occupational therapy, physiotherapy, speech therapy, language therapy)</li> <li>Exercise therapy</li> <li>Compensative strategies</li> <li>Psychosocial interventions</li> <li>Lifestyle interventions</li> </ul>	of comparable interventions global disability across diffe (online supplemental table 1 a high effect of the interven using Comprehensive Meta- Manager V.5.3.		
Control	<ul> <li>No intervention or placebo</li> <li>Standard care</li> <li>Another intervention</li> <li>Same intervention with a different dose or timing</li> </ul>	Investigation of heterogeneity ar We merged material diverse pants, setting, interventions assessed $I^2$ statistics to differ able, substantial, moderate of		
Outcomes	<ul> <li>Primary: global disability or dependence in daily living during the longest reported follow-up period (≥3 months from treatment start), for example,</li> <li>Modified Rankin scale</li> <li>Barthel Index</li> <li>Functional Independence measure</li> <li>Secondary: mortality, quality of life, for example,</li> <li>Stroke Impact Scale</li> <li>Stroke-specific Quality of Life Scale</li> <li>Neurologic disabilities, for example,</li> <li>Aphasia</li> <li>Dysphagia</li> <li>Cognition</li> <li>Paresis</li> <li>General stroke scores, for example,</li> <li>National Institutes of Health Stroke Scale</li> <li>Motor function scores</li> <li>Activity indices</li> <li>Functioning (walking/standing/limb functioning), for example,</li> <li>Walking speed</li> <li>Step lengthMetre walk time</li> <li>Minute walking distance</li> <li>Time up and go</li> </ul>	neity according to the <i>Coch</i> : analyses were planned to des odologic quality of studies (eg (eg, urban vs rural) and timen subacute vs chronic care). Du we performed only a subgroup geneity due to varying interve Risk of bias was described by two authors on the basis of of-Bias tool for RCTs <sup>39</sup> in five misation process, deviations fr missing outcome data, meas selection of the reported re concern' and 'high risk'. Disc discussion between the author Publication bias was investiga supplemental figure 1). <b>Patient and public involvement</b> No patients were involved.		
Publications	<ul> <li>Postural stability indices and scores</li> <li>Full- text publications according to CONSORT, SPIRIT or STROBE</li> </ul>	<b>RESULTS</b> We identified 3305 references base searches, including 289		
CONSORT, Co	onsolidated Standards of Reporting Trials; SPIRIT,	African databases, 121 regis		

Standard Protocol Items: Recommendations for Interventional Trials; STROBE, Strengthening the Reporting of Observational Studies in Epidemiology.

two authors. In all steps, disagreements were resolved in discussion with a third author (SU). Next, data extraction was performed by one author (LA), including the main

of all included studies. A ed all extractions.

e data to cover the included e also performed a metaogic interventions using a etric data described by mean ndardised MDs (SMDs). A hel score and the modified a benefit for the patient. All ed with their corresponding Ds to summarise the results s on our primary outcome, ferent measurement scales 1). SMDs above 0.8 indicate ntions.<sup>37</sup> Data were analysed -Analysis V.3.3 and Review

# nd risk of bias

e in methodology, particior outcomes studied. We erentiate between consideror not important heterogehrane Handbook.<sup>38</sup> Subgroup escribe differences in methg, RCT vs non-RCT), setting epoint of treatment (acute vs ue to the sparse data found, p analysis describing heteroentions (figure 2).

and judged independently f the revised Cochrane Riske different domains (randofrom intended interventions. surement of the outcomes, results) as 'low risk', 'some crepancies were resolved by nors or with a third author. ated via funnel plots (online

s in nine bibliographic datareferences from specialised African databases, 121 registrations from the International Clinical Trials Registry Platform, as well as 24 additional studies, and screened a total of 2810 references. 37 articles were potentially eligible, and 25 articles were included (see figure 1 and online supplemental table 1). Additionally, we dismissed one publication since the authors published data from the same participants the year before in another journal.<sup>40</sup> In the update search, we

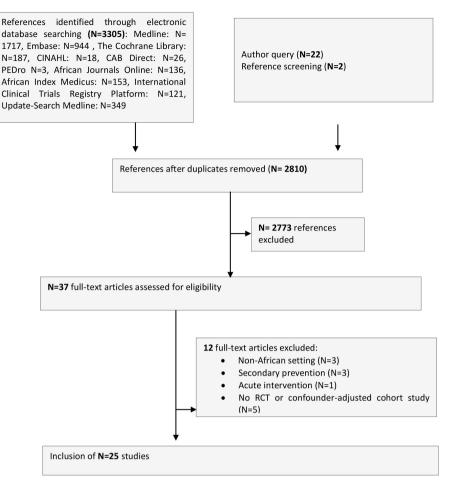


Figure 1 Flow chart describing the process of study selection. CINAHL, Cumulative Index to Nursing & Allied Health Literature; PEDro, Physiotherapy Evidence DatabaseRCT, randomised controlled trial.

found 349 new references. After abstract screening, none remained to be included.

# Study characteristics

# Setting

The studies were conducted in six countries. Almost half (n=11) were from Nigeria,<sup>41–51</sup> along with six from Egypt, three from South Africa<sup>52–54</sup> and one each from Uganda,<sup>55</sup> Benin<sup>56</sup> and Ebonyi State,<sup>57</sup> respectively. Most of the studies recruited patients from urban area hospitals. None of the studies had a specific rural focus (online supplemental table 1).

#### Population

The 25 studies involved 973 participants with a minimum of  $10^{47}$  and a maximum of  $144.^{52}$  The inclusion of females was reported in 21 studies, for which female prevalence ranged between 27% and 75%. The mean age of the participants ranged from 45 to 61 years, and weighted mean of the participant age was 53.8. Patients with stroke were included in the subacute (12 studies) and chronic phase (7 studies). In five studies, the phase of inclusion was not mentioned, and in one study the inclusion ranged from subacute to chronic. None of the studies specified pre-existing conditions relevant to stroke such as metabolic syndrome. Patients with

pre-existing disabilities or stroke were excluded from 24 of the 25 studies, and 9 of the 25 studies included only first-ever strokes.

7 studies used brain imaging to diagnose stroke,  $^{55\,58-63}$  1 used clinical signs for diagnosing stroke  $^{50}$  and 17 did not mention the diagnostic criteria.  $^{41-54\,56\,57\,64}$ 

#### Intervention

We subsumed the studied interventions in four categories: physiotherapeutic, electrophysiologic and psychotherapeutic interventions, and transitional care.<sup>24</sup> The first two categories aim to improve the sensorimotor functioning of the patient, whereas the psychotherapeutic interventions attempt to support the patient's QoL mentally. Transitional care addresses the patient's passage from the stationary to an ambulant home-based treatment.<sup>65</sup>

Nine studies (seven electrophysiologic interventions, two transitional care interventions) reported results on our planned primary outcome, global disability, using either modified Rankin scale, Barthel Index or the Activity Index.<sup>53 55 58-60 62 63 66 67</sup> Most of the interventions were provided by therapists (11 by physiotherapists, 3 by occupational therapists, 1 by a speech therapist) rather than physicians (6 interventions).

# Physiotherapeutic interventions for patients with stroke

 $\begin{array}{ccc} 12 & \text{studies} & \text{investigated} & \text{physiotherapeutic} \\ \text{measures}^{43\,45-52\,54\,57\,61} & \text{that we categorised as interventions} \\ \text{using therapeutic appliances, not using therapeutic appliances} & \text{and constrained-induced movement therapy.} \end{array}$ 

Appliances-based physiotherapy was scrutinised in five trials.<sup>43 50 51 57 61</sup> The use of a wobble board in addition to conventional physiotherapy improved static balance with closed eyes and dynamic balance.<sup>50</sup> The wobble board exercise was used as part of conventional physiotherapy in another study focusing on additional core strengthening exercises (eg, using a Swiss ball), but no supplementary effect of the core exercises in the balance tests could be demonstrated.<sup>57</sup> One study investigated dual motor task training in water compared with land-based exercises and showed significant benefits in multiple scores used (eg, overall stability index, walking speed and step length). The auxiliary use of a treadmill in comparison with overground walking showed an advantage concerning walking time and walking speed.<sup>43</sup> Badaru et al in 2012 compared physiotherapeutic use of treadmill and step bench and reported no positive effect of either of the therapeutic  $appliances^{51}$  (online supplemental table 1).

Five studies investigated constrained-induced movement therapy (CIMT), all conducted in Kano, Nigeria, by the same team.<sup>45–49</sup> CIMT was compared with other psychotherapeutic measures in three studies.<sup>45–48–49</sup> CIMT was more successful for improving motor function than proprioceptive neuromuscular facilitation<sup>45</sup> and standard physiotherapy, including passive movement and strength exercises.<sup>48–49</sup> Four studies compared different protocols of dosing control by repetition or time while using CIMT without significant differences in results.<sup>46–49</sup>

Two trials studied physiotherapy measures not using therapeutic appliances. Task-oriented exercises focusing on strength, balance and task management based on the movement science approach were compared with strength training alone of the lower extremities and a mere educational support showing an advantage in multiple stride parameter tests for both intervention groups.<sup>52</sup> The second study used individualised physio-therapy improving balance and stability scales<sup>54</sup> (online supplemental table 1).

#### Electrophysiologic interventions

Seven trials investigated the efficacy of electrophysiologic interventions supplementing standard physiotherapeutic and logotherapeutic care to strengthen motor recovery and coordination after stroke. Seven of the trials reported on global disability<sup>58–60</sup> <sup>62</sup> <sup>63</sup> <sup>66</sup> <sup>67</sup> (see figure 2). All studies reported positive effects of transcranial magnetic stimulation with a large pooled positive effect (SMD 1.26; 95% CI 0.72 to 1.79) despite substantial heterogeneity between studies ( $I^2$ =71%).

We separately calculated the results by Khedr *et al* from  $2013^{62}$  with transcranial current stimulation and found a large positive effect (SMD 4.21; 95% CI 3.07 to 5.34).

Two trials specifically treated patients with dysphagia with positive effects on dysphagia as well as on global disability.<sup>59 60</sup> Transcranial stimulation also had positive effects on global disability in patients with medullary infarction as opposed to brainstem infarction.<sup>59</sup> Four of the studies focused on the motor effects of transcranial magnetic stimulation after stroke with positive effects on global disability,<sup>58 63 66 67</sup> with one stating positive effects over 12 months.<sup>67</sup> Two different transcranial current stimulation application protocols showed clinically relevant effects on global disability for both application protocols.<sup>62</sup>

#### Psychotherapeutic interventions

Two trials explored the use of cognitive–behavioural therapy as part of tertiary intervention therapy, including cognitive behaviour language therapy, improving communication abilities of patients with aphasic stroke<sup>41</sup> and cognitive rehabilitation therapy that was superior to

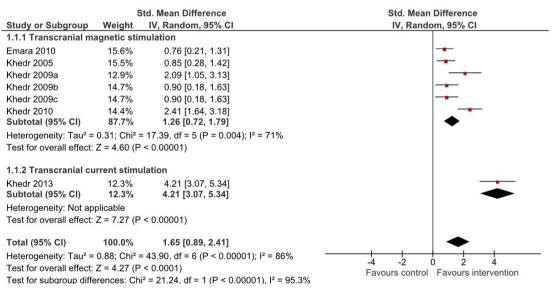


Figure 2 Standardised means differences of transcranial magnetic stimulation and transcranial current stimulation.

psychoeducation and usual care in reducing depressive symptoms.<sup>44</sup>

#### Transitional care

Out of four transitional care studies,<sup>42 53 55 56</sup> three were set at patients' homes and one occurred at the workplace. Global disability was reported in two of four studies.<sup>53 55</sup> Due to the heterogeneity of the interventions, we refrained from aggregating the results. The workplacetailored physiotherapeutic intervention of Kamwesiga et al in 2018 had a large effect on global disability (SMD 4.43; 95% CI 3.61 to 5.24),<sup>55</sup> whereas workplace-related interventions studied in Ntsiea *et al* in  $2015^{53}$  had no effect on global disability. However, the return to work rate was higher in the intervention group (60% vs 20%, OR 5.2 SD: 2.8).<sup>53</sup> A personalised, cell phone-supported, home-based occupational therapy intervention only showed an improvement tendency concerning global disability and subjective self-assessment of the patients.<sup>55</sup> A home-based self-rehabilitation protocol improved OoL

and motor functioning.<sup>56</sup> In-hospital physiotherapy with home-based physiotherapy revealed no benefit or harm regarding motor functioning and reintegration to normal life index.<sup>42</sup>

### **Risk of bias**

None of the studies fulfilled the requirements for an overall low-risk assessment. However, most of the studies reported methods leading to low risk of bias in domains 1-3 (figure 3). Studies scoring with high bias did not report data for all participants analysed or did not provide information about the number of randomised participants<sup>41 42 50 52 56–58 67</sup> (figure 3). Data from more than 90% of randomised participants were analysed in 11 studies, whereas in 4 studies data from less than 90% of randomised participants were analysed. Studies scoring with a high bias in domain 4 either had no blinding of the outcome assessor or did not report it.43 47 49-51 57 59 60 Nearly all studies scored with some concern in domain 5 because they did not report a prespecified analysis plan. A funnel plot on reporting of our primary outcome showed an under-representation of small studies, with negative results indicating a possible publication bias (see online supplemental figure 1).

#### DISCUSSION

This systematic review summarises high-quality evidence from 25 RCTs conducted in African countries on the efficacy of tertiary prevention interventions in the categories physiotherapeutic, electrophysiologic, psychotherapeutic interventions and transitional care and discusses the results for further use in national African stroke-specific guidelines.

#### Setting

The available evidence on tertiary prevention stroke research stems from only 6 out of 54 African countries,

with most studies set in countries with a comparably low score on the human development index (11 from Nigeria, 1 from Ivory Coast, 1 from Benin and 1 from Uganda). The great majority of the participants were from urban areas. The tenuous enrolment of patients from rural areas with still the highest population percentage might reflect organisational challenges recruiting patients for rehabilitation interventions and hint at the socio-economic barriers of the patients that can complicate access to rehabilitation.<sup>68–70</sup> Almost half of the studies were published by two authors, indicating a successful research community interested in tertiary prevention interventions in Nigeria (five studies by Abdullahi and colleagues)  $^{45-49}$  and Egypt (six studies by Khedr *et al*).  $^{59\ 60\ 62\ 63\ 66\ 67}$  Establishment of strong and productive research clusters in new settings is highly necessary and can be informed by such bestpractice examples.

# **Population**

Our review includes 973 patients with stroke without a remarkable gender bias. Many participants were younger than 55 years because African patients with stroke are generally younger in accordance with the findings of Yuyun *et al*<sup>11</sup> compared with HICs, which implicates a high potential for recovery.<sup>71 72</sup> Therefore, physiologic functional improvements of the patients, which take place anyway, might be even more accentuated and the comorbidity burden might be lower.<sup>72</sup> Thus, the applicability for elderly patients still needs to be addressed.<sup>73</sup> A total of eight studies with a total of 154 participants included patients with chronic stroke, while the best time point to start rehabilitation is the subacute phase, during which only 12 studies were conducted. These studied interventions might have shown improved patient outcomes if they had included patients earlier.<sup>24 74 75</sup>

Most studies exclusively included patients with a firstever stroke, possibly leading to an under-representation of patients with recurrent stroke. Recurrent stroke rates are estimated to be up to 22.5% within 5 years.<sup>5 76 77</sup> Patients suffering from recurrent stroke and thus having more impairments are in greater need of rehabilitative interventions than first-ever patients with stroke.

Besides, the diagnostic procedure was not sufficiently described in many studies. An uncertainty remains concerning the inclusion of patients with conditions that can mimic stroke such as epilepsy, subarachnoid haemorrhage, demyelinating diseases, migraine, functional disorders and others. Other neurologic diseases have a higher tendency to regression than stroke. This is likely due to an overall lack of radiologic diagnostic equipment.<sup>78</sup>

# Interventions

The research spans from the adaptation of established concepts such as physiotherapy with and without medical appliances<sup>43 50-52 54 57 61</sup> to the African context to cuttingedge research on transcranial magnetic stimulation with international recognition. Studies by Khedr *et al* were incorporated in European guideline development.<sup>79</sup>

Study ID	<u>D1</u>	<u>D2</u>	<u>D3</u>	<u>D4</u>	<u>D5</u>	<u>Overall</u>		
Abba 2020	+	+	+	+	!	!	+	Low risk
Abdullahi 2017	+	+	+		!	-	!	Some concerns
Abdullahi 2018	+	+	+	+	!	!	-	High risk
Abdullahi 2021	+	+	+	!		-		
Akabogu 2019				+		-	D1	Randomization process
Baradu 2012	!	+	+	•	!	•	D2	Deviations from the intended interventions
Danlami 2017	+	+	+		!		D3	Missing outcome data
Emara 2010	+	+		+			D4	Measurement of the outcome
Kamwesiga 2018	+	•	•	Ō	•	•	D5	Selection of the reported result
Khedr 2005	!	+	+	+	!	!		
Khedr 2009a	+	+	+		!	-		
Khedr 2009b	+	!	+	+	!	!		
Khedr 2009c	+	+	+		!	-		
Khedr 2010	+	+		+	!	•		
Khedr 2013	+	+	+	+	!			
Megan Knox 2018	+	!		!	!	-		
Natta 2021	!	+		+	!	-		
Ntsiea 2015	+	!	+	+	+	!		
Olaleye 2013	!	!		+	!	-		
Olawale 2009	+	+	+			-		
Olukolade 2017	+	!	+	+	!	!		
Onigbinde 2009	+	!				-		
Onwudiwe 2018	+	!			!	•		
Puckree 2014	!	+	+	!	!	!		
Saleh 2019	+	!	+	!	!	!		

Figure 3 Risk-of-bias analysis.

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Approved tertiary prevention interventions seem feasible with comparable benefits in African countries as in HICs. Therefore, research should focus on measures to implement established evidence-based tertiary prevention interventions. This is consistent with evidence from non-African low-income countries.<sup>80 81</sup> Known factors influencing rehabilitation uptake include level of education, travel burden, cost and religious beliefs.<sup>3 82</sup> Several rehabilitation approaches are being explored in low-income countries, not just in African countries, such as integrated care pathways, community health workers and the use of digital health technologies such as mobile health, videobased instructions and virtual reality.<sup>81</sup> However, most evidence is still of comparatively low quality.<sup>83</sup>

Most of the trials included physiotherapists, occupational therapists and speech therapists. Educational costs for these professions are usually lower than they are for physicians.<sup>84</sup> Task shifting and working in multidisciplinary teams could solve some allocation and educational shortcomings in low-resource settings, as has been recommended by the WHO<sup>85 86</sup> and multiple studies.<sup>87</sup> However, the availability of therapists in low-income countries in general is often low.<sup>82 88</sup> Therefore, task shifting to caregivers can also be a promising approach.<sup>81</sup> This process can be supported by telerehabilitation concepts.<sup>55</sup>

#### Physiotherapeutic interventions

The included studies showed promising results for the use of low-cost interventions. While the current rehabilitation guideline of the AHA does not clearly recommend water-based interventions<sup>24 89</sup> and treadmill exercises,<sup>24</sup> physiotherapeutic interventions concerning therapy optimisation of CIMT and physiotherapeutic intervention without medical appliances showed improvements on global disability measures and neurologic function scales in accordance with guidelines from HICs.<sup>85</sup> Especially physiotherapeutic interventions seem to be feasible in African contexts because they require no or little technical equipment.

#### Electrophysiologic interventions

Most of the electrophysiologic studies were authored by Khedr and colleagues and conducted at the Assiut University Hospital in Egypt. The electrophysiologic interventions in this review focused mainly on transcranial magnetic and current stimulation, which showed benefits for dysphagia and motor functioning. However, these treatment options are still the objects of further and multicentre research.<sup>90 91</sup> They are not yet considered part of usual rehabilitation.<sup>24</sup> Professional equipment for transcranial magnetic and transcranial current stimulation is costly.<sup>92</sup> Considering cost and the still incomplete evidence, physiotherapy should be prioritised.

#### Psychotherapeutic interventions

Cognitive–behavioural therapy improved psychologic outcome measures, in line with the results of a current systematic review.<sup>93</sup> A Cochrane review from 2022 also suggested the use of psychotherapeutic interventions<sup>94</sup> to treat post-stroke patients with depression with low-certainty evidence. Psychotherapeutic interventions for post-stroke depression are not mentioned in the current AHA guideline.<sup>24</sup> However, other guidelines from HIC (eg, German and Australian) on stroke rehabilitation rather advise the use of serotonin reuptake inhibitors.<sup>95 96</sup> The inclusion of psychotherapeutic interventions as part of a patient-centred and biopsychosocial model of rehabilitation community.<sup>97</sup>

#### **Transitional care**

The positive patient outcomes of the included transitional care studies indicate a high potential of promoting self-sufficiency and QoL of patients with stroke in line with the WHO promotion of community-based rehabilitation<sup>98</sup> and task shifting,<sup>86</sup> as well as the South African stroke guideline for under-resourced areas.<sup>99</sup> Additionally, the AHA guideline mentions benefits in ambulation, mobility, self-care, functional independence and patient and caregiver satisfaction.<sup>24 100-103</sup>

#### **Outcomes**

The outcome measures primarily focused on scales of neurologic functioning (17 out of 25) and do not report QoL or global disability. Thus, it often remains unclear if the benefits in these scales translate into an improvement in real life.<sup>104</sup> None of the included studies reported on cost-effectiveness, so statements regarding resource allocation are not possible.

#### **Strengths and limitations**

We included high-quality studies based on a comprehensive systematic search that included specifically African databases and a thorough literature search with reference screening and author inquiry. We did a study registration and published a study protocol ensuring transparency of the research methods used. Additionally, we worked in close collaboration with researchers from Ethiopia and Cameroon. A first limitation is the lack of inclusion of non-English publications that we addressed by reference screening and contacting of study authors to close the gap. Second, owing to the heterogeneity of the studies we could only perform a small meta-analysis, so to merge some results of the interventions, we therefore narratively summarised the existing data. Moreover, almost half of our studies stem from two research groups, which makes it difficult to draw general conclusions. Third, the questionable diagnostic accuracy of stroke due to the lack of radiologic equipment might limit the validity of the results.

Finally, none of the trials we considered provided a low risk of bias. Especially, prespecified analysis plans or protocols have not been reported. Only four studies were double-blinded. However, it must be considered that blinding participants to their intervention in rehabilitation studies often is impossible due to the nature of the interventions.<sup>46 55 56</sup> Positively, most of the studies reported details on their randomisation process, did not deviate from the planned intervention and reported results on most randomised patients, thereby implicating reliable data.

#### Recommendations

As the adherence to reporting guidelines was insufficient in most studies, efforts to improve the adherence to standardised reporting guidelines are advisable.<sup>104 105</sup>

While the existing research shows the effectiveness of physiotherapeutic interventions in African patients, uptake of tertiary prevention after hospital discharge is a major barrier. Health services research on how to effectively implement tertiary prevention interventions in real-world setting is necessary.<sup>3</sup> The WHO's community-based rehabilitation guidelines could be used as a starting point.<sup>106</sup>

#### CONCLUSION

There is a growing body of research from African countries covering important areas of tertiary prevention. Several strategies, including rehabilitation measures like physiotherapy, psychotherapy, transitional care and electrophysiology, have been implemented in trials with beneficial results in African settings. Some studies informed about local adaptations of the rehabilitation process, and the Khedr *et al* studies on transcranial magnetic stimulation also supplemented international guidelines. Overarching is the need to politically recognise tertiary prevention as an important part of the healthcare system to increase the years that patients who survived stroke can live meaningfully and autonomously.

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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 and public involvement** Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval Not applicable.

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 supplementary information.

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