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Strategies to Improve Stroke Care Services in Low- and Middle-Income Countries: A Systematic Review

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Keywords
Low and Middle Income Countries (LMICs) · Stroke services · Strategies · Stroke units · Pre-hospital stroke transport

Abstract
Background: The burden of stroke in low- and middle-income countries (LMICs) is large and increasing, challenging the already stretched health-care services. ***Aims and Objectives:*** To determine the quality of existing stroke-care services in LMICs and to highlight indigenous, inexpensive, evidence-based implementable strategies being used in stroke-care. ***Methods:*** A detailed literature search was undertaken using PubMed and Google scholar from January 1966 to October 2015 using a range of search terms. Of 921 publications, 373 papers were shortlisted and 31 articles on existing stroke-services were included. ***Results:*** We identified efficient models of ambulance transport and pre-notification. Stroke Units (SU) are available in some countries, but are relatively sparse and mostly provided by the private sector. Very few patients were thrombolysed; this could be increased with telemedicine and governmental subsidies. Adherence to secondary preventive drugs is affected by limited availability and affordability, emphasizing the importance of primary prevention. Training of paramedics, care-givers and nurses in post-stroke care is feasible. ***Conclusion:*** In this systematic review, we found several reports on evidence-based implementable stroke services in LMICs. Some strategies are economic, feasible and reproducible but remain untested. Data on their outcomes and sustainability is limited. Further research on implementation of locally and regionally adapted stroke-services and cost-effective secondary prevention programs should be a priority.

Introduction

Globally, stroke is the second most common cause of death and disability [1]. The mortality rate of stroke has reduced to half in high-income countries but only 15% in low-and middle-income countries (LMICs) [1]. In LMICs, stroke patients are younger than those in high-income countries [2–4], use tobacco more often [5–7], have a greater prevalence of diabetes mellitus, hypertension, cardiovascular diseases, dyslipidemia and obesity [4, 8], have lower prevalence of atrial fibrillation [9, 10], and have a greater case fatality rate [11]. It is uncertain whether current healthcare systems in most LMICs are well equipped to deal with this enormous burden of stroke.

Aims and Objectives

The objective of this systematic review is to determine the quality of existing stroke-care services in LMICs and to highlight indigenous, inexpensive, evidence-based implementable strategies to improve stroke-care.

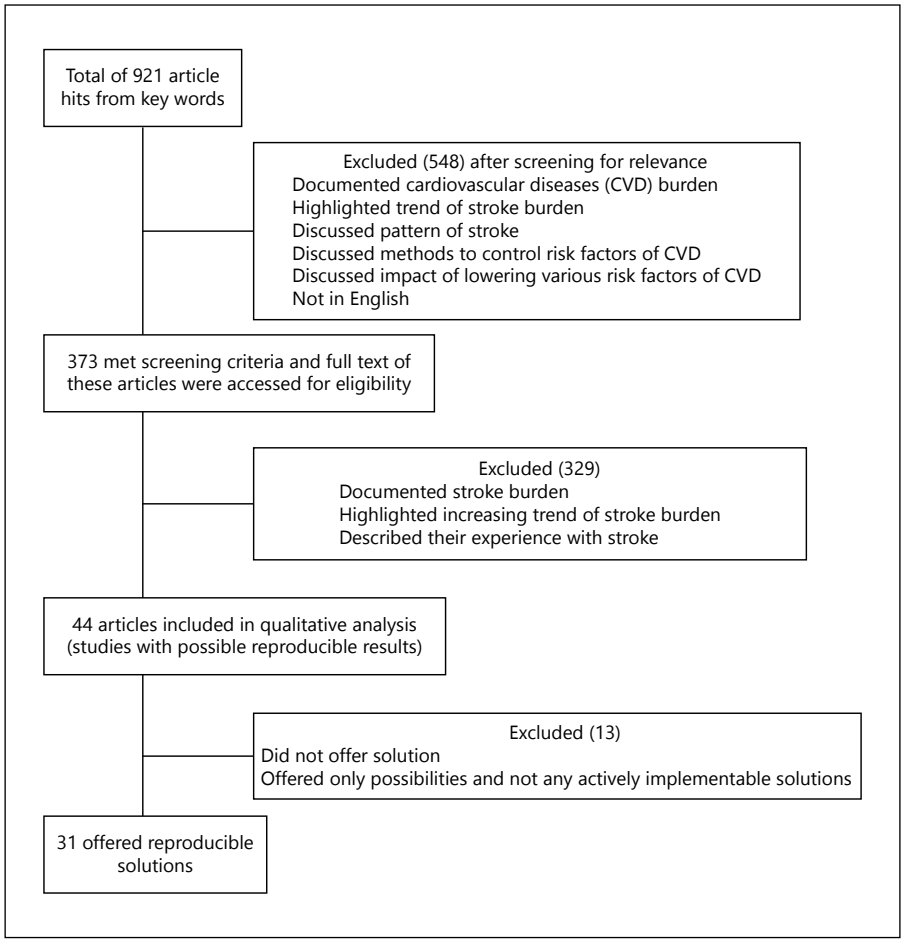

Fig. 1. Flowchart showing the selection of articles.

Methods

A literature search was conducted using PubMed and Google scholar to find articles published between January 1966 and October 2015 that included details of stroke care and improvements in this care in LMICs. For this review, we used the World Bank classification of the year 2015. According to this classification, a gross national income per capita for the previous year of less than USD 1,025 classified a country as "low income," while income between USD 1,026 and USD 4,035 classified a country as "lower-middle income." The literature search was conducted using the following key words: stroke, hemiplegia, ambulance, low to middle-income country(ies), developing country(ies), pre-hospital transport, stroke units (SUs), district hospital, government hospital, thrombolysis, tissue plasminogen activator (tPA) cost and dose, post-stroke care, caregiver depression, rehabilitation, physiotherapist, speech therapist, social worker, public awareness and healthy lifestyle. A further search was conducted among all individual LMICs using 3 key words – stroke registry, thrombolysis and SU. The search was limited to original studies and review articles were published in the English language. We identified 921 articles, out of which 373 articles met the screening criteria, that is, they offered the possibility of a stroke care strategy feasible in LMICs (Fig. 1). Among these, 329 articles provided data on stroke burden or included data only on structure and process of service provision. The remaining 44 articles were reviewed by A.G.W. and J.D.P. When there was disagreement between reviewers, the decision of J.D.P. was binding. Thirty one of the 44 articles provided information of reproducible, low inputs stroke care methods Table 1.

Results

Stroke care services encompass pre-hospital recognition, assessment and transport, acute stroke care (rapid triaging in emergency department, ED), SU care and rehabilitation and community support. In LMICs there are many barriers in the establishment of stroke care services (Table 2). A typical stroke pathway is shown in Figure 2.

Pre-Hospital Services

There is limited data on government-run pre-hospital systems from LMICs [12–14] and within these the ambulances are either not well equipped, or do not have trained

Table 1. List of the various reproducible low input strategies used in various LMICs

Reference number	Title	Observations and potential area of improved care	Country(ies)	Strategy	Limitation
Pre-hospital transport					
16	Factors delaying admission to a hospital based stroke unit in India.	– Time lost in consulting a local doctor.	India	Local doctors can be updated about functioning stroke units to refer patients in a timely manner.	Educating general population Keeping local doctors up to date about stroke units that thrombolyse.
18	Factors associated with prehospital delays in the presentation of acute stroke in Urban China.	– Merged multiple existing emergency systems.	China	To cover a large area, consider merging already functioning systems. Make use of already established co-ordination between local doctors and ambulance services	Needs legislative backing for implementation
24	Role of pre-hospital care and ambulance services in Karachi.	– Observed and elucidated public perception of ambulance services. This emphasizes role of public knowledge. – Used local infrastructure – Edhi and Chippa Foundation- training volunteers (Edhi has 400 ambulances) – Rearranged ambulance stations	Karachi, Pakistan	Private independent ambulance services can function efficiently. Ambulance stations can be arranged to match population density. Quality indicators for ambulances can be individualized according to local culture	Not exclusively for stroke Cost may be limiting for common man
25	Establishing a successful pre-hospital emergency service in a developing country: experience from rescue 1,122 service in Pakistan.	– Retrained already working personnel – Provide ambulance with 2 emergency technicians – Use local infrastructure	Pakistan	Can supplement the training of paramedics Ambulance stations can be established according to response time.	Needs legislative and economic support for sustainability
20	An overview of Shiraz emergency medical services, dispatch to treatment	– Ambulance services updated. – Ambulance has one general practitioner along with paramedic staff – Ambulance nurse trained in anesthesia – Paramedic trained in basic life support	Iran	Supplementing training of nurses and paramedics Each ambulance has one general practitioner, one nurse and one paramedic	Not dedicated for stroke
28	Curitiba acute ischemic stroke protocol.	– Use of already existing cooperation between SAMU and hospital – Linking SAMU to tertiary care centre – Training EMS in LAPSS. If acute ischemic stroke was suspected (<2 h) patient was taken to university hospital where neurologist, CT technician, laboratory staff were waiting – Neurological evaluation done in CT room – Of the 15 patients thrombolysed, 13 were treated within 60 min	Brazil	EMS personnel do primary evaluation Coordinate among centres such that EMS personnel can take suspected stroke patient directly to tertiary centres Patient is be transported to CT scan directly Neurological evaluation done in CT room	

Table 1. (continued)

Reference number	Title	Observations and potential area of improved care	Country(ies)	Strategy	Limitation
Pre-tPA investigtions					
31	Hyperacute thrombolysis with IV rtPA of acute ischemic stroke: efficacy and safety profile of 54 patients at a tertiary referral centre in a developing country.	– tPA given without investigating coagulation profile	India	Thrombolysis in carefully selected patients.	Prudent selection
35	A low-cost tele-imaging platform for developing countries	– Two camera systems installed one at "remote/patient" and the other at "expert" centre. – Using LogMeIn software – Allows audio and video communication – Allows file and data transfer – Allows expert centre radiologist to take control of the computer at the remote site – Allows the expert to see the images and give their opinion	Togo, Africa	Neurologist can provide tele consultation from "expert" centre	Needs one time set up and continuous internet connection
36	Initial Brazilian experience of Telestroke for thrombolysis in a community hospital	– Remote consultation between secondary community hospital and a private tertiary hospital. – Imaging done at secondary hospital. A TeleMedicine Central Command located at the tertiary centre with endpoint 97 MXP Cisco solution and a mobile Intern MXP ISDN/IP Cisco for secondary hospital. This helps to exchange images.	Brazil	Teleconsultation	Needs input for one time set up
37	Intravenous thrombolysis guided by a telemedicine consultation system for acute ischaemic stroke patients in China: the protocol of a multicentre historically controlled study.	– Developed a two-way interactive audio-visual wireless system, compatible with iPhone operating system, smart phones and tablets. – Connecting one hub and 14 spoke hospitals	China	Teleconsultation Results awaited	
34	Design of a standard Iranian protocol of Intravenous thrombolysis with tissue plasminogen activator: a national project.	– With modified NIHSS, stroke severity assessment is easier to assess by paramedics and doctors.	Iran	Simplified NIHSS Removed- level of consciousness, ataxia, facial palsy and dysarthria	Validity is yet to be established on a large scale
Emergency department					
39	The state of emergency care in the republic of the Sudan	– Nursing staff and emergency medical officers were sent to countries with well-established EDs to learn – Consequently EM residency was started in 2011	Sudan, Africa	Train a few staff in well-established EDs so they in turn train local staff	Needs legislative involvement of developed countries also. These candidates need to be sponsored by the hospital or another philanthropic body

Table 1. (continued)

Reference number	Title	Observations and potential area of improved care	Country(ies)	Strategy	Limitation
40	The first year of a formal emergency medicine training programme in Papua New Guinea.	– EM was established as a specialty – Experienced emergency nurse from Australia was invited to educate local nurses – Training medical students in emergency medical care was initiated	Papua, New Guinea	EM added to the curriculum of medical students EM training started and was structured If local educational support is limited, help can be sought from developed institutions/countries	Needs motivation, sustained effort
41	Capacity building in emergency care: an example from Madang, Papua New Guinea	– Australasian emergency physicians and emergency registrars teach their ER skills in the local hospitals of New Guinea	Papua, New Guinea	ER officers from well-established ERs teach in less developed ERs	
Stroke Units (SUs)					
27	Past, present, and future of stroke in middle-income countries: the Brazilian experience	– National Stroke Policy Act – Increased SUs from 20 to 37 in public sector and 15–45 in private sector – Increased thrombolysis rate – Reimbursement for each patient stay increased to US$ 190/day with additional for CT, ECHO and carotid duplex – Negotiating salt reduction in processed food	Brazil	The government supported establishment of SUs Made reimbursement easy and directly from the government Increased thrombolysis rate in the country	Needs government support
45	Burden of stroke in Egypt: current status and opportunities.	– Observed that medical students receive insufficient teaching about stroke – <1% of patients are thrombolysed	Egypt	Establish stroke units	Needs economic and legislative support
46	Does multidisciplinary stroke care improve outcome in a secondary level hospital in South Africa?	– Reduced in-hospital mortality in SUs from 33 to 16% – Rate of referral to inpatient rehabilitation increased from 5 to 19% – Length of hospital stay increased	Cape Town South Africa	Establish SUs Encourage referral of inpatients to physiotherapist and social workers	
47	Quality of ischemic stroke care in emerging countries: the Argentinian National Stroke Registry.	– SUs reduced complications and mortality – Creating network of stroke-care services – Academic hospitals AH admitted more patients in SUs (8.5 vs. 3.2%, $p < 0.001$) – AH had shorter length of hospital stay (6.3 vs. 9.5 days, $p < 0.001$) – AH had fewer pneumonia (9.6 vs. 15.5%) – AH had lower risk adjusted in-hospital mortality (7.1 vs. 10.6%).	Argentina	Centralized reimbursement of tPA Decentralization-establishing multiple stroke units Stroke education campaigns Demonstrating economic benefits to health authorities Reducing the cost of tPA Creation of "line of stroke care"	Needs active co-operation from the government.
Thrombolysis					
51	Abstract MP25: Intravenous thrombolysis in India: the Indo–US stroke project	– Eleven percent (227/2066) patients thrombolysed	India	Establishing SUs in teaching referral hospitals can dramatically improve thrombolysis rate	
52	Telestroke in resource-poor developing country model	– Telestroke between 2 tertiary care hospitals (with neurologist) and 17 district hospitals (without neurologist) between June 2014 and May 2015, thrombolysed 26 patients	Shimla, India	tPA is offered free of charge by the state government Telestroke is feasible	Needs government support

Table 1. (continued)

Reference number	Title	Observations and potential area of improved care	Country(ies)	Strategy	Limitation
53	Problems and limitations in thrombolysis of acute stroke patients at a tertiary care centre	– In this retrospective audit, lack of triaging stroke patients at every level was identified as a potential area for saving time. – Educating EM staff about triaging stroke patients – Suggested that incase the first on call neurologist is busy, a second neurologist can be on call only for patients with acute stroke. – Suggested to establish a "stroke-code". This code is a pre-notification call to all the concerned departments about any stroke patient within the hospital	Pune, India	Pre-notification within the hospital can reduce door to needle time Second on call neurologist/ stroke expert only for patients with acute stroke in ED may be helpful	
Post-stroke care					
56	FAmily-Led RehabiliTaTion aftEr Stroke in INDia: the ATTEND pilot study.	– Care-giver of patient with stroke is trained in giving physiotherapy while the patient is admitted – Physiotherapy can be continued upon discharge	India	Caregivers of stroke patients from rural areas can continue to give physiotherapy at home without additional cost	Can only be offered to patients hospitalized in centres offering physiotherapy
57	Caregiver-mediated intervention can improve physical functional recovery of patients with chronic stroke: a randomized controlled trial.	– For patients in intervention arm, physical therapist charted a personalized schedule for each patient – A physical therapist visited each patient weekly. – Taught personalized rehab skills to the patient and taught care-givers to assist and help the patients – Patients in intervention arm had better strength (15.5:1.4, $p = .002$), mobility (13.7 vs. 0.5, $p < 0.001$), composite physical (11.2 vs. 0.7, $p < 0.001$), and general recovery domain (17.4 vs. 0.2, $p < 0.001$), free-walking velocity (7.5 vs. −1.4 cm/s; $p = 0.006$), 6-min walk distance (15.8 vs. −10.5 m; $p = 0.003$), Berg Balance Scale score (4.5 vs. −0.8, $p = 0.006$), and Barthel Index score (7.2 vs. 0.6, $p = 0.008$). CHI did not significantly increase caregiver burden at endpoint.	Taiwan	Train care-givers in basic physiotherapy techniques	
58	Methodology of the Stroke Self-Management Rehabilitation Trial: an international, multisite pilot trial	– Rehabilitation techniques were given to patients in the form of digital video discs (DVDs). – Patients were encouraged to exercise 5 days/week – Weekly phone calls to patients in intervention arm. To the patients in control group only baseline and 2 months assessment was made	Two centres in India and Nigeria each	Use of a simple DVD at home for self-rehabilitation	Needs individual motivation
Secondary prevention					
59	Randomized controlled trial of a multipronged intervention to improve blood pressure control among stroke survivors in Nigeria	– THRIVES is testing whether a Chronic Care Model-based multipronged, culturally sensitive and system-appropriate intervention significantly improves blood pressure control after stroke. The interventions include: (1) in-clinic educational video; (2) patient report card; and (3) text messaging with motivational information and clinic reminders.	Nigeria	Ongoing trial	–

Table 1. (continued)

Reference number	Title	Observations and potential area of improved care	Country(ies)	Strategy	Limitation
6	Project Quit Tobacco International Group. Introducing tobacco cessation in developing countries: an overview of Project Quit Tobacco International.	– Methodically developed culturally acceptable methods of tobacco cessation. – Also made efforts to understand and overcome the barriers to quitting – Team members conducted tobacco cessation counseling in government hospitals.	India Indonesia	Culturally accepted and appropriate methods of tobacco control	Time consuming Needs persistent funding for sustenance
68	The effect of tobacco-control measures during a period of rising cardiovascular disease risk in India: a mathematical model of myocardial infarction and stroke.	– Developed a mathematical model to study which strategy will be most effective as tobacco-control strategy. Models tried – Tobacco taxation (300% increase in cigarette and bidi tax rate can avoid 0.6 and 0.5 million stroke deaths over the next 10 years respectively. – "Smoke free" laws – Cessation advice by maybe the least effective measure – Anti-hypertensive therapy can help avoid 1.6% of stroke deaths	India	Increased taxation on tobacco products Smoke-free laws	Mathematically projected analysis
69	An empirical analysis of cigarette demand in Argentina.	– A 10% rise in the price of cigarettes can result in a 3.1% reduction in its consumption	Argentina	Increase tax on cigarettes	Needs legislative support for sustenance
72	Developing a national salt reduction strategy for Mongolia.	– Establishing data (2011–2013) – Mean salt intake (grams per day) in males was 11.68 (6.15) as compared to 10.54 (5.81) in females – Mean salt intake in urban areas was 11.32 (6.06,) while that in rural area was 10.64 (5.86) ($p < 0.005$) – People who drank salty tea daily consumed 11.81 (6.34), while those who did not consume 10.20 (5.43) g of salt per day; mean difference of 1.61 (95% CI 1.10–2.22; $p < 0.002$) – Pinch Salt Mongolia-2011 – Objective- reduce salt intake of employees of 3 main food processing factories (Makh Impex, Talkh Chikher and Goyo). – Educating the staff about potential adverse effects of high salt intake and educating them how to consume less salt – In post-intervention 24 h urine test – salt intake reduced from 11.48 (7.32) g per day in 2011 to 8.65 (4.26) g per day in 2013. The number of staff who didnot know salt content in foods declined from 18.5% (95% CI 14.0–23.9) to 2.9% (95% CI 1.1–7.4) during the same period – The first company to reduce salt in bread was – Talkh – Chikher. It reduced salt in "Atar" bread by 12% in May 2011 – Other companies soon followed, reducing salt content in 10 breads and bakeries declining salt by 1.6% after May 2011 – Sausage industry also agreed to reduce salt content by 10%	Mongolia	Reduce salt in processed food, (bread, meat) Reduce salt content in locally made food e.g. bakeries Results by 2025	Needs continued government support

Table 1. (continued)

Reference number	Title	Observations and potential area of improved care	Country(ies)	Strategy	Limitation
73	WHO's supported interventions on salt intake reduction in the sub-Saharan Africa region.	– Collection of salt intake data through STEPS survey methods – Documents progress made by various countries	Sub-Saharan Africa	Government commitment to increase awareness among people (consumers) and making laws to reduce salt in processed food. Results by 2025	–
75	Hypertensive patients using thiazide diuretics as primary stroke prevention make better functional outcome after ischemic stroke.	– Among 140 patients who completed 3 months follow-up, 21 patients were taking thiazide prior to stroke. No difference in stroke subtypes/ comorbidities observed between the 2 groups. Thiazide group had lower NIHSS (4 vs. 6) and better outcome mRS≤2 (42.4 vs. 26.9%, $p = 0.02$)	Taiwan	Long-term thiazide use reduces stroke severity Cost-effective way	Small study

SAMU, Serviço de Atendimento Móvel de Urgência (Pre-hospital emergency medical system in Brazil); LAPSS, Los Angeles pre-hospital stroke screen; EMS, emergency medical services; ECHO, echocardiography; tPA, tissue plasminogen activator; NIHSS, National institute of health stroke scale; ED, emergency department; EM, emergency medicine; ER, emergency room.

Table 2. Barriers at each level in the establishment of stroke care services in LMICs

Level of barrier	Type of barrier	Reference number
Pre-hospital	Lack of stroke helpline Insufficient infrastructure Unavailable/inadequate transportation facilities (Ambulance)	[12–14, 16, 18, 19, 25, 37]
Hospital triage	Under-resourced emergency departments Under-resourced imaging and radiologist	[38, 39, 41] [16, 32, 33, 35]
Stroke unit	Lack of neurologist/stroke experts in rural areas Lack of trained personnel High cost of drugs	[45, 48] [94] [45, 88, 92]
Post stroke care	Limited rehabilitation facilities Deficient numbers of physiotherapists speech therapist and occupational therapists	[94] [32]
Community support	Lack of social workers	[94]

personnel [15]. Most patients prefer to use their own vehicle(s) (personal or hired) to seek medical help [16–19]. The ambulances in these countries predominantly transport patients with trauma injuries and obstetric emergencies [20, 21], while medical emergencies such as stroke are not given priority.

Asia

The Government of India with private public partnership has established ambulance services in 29 States. The most popular model is the "dial 108" model. This ambulance service is provided free of charge by the government [22]. Similarly, Iran has made ambulances available in rural areas, but their impact on stroke-care services needs to be explored [23].

In Pakistan, ambulance services are offered by both private and government organizations [19, 24]. These ambulances are equipped with paramedics, emergency drugs and they keep up the World Health Organization's (WHO) standard of care [24].

In an unprecedented initiative in Pakistan, a trauma surgeon trained Emergency Medical Technicians (EMTs)

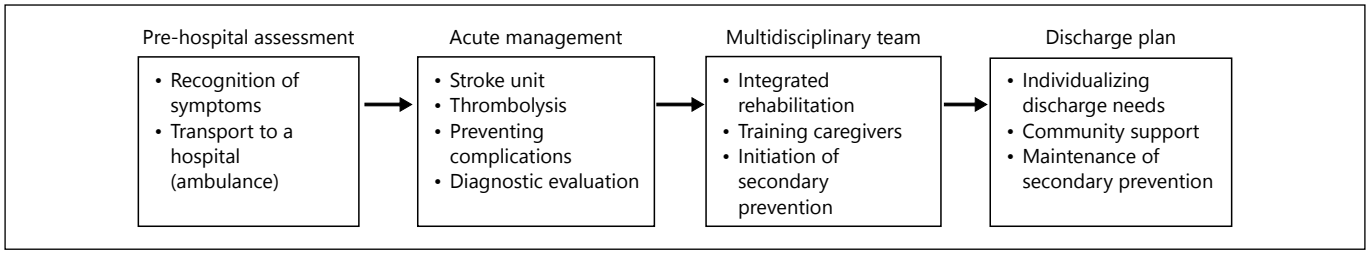

Fig. 2. Components of stroke-care services.

in triage, rescue, spine immobilization, using external defibrillators and other similar medical equipment. After the success of this service it was expanded to all 35 districts of Punjab, Pakistan. Ambulance stations were strategically located in a circular fashion, such that each station can respond to a call within 7 min; 14 such stations were built to cover the entire city. Every ambulance was staffed with one driver and 2 EMTs. They used locally available infrastructure for all ambulances and other hardware. The pre-hospital assessment of stroke is not incorporated in this system [25].

In China, the "Chinese Association of Emergency Medicine" was established in 1986 [26], while the Administrative committee of Emergency Medical Center (First Aid Station) Branch of the Chinese Hospital Association was established in 2002. The Chinese government mandated the use of "120" as the official medical emergency phone number in 1996; however, multiple emergency numbers still exist simultaneously within the same geographic region, for example, "120," "119," "110," "122" and "95120". These include private ambulance services, stand-alone emergency centres and hospital-based ambulance services. To make these systems efficient, 2 operational medical emergency systems in Beijing were merged. One was "120" system managed by Beijing Health Bureau, while the other was "999" system operated by the Beijing Red Cross. The 2 systems were combined in 2011. However, these services are not being used to bring patients with stroke to hospital.

South America

The Brazil National Stroke Project was launched in 2008. Under this project acute stroke centres were constructed; pre-hospital training, transport and acute hospital care were improved. "*Servico de Atendimento Movel de Urgencia*" (SAMU), which is an established pre-hospital emergency medical system in Brazil was also included. In 2012, the government launched "Brazil National Stroke Policy Act". This system has a "stroke line," comprising a local network that works towards primary/secondary prevention, pre-hospital assistance, acute and post-acute care and rehabilitation centre in each city for stroke patients. Thus, any patient with stroke needing assistance is directed to a stroke centre by the central regulation centre (SAMU) [27].

The second strategy implemented was "call before arrival or pre-notification." Emergency Medical Service personnel, who suspected acute ischemic stroke in a patient for less than 2 h, evaluate the patient using a standard checklist based on the Los Angeles Pre-hospital Stroke Screen and thrombolytic criteria. After a quick evaluation, the hospital was informed and the patient taken directly to CT scan room, where a neurologist, CT technician and laboratory technician were waiting. This helped Emergency Medical Service personnel to detect stroke patients in time and radically reduce the transit time, imaging time and time for consultation by a neurologist. Of the 433 stroke patients evaluated, 50 potentially eligible thrombolysis patients were transferred to the hospital within 3 h. Among them, 15 (15/433, 3%) patients received tPA. Thirteen patients were treated within 60 min and the remaining 2 received thrombolysis within 90 min of symptom onset [28].

In some countries, due to a large number of cars and poor traffic infrastructure, ambulance service might result in a delay of transit. Use of an ambulance maybe feasible if operated in small cities within a distance of up to 15 km from a stroke centre [15, 16, 25, 29, 30]. Hence, the risk of losing time in transit must be carefully balanced against the services potentially offered by these ambulances.

Acute Management

Investigations and Imaging

Delays in investigations prior to administering tPA excludes a large number of eligible patients from the treatment time window [16]. This delay was systematically analyzed in a small study conducted in India. In this

study, 54 patients were carefully selected after excluding those with bleeding predilection, for example, liver or renal disease, bleeding diathesis, intracranial hemorrhage, old hemorrhagic stroke or recent myocardial infarction and so on. These patients were thrombolysed without investigating coagulation profiles. Hemorrhagic transformation was seen in 5 patients, while symptomatic and fatal haemorrhage was not seen. At 1 month follow-up, 1 patient developed small frontal lobe haemorrhage and recurrent stroke [31].

Similarly, in a small study in Iran involving 625 patients, only 50 patients reached within the 3-h window period. Of those who arrived early, 56% of patients were within the 3-h time window even after completing the investigations**.** To overcome this hurdle, a "stroke code' was established. This was with one resident doctor directly involved in the care of each patient, and a neurologist available 24 h each day. The team also established a new protocol for patients eligible for tPA that included illustrations of imaging and clinical exclusion criteria. All doctors and nurses were trained in this acute stroke care protocol and their knowledge was supplemented with regular refresher courses [32–34].

To extend imaging facilities in underprivileged rural areas, "low cost tele-imaging" strategy was tested in Togo, Africa. Two camera systems were installed; one at the remote/patient centre and the other at the expert centre. By using LogMeIn software it was possible to teleconsult with the stroke expert from a remote centre. This software allowed to and fro communication (audio and video), transfer data/file and even take control of the computer at the patient centre. It enabled the neurologist/stroke expert to make decision for a patient at the remote centre without having to leave the expert centre, thereby promoting early diagnosis [35].

A similar pilot project testing the tele-stroke consultation system was done in Brazil. Before this project, no patients were thrombolysed. Upon initiating tele-consultation, 6 patients were thrombolysed in 30 days [36]. This telestroke facility for stroke patients is being tested in China [37]. In this study, an interactive two-way wireless system compatible with iPhone Operating System, smartphones and tablets was developed by the School of Biomedical Engineering. This study is actively recruiting patients.

Emergency Department

To quantify the time lost while waiting to be seen in ED, a study was done in Aga Khan University Hospital, Karachi, Pakistan. This is a private hospital in an urban area. During the study period of 9 months, 38,762 patients visited the ED and more than 32% of patients waited for >180 min before leaving without being seen. The average waiting time before leaving ED unseen/unattended was 154 and 171 min for paediatric and adult patients, respectively [38].

In Sudan, triage-based emergency care was introduced for the first time in 2001 by the Ministry of Health. It was done in the 3 largest hospitals in the county; Khartoum Teaching Hospital, Khartoum North Teaching Hospital & Omdurman Teaching Hospital. This helped in understanding the difficulties in delivering Emergency Medical (EM) care. Hence, 5 senior nurses were sent to Malaysia in 2001 for training in Malaysian triage system. Following this in 2007, emergency medicine officers were sent to pursue their Masters Degree in EM. In 2011, the EM residency programme was established in Sudan. As a quantifiable measure of improvement in EM services, mortality in Omdurman Accident and Emergency Hospital decreased from nearly 18% in 2005 to <0.05% in 2011. This is despite the increase in the number of patients attending ED [39].

In Papua New Guinea, the first efforts to launch EM were made by introducing "Master of EM" course. This attempt was unsuccessful because of lack of specialist support. In 2002, Australian Agency for International Development supported the development of EM. Australian Agency for International Development supported a resident Emergency Physician, but it was short lived since the agency closed. The University of Papua New Guinea supported by establishing the position of "senior lecturer" in January 2003. Under this programme, EM training was structured, EM was added to the curriculum of medical students, ED was supported with senior staff and research projects. They also involved an experienced emergency nurse from Australia to educate their nurses [40, 41].

A survey done in China to evaluate the preparedness of hospitals regarding public health emergencies in 400 hospital showed that hospital preparedness was in the early stages of development and a lot could be done [43]. In India, Emergency Medicine was established as a separate specialty in July 2009 [42]. Emergency Medicine is offered as a specialty in 7 states across India [43].

Stroke Units

Patients managed in SUs have better outcomes; therefore, all district or primary government hospitals and teaching institutes must strive to have at least one primary SU [44]. If primary government hospitals run by physicians cannot have independent SUs, they can be linked to tertiary teaching care hospitals that have SUs. In

Brazil, as a target for "National Stroke Policy Act" multiple SUs were established across the country between 2008 and 2012. During this time, the number of SUs increased from 20 to 37 in the public sector and from 15 to 45 in the private sector, an increase of 47 SUs in total. To further convene stroke patients, the reimbursement for stroke rose from USD 400 for 7–14 days stay in an SU including basic investigations (2 brain CT scans, Echocardiography and carotid duplex ultrasound) to USD190/day of stay in an SU with separate reimbursement for CT, ECHO and carotid duplex. All reimbursement is provided directly by the Ministry of Health [27]. In Egypt, there are nearly 10 SUs [45]. In South Africa, SUs have reduced mortality rates from 33 to 16%, and improved referral to inpatient rehabilitation from 5 to 19% [46]. In Argentina, stroke-care quality indicators were analyzed using various parameters. Comparison was made between outcomes at academic and non-academic hospitals. Results showed that more patients in academic were admitted in SUs (8.5 vs. 3.2%), had fewer in-hospital pneumonia (9.6 vs. 15.5%) and had lower risk adjusted in-hospital mortality (7.1 vs. 10.6%) [47]. In India, there are approximately 35 SUs mostly situated in private sector hospitals [48, 49].

Thrombolysis in Acute Stroke

In Porto Alegre, Brazil, a pilot study was conducted to estimate the impact of introducing thrombolysis in the public health system. Part of the intervention comprised of training the pre-hospital rescue team in 5 stroke centres resulting in an increase in thrombolysis rate from 1.7% (65/3,824) to 5.3% (206/3,860). Following its success, "Brazilian National Stroke Policy Act" was implemented, which reduced the cost of rTPA from USD 2,000/patient to USD 540/patient [27]. In Egypt, <1% of eligible patients were thrombolysed [45], while no more than 2% of patients are thrombolysed in Pakistan and Iran [34, 50]. This figure is somewhat better in the "Indo-US Collaborative Stroke Project," where 227 of 2066 (11%) patients in 5 centres across the country received thrombolysis. Of those who did not receive the drug, 47 patients (8.8%) did not get tPA because of their inability to pay for the USD 1,100–2,200 required [51].

In various states in India, thrombolysis is being encouraged.

The state government of Himachal Pradesh provides tPA free of cost in 10 district hospitals. A neurologist based in the state capital of Shimla is available 24 h a day for consultation by mobile consultation or via WhatsApp at these 10 district hospitals. Between June 2014 and May 2015, a total of 26 patients were thrombolysed [52].

A retrospective audit in Pune found that prioritizing patients in ER, SUs, and imaging unit (s) reduced the door-to-needle time. Stocking tPA and thrombolysing patients in ER also helped in reducing time [53].

In another model in a small town of "Akluj" in Maharashtra state, a team of 6 physicians has initiated stroke service that has a stroke expert, simple imaging facilities and thrombolysis available round-the-clock [54].

In a new initiative in Punjab, district hospitals in the 5 cities of Jalandhar, Ludhiana, Bhatinda, Sangrur and Fazilka and 3 government medical colleges and hospital have implemented SU care and thrombolysis by the hub (Christian Medical College and hospital, Ludhiana, All India Institute of Medical Sciences, New Delhi and Post-Graduate Institute of Medical Education and Research, Chandigarh) and spoke model [55].

Post-Stroke Care

The "FAmily Led RehabiliTaTion AftEr Stroke in INDia" trial was undertaken across 14 centres in India. In this trial, caregivers of patients who were randomized to the intervention arm were trained by a physiotherapist for 3 sessions (one-hour each), while the patient was still in hospital. Upon discharge, the same physiotherapist undertook 4–6 home visits over a 2-month period. At the end of 3 and 6 months, patients were evaluated by a blinded examiner [56]. They were compared to patients in the control arm who received conventional hospital and outpatient rehabilitation. Although there were no clear benefits in this approach, it is important to note that training a caregiver could ensure continued physiotherapy to the patient without adding to the economic burden.

Another trial "Caregiver-mediated intervention can improve physical functional recovery of patients with chronic stroke: a randomized controlled trial" was conducted in Taiwan. In the intervention arm, an individualized 3-phase therapy plan was charted for each patient. A physical therapist visited each patient weekly to teach the rehabilitation skills, to help the caregiver in assisting and record the frequency of training. Physical therapist visited patients in the control group, but they were not given personalized rehabilitation skills. Patients in the intervention group had better outcome strength (15.5 vs. 1.4, $p = 0.002$), mobility (13.7 vs. –0.5, $p < 0.001$), activities of daily living/instrumental activities of daily living (8.5 vs. –0.2; $p = 0.022$), hand function (8.8 vs. –3.7; $p = 0.039$), communication (5.7 vs. –2.3; $p = 0.030$), 6-min walk test (15.8 vs. –10.5 m, $p < 0.01$) and Berg Balance Scale (4.5 vs. –0.8, $p < 0.01$) among other parameters assessed. This did not worsen the care-giver's burden [57].

In the 'Stroke Self-Management and Rehabilitation Trial," a pilot trial, patients in the intervention group were provided with digital video discs that they took home with them on discharge. This trial included 2 centres from India Nigeria each. This digital video disc offered 40 different care and rehabilitation techniques based on best available evidence delivered by people from different ethnicities. Patients were encouraged to exercise at least 5 times/week. Weekly phone calls were made to monitor adherence to the therapy and the resulting changes. The control group received only baseline and 2 month follow-up assessment [58]. This trial proves that such self-management strategy is feasible with local and global support.

'Tailored Hospital–based Risk Reduction to Impede Vascular Events after Stroke' is an ongoing trial among stroke survivors in 2 Nigerian cities of Ibadan and Abeokuta. The interventions are at 3 levels: (1) In-clinic educational video; (2) patient report card; and (3) text messaging with motivational information and clinic reminders. Tailored Hospital–based Risk Reduction to Impede Vascular Events after Stroke aims to test if this model improves blood pressure control, functional status, cognitive function and quality of life [59].

Task-shifting Strategies to ameliorate shortage of relevant stroke expertise – this study was conducted in Nigeria to examine if training health workers can improve their stroke knowledge. Two hundred and ten health-workers drawn from 53 local government areas of Ogun and Oyo states participated. Participants completed a pre-workshop questionnaire survey of stroke knowledge following which an intensive, multicomponent one-day stroke workshop was held. The participants' knowledge significantly increased at the end of the training on stroke risk factors ($p < 0.001$), stroke symptoms ($p < 0.001$) and how stroke develops ($p = 0.009$). However, further studies are needed to show that improved knowledge results in better care despite resource limitation [60].

Secondary Preventive Strategies in LMICs

The studies on secondary prevention identified had a focus on lifestyle modification and adherence to medications. To discuss primary preventive strategies in detail is beyond the scope of this review; only secondary prevention is discussed here. (Table 2).

Secondary Prevention

Lifestyle Modification

Altering one's lifestyle to minimize the possibility of recurrent stroke demands commitment from the individual and government alike.

Smoking

Argentina, Namibia and India have passed laws that discourage people from consuming tobacco and related products in public places [61–64]. In India, sale or consumption of tobacco within 100 m of an educational institute is also forbidden [65–69].

Salt Intake Reduction

Reducing salt intake in the general population is one of the simplest, most cost-effective ways of reducing cardiovascular and all-cause mortality [70]. Salt reduction lowers blood pressure and can lower stroke deaths in 8–13% of the cases [71]. A systematic alliance between the government and private food-processing sectors along with the marketing sector is needed for sustainable change. Mongolia, Brazil and 15 countries from West African Health Organization already have a strategy in place to implement this change [72, 73].

Physical Activity

Physical activity lowers 2 leading risk factors: blood pressure and the risk of developing diabetes. This is a highly cost-effective intervention for the 2 common risk factors [74].

Medication for the Management of Risk Factors

Medication to control risk factors such as hypertension, dyslipidemia and atrial fibrillation reduces the risk of stroke. Drugs such as acetylsalicylic acid, thiazide diuretics [75] and oral anti-coagulants (OACs) [76] can prevent or even minimize the functional outcome of stroke. Patients on OACs need regular International Normalized Ratio (INR) monitoring. Most patients do not have access to regular INR monitoring facilities. Furthermore, in LMICs, INR testing is neither centralized nor standardized. This makes physicians reluctant to start patients on OACs [77]. To reduce the cost and improve compliance, polypill was introduced. It is usually a combination of 2 antihypertensive drugs, 1 antithrombotics and 1 statin. But availability of individual drugs and polypill remains inconsistent in many LMICs. Currently, there are 15 ongoing clinical trials on various combinations of polypills. Four of these are being conducted in LMICs – one each in Iran and Sir Lanka and 2 in Brazil. In one multicentric study, India is one of the centres [78].

These medicines can be included in the WHO "list of essential medicine" for individual countries and can be made available in primary/district hospitals or government health centre in rural areas. They can even be provided at a reduced cost.

WHO (Package of Essential Non communicable disease intervention) approach: This is a set of interventions that can be easily delivered by a physician or a healthcare worker. These are interventions involving lifestyle modifications that are cost effective.

Thus, controlling the risk factors with government and public partnership can help reduce stroke burden.

Stroke Riskometer app: It is a unique mobile tool programmed to assess one's own risk of developing stroke within the next 5 and 10 years. It can be used to educate individuals about stroke, its risk factors and how to reduce them (including secondary stroke prevention). It compares one's risk with that of another person of the same age and gender without risk factors. It is a freely downloadable application, endorsed by the World Stroke Organization and other major international stroke/cardiology organizations. It is compatible with most iPhone operating systems and android phones. It is also available in different languages such as Hindi, Mandarin, Farsi, Portuguese, Bengali, Russian, Italian, Spanish, Malay, and French among others [79]. As a preventative tool, the app is being successfully trialed in New Zealand and the preliminary results are encouraging. If proven effective, it should be included in the WHO "list of essential devices" for individual countries and can be made available in primary/district hospitals for not only primary but also secondary stroke prevention. Global trial of primary prevention using stroke riskometer is being planned and results of the pilot randomized controlled trial will be submitted for publication soon (Feigin et al.) [80].

Discussion

Ambulance services exist in LMICs but are underutilized for stroke patients. Training EMTs to recognize stroke, notify the ED, neurologists and radiologists before the arrival of a stroke patient can reduce time lost in transit, ED and investigations. If the nearest centre does not have an imaging facility, patients can instead be taken to centres with these facilities after pre-notification. Time lost in ED can also be reduced by establishing standard stroke protocols that are tailored to regional and local needs [25, 31, 81–83].

Basic imaging equipment can be made available in primary/ government hospital. Linking it to a tertiary or academic centre via tele-stroke will make imaging, evaluation and thrombolysis possible in rural setups [35, 84].

The World Stroke Organization established Global Stroke Guidelines and Quality Committee to facilitate stroke care especially in areas where healthcare resources are limited [85]. It categorizes stroke care services into 3 levels: minimal healthcare services, essential stroke services and advances stroke services. It also provides key quality indicators and health system indicators to track the progress. Minimal healthcare service offers care by the local communities with limited or no access to physicians, diagnostic or imaging facility. At essential stroke service level, patients with stroke have access to diagnostic services, nurses, physicians (not neurologists), tPA and members of the stroke team, but they do not have access to advanced diagnostic services (interventional radiology) and access to stroke experts, rehabilitation therapists and well-coordinated stroke team, which is available only with advanced stroke services.

In areas where the healthcare system is limited, establishing a minimal model of SUs can be initiated by reserving 3–6 beds for stroke patients. After thrombolysis, patients can be transferred to advance SUs for further management and rehabilitation [35]. Supplementing the training of current staff to monitor parameters with clear evidence of benefit can maximize their efficacy at no additional cost [86, 87]. By decentralizing SUs and supplementing nursing care, more patients benefit from SU facilities.

Since the cost of tPA is a limiting factor [88], government subsidy or free provision of tPA in government hospitals can improve thrombolysis rate. The government can also include it in medical insurance.

During hospital admission or stay in SU; family members and/or caregivers can be trained under direct supervision of a physiotherapist. This can be continued after discharge. This system could be effective in improving physical and functional recovery without significantly increasing economic or emotional burden on the caregiver or prolonging hospital stay [56, 57, 89, 90, 94]. Countries from Eastern Europe had very limited information on SUs, imaging and rehabilitation services.

In secondary prevention, the use of anti-platelet drugs, anti-coagulants, drugs for hypertension and lipid control, and tobacco cessation are of proven benefit. All these medication should be made available at primary healthcare centres or government health centres in rural areas [91]. Primary and secondary prevention can prove

to be very cost-effective tools in reducing stroke burden [92].

Smartphone use has increased significantly in the last few years in LMIC. Developing web-based applications to alert patients about their medications, investigations and doctor visits can improve compliance. Another strategy is to contact family members and friends of patients admitted in SUs or hospitals. Helping them understand *their* risk will sensitize them to cardiovascular prevention. This method is called contact tracing, which is used in infectious disease control [93].

Limitations

This review has a few limitations. First, data from LMICs on stroke-care services and rehabilitation was very limited. Most articles from LMICs described the stroke burden and individual experience. The search was restricted to publications in English language only. Furthermore, risk of publication bias cannot be removed completely. Some of these countries were in the process of establishing a stroke care registry at the time of preparation of this manuscript, and so this may promote changes in these countries.

Conclusion

In our systematic review, we found several reports on evidence-based implementable stroke services in LMICs. Some strategies are economic, feasible and reproducible but remain untested. Data on effects on outcomes and sustainability of changes were very limited. Further research of implementation of locally and regionally adapted stroke services should be prioritized.

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