Stroke

COMMENTS AND OPINIONS

Inpatient Management of Acute Stroke of Unknown Type in Resource-Limited Settings

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ABSTRACT: Stroke is the second leading cause of death and disability worldwide, with a disproportionate burden on low- and middle-income countries. Critical elements of guideline-based stroke care developed in high-income countries are not applicable to resource-limited settings, where lack of access to neuroimaging prevents clinicians from distinguishing between ischemic stroke and intracranial hemorrhage, requiring challenging clinical decision-making, particularly in the acute setting. We discuss strategies for acute inpatient management of stroke of unknown type with a focus on blood pressure management and antiplatelet therapy when neuroimaging is unavailable, and review some of the challenges and strategies for successfully implementing stroke unit care in resource-limited health care settings.

Key Words: blood pressure ■ cause of death ■ clinical decision-making ■ inpatient ■ neuroimaging

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Stroke is the second leading cause of death and disability worldwide, accounting for nearly half of global disability and more than two thirds of global mortality due to neurological disease.[1,2] Stroke-associated morbidity and mortality fall disproportionately on low- and middle-income countries (LMICs), where 57% of worldwide strokes and 67% of stroke-associated mortality occurs.[3] In 2016, the case fatality rate from stroke was 56% in LMICs compared with 29% in high-income countries (HICs), and the average disability-adjusted life years lost per stroke was 13.4 years in LMICs compared with 4.6 years in HICs.[3] Compared with patients in HICs, those in LMICs have significantly higher stroke severity at presentation, greater rates of intracerebral hemorrhage (ICH), and lower access to specialized stroke care, neuroimaging, acute stroke interventions, and rehabilitation services.[4]

In HICs, acute stroke care relies on rapid access to neuroimaging to determine eligibility for interventions such as thrombolysis and thrombectomy, which have transformed outcomes in recent decades.[5] Inpatient stroke care in HICs takes place in dedicated stroke units where bedside monitoring, specialized nursing, and rehabilitative care are protocolized to mitigate poststroke complications, optimize neurorecovery, and reduce mortality.[6] Health care providers in HICs prescribe optimal antiplatelet, lipid-lowering, and antihypertensive medications for secondary stroke prevention at high rates.[7] Anticoagulation services are widely accessible after stroke when indicated.[8]

In LMICs, inpatient stroke care is commonly delivered by physicians and nurses with no specialized training given the dearth of neurologists in LMICs.[8] Access to computed tomography (CT) in LMICs is extremely limited, with just 1.3 CT scanners per 1 million population (compared with 21.2 CT scanners per 1 million population in HICs).[9] Even where CT is available in LMICs, patients may lack access because of location concentrated in urban areas, cost,[10] and inconsistent device function.

Lack of access to neuroimaging in many LMICs not only places thrombolysis and endovascular interventions out of reach for patients with ischemic stroke (IS) but precludes clinicians from accurately distinguishing between IS and ICH given the poor reliability of clinical

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Nonstandard Abbreviations and Acronyms

APT	antiplatelet therapy
BP	blood pressure
CAST	Chinese Acute Stroke Trial
HIC	high-income country
ICH	intracranial hemorrhage
INTERACT-2	Implementation of Intensive Blood Pressure Reduction in Acute Cerebral Hemorrhage Trial
IS	ischemic stroke
IST	International Stroke Trial
LMIC	low- and middle-income country
SOUT	stroke of unknown type

findings for this purpose.[11] Without neuroimaging, acute management strategies must balance the competing priorities of adequate cerebral perfusion in the event of IS while minimizing risk of hematoma expansion in the event of ICH and must weigh the antithrombotic benefit of aspirin for IS against the risk of impaired hemostasis in the event of ICH. Existing evidence-based guidelines for managing patients with IS[5,12,13] and ICH[14] are applicable only where CT is available and therefore cannot be applied in many resource-limited settings. As a result, many LMICs lack comprehensive, context-appropriate guidelines for stroke care.[15]

Here, we review best practices for managing stroke of unknown type (SOUT) in resource-limited settings based on existing literature from HICs and author experience in LMICs—contexts that would be classified as having "minimal" capacity per the World Stroke Organization.[16] We focus specifically on strategies for blood pressure (BP) management and use of antiplatelet therapy (APT) when no CT scanner is available to differentiate between acute IS and ICH. We further discuss the role of dedicated stroke units in caring for both IS and ICH, and the challenges and opportunities for their implementation in LMICs where there are few or no neurologists.

BLOOD PRESSURE MANAGEMENT IN SOUT

Optimal BP management following both IS and ICH is not known. In acute IS, BP is commonly allowed to autoregulate up to ≤220/120 mmHg in the first 24 hours after stroke to optimize perfusion to at-risk brain tissue, although this particular BP target has not been validated in a randomized trial. Available evidence from observational studies suggests that hypotension may be harmful.[17,18] In patients who receive intravenous (IV) thrombolysis, BP is maintained below 180/105 mmHg, a target that appears to be well-tolerated among those requiring pretreatment BP reduction to become eligible for tPA treatment.[19]

Despite 2 large randomized controlled trials, the INTERACT-2 (Implementation of Intensive Blood Pressure Reduction in Acute Cerebral Hemorrhage Trial)[20] and Antihypertensive Treatment of Acute Cerebral Hemorrhage,[21] optimal BP management after ICH also remains unclear. While INTERACT-2 demonstrated improved functional outcomes in patients with SBP<140 mmHg, neither trial revealed differences in mortality or severe disability between aggressive BP control (SBP<140 mmHg) and usual care (SBP<180 mmHg), and Antihypertensive Treatment of Acute Cerebral Hemorrhage revealed a higher risk of renal injury in patients receiving more aggressive BP control. More recent studies have suggested that high BP variability[22] and rapid BP correction[23] in the acute period after ICH onset are associated with worse functional outcomes.

Based on these data, when managing BP in the first 24 hours after acute SOUT, targeting a maximum SBP of 180mmHg while avoiding a minimum mean arterial pressure (MAP) of <65 mmHg is likely to be safe for both IS or ICH. In IS, this BP range avoids the hypotension that seems to be harmful and is unlikely to exacerbate cerebral ischemia based on data from tPA trials. If patients show worsening neurological deficits with BP reduction, the BP goal can be increased and a trial of BP augmentation with IV fluid resuscitation can be considered.[24] In ICH, this BP range does not seem to increase risk of death or severe disability and may prevent the rapid correction and variability in BP that appear to be harmful in ICH.

Current guidelines for IS recommend that in patients who do not undergo thrombolysis or thrombectomy it might be reasonable to lower BP by 15% within the first 24 hours but comment that the benefit of treating hypertension within the first 48 to 72 hours is unclear.[5] Many resource-limited settings lack access to vessel imaging to detect critical stenoses, titratable short-acting antihypertensives, intraarterial BP monitoring, and frequent neurological examinations to detect deterioration at lower BPs should it occur. Therefore, in SOUT, a period of autoregulation (up to 180/105 as above) lasting 48 to 72 hours may be considered before beginning to pursue long-term control of blood pressure in the normotensive range. A reasonable medium- and long-term BP goal is ≤130/80 mmHg, although this can be tailored as needed based on premorbid BP, age, and life-expectancy.[25]

Of note, rapid access to health care facilities may be limited in LMICs, such that patients may present for evaluation in a health care setting several days after stroke symptom onset. In such cases, clinicians would manage BP based on the last known well time rather than the time of hospital arrival. After the first 72 hours from time last known well, BP goals to gradually target normotension will be identical in SOUT.

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Hypertension is a critical treatable risk factor for both IS and ICH, and close primary care follow-up in the outpatient setting is vital for secondary stroke prevention. There is considerable heterogeneity in the cost and availability of antihypertensive medications across LMICs,[26] and medication selection should be determined by local availability of individual agents as well as patient-specific factors. Beyond long-term BP control, lipid-lowering therapy has long been recognized as an important component of secondary stroke prevention[27] and appears to confer no increased risk of ICH[28] although access to statins is limited in LMICs because of cost.[7] The use of a polypill containing a combined formulation of antihypertensives and a statin was recently shown to decrease cardiovascular events in an LMICs setting[29] and may hold promise for secondary stroke prevention in LMICs as access to such agent becomes more widespread.

APT IN SOUT

The benefit of aspirin for acute IS was established in 2 large randomized controlled trials that included patients from resource-limited regions, the IST (International Stroke Trial)[30] and the CAST (Chinese Acute Stroke Trial).[31] Both studies demonstrated small but significant decreases in recurrent stroke risk in participants started on aspirin within 48 hours of stroke onset.[32]

Aspirin is inexpensive, widely available, and on the WHO List of Essential Medicines. Despite the accessibility and established benefit of aspirin in preventing recurrent stroke, its use in resource-limited settings remains low. In the PURE study,[7] aspirin use for secondary stroke prevention was found in 53.1% of patients in HICs compared with 28.2% of patients in LMICs and only 3.8% of patients in LICs. While the root causes of this disparity are likely multifactorial, reluctance to prescribe aspirin when ICH cannot be ruled out by neuroimaging may be an important contributor.

When CT is not available, clinicians must decide whether to prescribe aspirin in the acute setting and whether to continue it for chronic secondary prevention after SOUT. While no randomized controlled trials have assessed these decision points, available data from multiple studies suggest that aspirin for acute management and secondary prevention is likely safe and effective in SOUT.

Should APT Be Started in the Acute Setting for SOUT?

Among the roughly 40 000 participants in IST and CAST, 9000 were randomized before CT, with no apparent difference in rates of subsequent IS or ICH compared with those who underwent initial CT to exclude ICH. Among these participants, 773 were subsequently found to have ICH, of whom 398 received aspirin. There was no increased risk for adverse events among these participants, and they appeared to have a lower rate of subsequent IS and SOUT.[32] While these trials were not designed to evaluate APT safety in patients with ICH, these data support the use of APT for SOUT.

This question was further explored in a decision analysis of aspirin use for SOUT in resource-limited settings.[33] Using data from IST and CAST, the analysis compared a strategy of treating all SOUTs with empirical aspirin for the duration of hospitalization against a strategy of withholding aspirin from all such patients. This model suggested that providing aspirin within 48 hours of symptom onset for all patients with SOUT would decrease in-hospital mortality by 4 per 1000 patients and recurrent stroke by 8 per 1000 patients, with the empirical aspirin strategy comparing favorably even in settings with the highest estimated incidence of ICH (up to 60% of strokes).

Taken together, these data support the safety and efficacy of aspirin for SOUT. There is no established evidence to guide the dosing or timing of aspirin when the etiology of stroke is unknown. IST and CAST used initial doses of 300 and 160 mg/day, respectively. After an initial loading dose within 48 hours of time last normal, doses between 75 and 150 mg/day are accepted as providing similar antithrombotic protection with lower bleeding risk.[34] As the risk of hematoma expansion after ICH is the greatest in the first 24 hours after symptom onset, it is reasonable to defer a loading dose and delay initiation of aspirin until 25 to 48 hours after onset of SOUT. Depressed mental status and/or oropharyngeal dysphagia may pose a prohibitive risk of aspiration pneumonia from oral medications in the acute setting, requiring administration rectally or crushed via nasogastric tube.

Finally, while no scoring system or set of clinical signs reliably distinguishes between IS and ICH,[11] certain clinical features may indicate a higher likelihood of ICH or subarachnoid hemorrhage. These include depressed level of consciousness, vomiting, seizure at symptom onset, hypertension on presentation, meningismus, oculomotor palsy, or thunderclap headache in the hyperacute period. While none of these signs or symptoms alone or in combination can definitively distinguish ICH from IS, it may be reasonable to withhold APT in the acute setting if clinical suspicion for ICH is high.

Should Antithrombotics Be Used for Long-Term Secondary IS Prevention After SOUT?

It is well established that daily APT reduces the risk of recurrent IS among IS survivors.[35] ICH survivors share many of the risk factors for IS for which APT may be beneficial but also carry greater risk for recurrent ICH. There is no established consensus on the timing of APT

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resumption after ICH. The 2019 RESTART trial,[36] randomized 537 participants with ICH who were previously on an antithrombotic to receive or avoid open-label APT 24 hours after spontaneous ICH, with median enrollment at 76 days. Over 2 years of median follow-up, rates of recurrent ICH, major bleeding, or major occlusive vascular events did not differ between study arms. A subsequent analysis of this cohort with median follow-up extended to 3 years continued to show no difference in these outcomes between groups.[37] A subgroup analysis of RESTART participants with cerebral microhemorrhages on MRI further suggested that APT is safe in this population.[38] In a meta-analysis of 2801 patients with ICH, 288 received APT at 7 to 39 days and appeared to have no increased risk of death or disability at 3 months.[39] These studies constitute a considerable evidence base supporting the use of APT in patients with ICH, even those with neuroimaging features indicating increased hemorrhage risk.

In addition to these studies from HIC settings, a decision analysis[40] assessed empirical aspirin for long-term stroke prevention after SOUT in resource-limited settings. The model incorporated data from multiple published stroke datasets and compared lifelong aspirin after SOUT to no aspirin. The model predicted that the lifelong aspirin therapy after SOUT would prevent 84 492 strokes and 4056 stroke-related deaths in LMICs annually compared with not administering APT to any patients with SOUT. The benefits of long-term aspirin were predicted to be consistent across the age spectrum and in settings with the highest prevalence of ICH.

Although there are increasing data supporting use of nonaspirin antiplatelet agents such as clopidogrel, cilostazol, ticagrelor, and dipyridamole in secondary stroke prevention in certain scenarios,[36,41–44] there is insufficient data to determine what role they may play in SOUT. Given the cost and limited availability of nonaspirin antiplatelet agents outside of high-income settings, aspirin remains the preferred and most widely available secondary prevention agent for patients with SOUT in resource-limited settings.

Systemic anticoagulation therapy is unavailable in most LMICs, with warfarin (and associated monitoring) being reliably available for outpatient use in only 14% LMICs.[8] Direct oral anticoagulants are generally unavailable outside of HICs owing to prohibitive costs, although their recent inclusion on the WHO Essential Medicines List may increase their use in LMICs in the coming years.[45] Given that aspirin provides some protection from stroke secondary to atrial fibrillation (albeit inferior to anticoagulation),[46] it could serve as an affordable and widely available secondary prevention agent in patients with atrial fibrillation while awaiting greater availability of DOACs.

In sum, the long-term use of APT seems to be safe and beneficial for the long-term prevention of recurrent IS and stroke-associated mortality after SOUT and does not appear to increase risk of recurrent ICH, death, or severe disability in patients with ICH.

TOWARD IMPLEMENTATION OF PROTOCOLIZED STROKE CARE: THE ROLE OF STROKE UNITS

Stroke units are proven to reduce stroke morbidity and mortality.[6] Dedicated stroke units physically colocalize care staffed by multidisciplinary teams that include physicians, nurses, physical therapists, occupational therapists, speech-language pathologists, and social workers. Evidence-based care is protocolized to ensure consistent implementation of proven interventions through the continuum of acute, subacute, and rehabilitative care. The majority of care provided in these settings is applicable to both IS and ICH. While a comprehensive review of stroke unit care is beyond the scope of this article, guidelines for global stroke care have been established by the World Stroke Organization[16] and some of the fundamental components that are likely to be beneficial and feasible in resource-limited settings are enumerated in the Table.

In a large systematic review of multiple clinical trials comparing stroke unit care to usual care in a nonspecialized health care setting, stroke unit care appears to significantly improve patient survival, neurological outcomes, and functional independence.[6] These benefits have been demonstrated in both IS[6] and ICH,[69] patients of all ages, across the spectrum of stroke severity (with patients with severe strokes deriving the greatest survival benefit)[6] and in LMIC health care settings in Asia, Africa, South America, Eastern Europe, and the Middle East.[70] Of note, stroke units appear to confer benefits even in settings where CT is not broadly available.[70]

Stroke units confer benefits through low-tech and inexpensive interventions such as vital signs monitoring, prevention of common nosocomial complications such as aspiration pneumonia and pressure ulcers, and engaging patients and their families in the rehabilitation and discharge planning process. For example, implementation of protocolized vital sign monitoring and supportive care in a newly established stroke ward in Guinea led to significant reductions in poststroke chest infections, urinary tract infections, decubitus ulcers, and 28-day mortality.[71] The implementation of stroke units requires a reorganization of human and material resources, but they seem to be cost-effective over the long term in resource-limited settings.[72] Moreover, patients with stroke need not meet any inclusion criteria to benefit from stroke unit care. tPA and thrombectomy are known to improve outcomes, but the proportion of patients eligible to receive them is small, even in the most well-resourced settings. Because any patient with stroke can be cared for in a stroke unit, the benefits of protocolized stroke care can reach a significantly greater share of this patient population. As access

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Table. Basic Elements of Poststroke Care That Can Be Implemented in Most Resource-Limited Settings

	Management considerations	Diagnostic evaluation	Therapeutic interventions
Early diagnosis and stabilization			
Volume status	Hypovolemia and hypotension likely harmful in acute stroke[17,18]	Bedside assessment of volume status and BP	Gentle IV hydration with crystalloid fluids
Fever control	Temperatures >39 °C associated with increased risk of mortality after acute stroke[47]	Blood cultures	Antipyretics may improve functional outcomes after stroke[48]
		Urinalysis	Antibiotics as indicated
		Chest plain film	
Dysglycemia	Persistent poststroke hyperglycemia associated with worse outcomes[49]	Regular point-of-care glucose checks, as available	Correctional insulin for goal serum glucose 140–180 mg/dL (should only be administered in settings equipped to serially monitor serum glucose)
HOB position	HOB elevation may help lower risk of aspiration pneumonia[50]		Reasonable to elevate HOB to ≥30° for all SOUT patients, unless neurological worsening is seen with HOB elevation
	HOB elevation lowers intracranial pressure; may worsen cerebral perfusion in patients with IS penumbra		May be necessary to use supporting objects (blankets, boxes) beneath HOB if bed lacks recliner mechanism
Mitigation of complications			
PSAP	Common complication of stroke, may be particularly prevalent in resource-limited settings[51]	Blood cultures and chest plain film if clinical suspicion for pneumonia	Dysphagia screening decreases PSAP risk[57–59]
	Associated with increased mortality and worse neurological outcomes[52–56]		Twice oral hygiene care (supervised tooth brushing) likely decreases PSAP risk[60,61]
			Enteral feeding via nasogastric tube in patients with dysphagia
DVT	Greatest risk poststroke days 2–7,[62] and in patients with severe paralysis, advanced age, and atrial fibrillation.[63,64]	Lower-extremity ultrasound unavailable in most resource-limited settings	If available, consider DVT prophylaxis with unfractionated or low-molecular weight heparin
			Seventy-two hours after SOUT onset for patients with stable neurological exam.
			Patients who are able to ambulate may be encouraged to do so 2–3 times per day under close supervision to minimize fall risk.
			Maintenance of euvolemia may be protective.[65]
	Pharmacological DVT prophylaxis contraindicated in acute phase of ICH		
Skin care and pressure ulcer prevention	Pressure ulcers are common after acute stroke[66]	Daily skin assessments for ulcer formation/skin breakdown	Regular patient turning
			Skin hygiene
			Minimize skin moisture
	Associated with increased mortality[67] and resource utilization[68]		Bedside family members may be able to help
Approach to diagnostic evaluation of stroke etiology			
Diagnostic workup will vary by setting, local epidemiology, and resource availability. Serum diagnostics to consider include complete blood count, basic metabolic panel, screening for diabetes (eg, random or fasting blood glucose, hemoglobin A1c), lipid panel, and troponin. Where local prevalence is high, HIV and RPR should also be included. A cardiac workup should be undertaken to evaluate for atrial fibrillation and other arrhythmias as well as acute cardiac ischemia and could include ECG, echocardiogram, continuous cardiac monitoring during the inpatient admission, and 30-d outpatient cardiac monitoring as resources allow. Carotid ultrasound and vascular imaging could also be considered where available. However, it is also important to ensure that resources are available to intervene on abnormalities identified before an investigation is undertaken. For example, if vascular surgeons and interventional radiologists are not locally available, then carotid imaging is also unlikely to change management even if stenosis is identified.		

DVT indicates deep vein thrombosis; HOB, head-of-bed; ICH, intracranial hemorrhage; and PSAP, poststroke aspiration pneumonia; and RPR, rapid plasmin regain.

to advanced acute stroke therapies broadens to more LMIC settings, stroke units will be an important prerequisite to sustain beneficial outcomes from such interventions. If implemented at scale in LMICs, stroke units could begin to mitigate the disproportionate disability and mortality experienced by patients with stroke in these settings.

Implementation Challenges

While stroke units may be inexpensive, cost-effective, and low-tech, broad adoption requires adequate "staff, stuff, space, and systems"[73] for implementation. A key issue in many LMIC settings is the lack of workforce for providing specialized stroke care. Staffing shortages may apply not only to trained neurologists but also to nurses with expertise in bedside stroke care, rehabilitative therapists with knowledge of the unique motor, neurocognitive, and swallowing issues common after stroke, and social workers versed in post-discharge needs of stroke survivors and their caregivers. A common result is that family members with no medical expertise provide much of the acute and long-term care.

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A baseline level of material resources is required to provide poststroke care, including devices necessary to monitor and record vital signs, availability of supplemental oxygen, nasogastric tubes for enteral nutrition and medication delivery, and access to essential medications such as IV fluids, antihypertensives, and aspirin.

Beyond staffing and material shortages, LMIC hospital wards may lack the physical space required to create a ward dedicated solely to the care of patients with stroke. Protocolized stroke care delivered in a geographically defined stroke ward appears to significantly improve survival and long-term functional independence compared with stroke care on general medical wards with guidance from a consulting stroke team,[74] particularly for patients with more severe stroke syndromes.[75] The benefits of a dedicated stroke ward are likely conferred through more consistent monitoring for physiological derangements, prevention of aspiration pneumonia, and early nutrition.[76] A physical ward can also facilitate education, data collection, and cultures of care that serve to improve quality of stroke care over time. Despite these proven benefits, it may be difficult for resource-limited health care facilities to allocate space and staffing for this purpose.

Recovery from stroke is a gradual process that takes place over weeks to months, particularly in patients with severe strokes. Most HIC health care systems provide guideline-directed rehabilitative services,[77] and stroke unit care in these settings is organized around the goal of a safe transition to inpatient, subacute, or in-home rehabilitative care. Access to these services is severely limited in LMICs,[4] and the majority of postdischarge stroke care falls upon the families of patients, who may be unprepared to handle the complex needs of early stroke survivors. Task-shifting to educate patients' family members in postdischarge rehabilitation interventions is a potentially viable strategy,[78,79] although two recent randomized controlled trial of stroke survivors in LMICs showed no benefit of family based rehabilitation,[80,81] and further work is needed to determine whether family delivered rehabilitative care can be successful.

Strategies for Implementation

While numerous challenges exist in successfully implementing stroke unit care in LMICs, they are not insurmountable. Each LMIC health care setting has a unique set of assets and resource-limitations, and a reasonable starting point for the implementation of protocolized stroke care in any particular setting is a needs assessment, preferably derived from a combination of quantitative and qualitative data, that accurately describes gaps in care and highlights local opportunities for innovation. The WSO has developed a freely available online quality assessment tool[82] to guide individual health care organizations in next steps for improving stroke care capacity, which may provide a useful starting point for local stroke unit champions. A set of checklists for quality assurance across the multiple stages of inpatient stroke care is available from the Angels Initiative[83] and may be adapted to suit local needs in LMIC settings.

The creation of a hospital stroke registry, in which stroke cases and salient clinical data points are logged into a database, is feasible in resource-limited settings with existing staffing and technological infrastructure.[84] Multiple online registry tools for stroke care quality have been developed by international organizations including the Safe Implementation of Treatments in Stroke and the Registry of Stroke Care Quality,[85,86] and may be useful in settings with reliable internet access. Stroke registries can provide valuable information about the current state of stroke volume and inpatient stroke mortality, and capture common inpatient issues specific to a particular setting. After an intervention, the same stroke registry can prospectively monitor implementation metrics including rates of dysphagia screening or APT prescribing, as well as clinical outcomes such as in-hospital complications and mortality. These data can support clinicians in leadership positions as they work with hospital administrators, inpatient staff, funding agencies, and government health ministries to establish the need to create and sustain stroke units.

Effective health care delivery reorganization requires collaborations that benefit from the unique perspectives offered by providers at each level of the system. Stroke unit implementation depends on a stroke champion leading a multidisciplinary team including hospital leadership, physicians, nurses, rehabilitative therapists, social workers, and community health workers who can help patients transition into outpatient care. A potential starting point for the team is to identify dedicated ward space to co-localize at least some stroke patients, reorganizing existing hospital beds rather than increasing them. Given the known clinical benefits of a physical stroke ward, the creation of dedicated stroke beds could catalyze further collaborative restructuring while also improving stroke care.

While many LMIC inpatient settings will not be staffed by a neurologist, many benefits of stroke unit care can be realized by the use of protocols by physicians and nurses without formal training in neurology. Task shifting to non-neurologist health care workers has been shown to increase knowledge of routine stroke care across multiple hospitals in Nigeria,[87] although data on whether this affects stroke outcomes remains sparse. Development of a nurse-driven protocol for epilepsy care in rural Cameroon showed significant reductions in seizure frequency in a prospective cohort of patients with epilepsy,[88] suggesting that task-shifting can translate into clinical benefits for individuals with neurological disorders. Coupling the education of non-neurologist work forces with the establishment of clear protocols for poststroke care is likely to broaden the

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range of providers who can participate in stroke unit implementation. Moreover, because stroke units can serve as hubs of specialized expertise, they may foster a virtuous cycle that helps to train an increasing number of providers in stroke care.

CONCLUSIONS

Stroke represents a leading driver of disability and death worldwide, with a disproportionate burden on LMICs, placing heavy demands on strained health systems. Lack of access to neuroimaging is a key challenge to translating current guidelines for inpatient stroke management to resource-limited settings. The resulting uncertainty regarding an individual patient's underlying stroke etiology requires dedicated protocols that include the optimal management of blood pressure and antithrombotic choice in SOUT. Available evidence suggests a liberal BP strategy that seeks to avoid extreme hypertension or hypotension in the first 48 to 72 hours is likely to optimize the competing priorities of cerebral perfusion for IS and prevention of hematoma expansion for ICH when the etiology of stroke is unknown. Clinical trial and modeling data supports the safety and efficacy of empirical aspirin for SOUT. Increasing the use of aspirin after SOUT may prevent a significant number of recurrent strokes and stroke-related deaths in resource-limited settings worldwide. Organizing care delivery into stroke units with established protocols for high-quality stroke care has been shown to be a cost-effective means of improving stroke outcomes in both high- and low-resourced settings. Initiatives to scale up the implementation of stroke unit care in LMICs through collaborative training, reorganization of existing resources, and dedicated management protocols for SOUT offers a promising opportunity to improve the delivery of inpatient stroke care in resource-limited settings.

In parallel with efforts to improve stroke care with existing resources as outlined here, advocacy for greater access to CT is essential to improve diagnostic capacity and develop the infrastructure needed for thrombolytic therapy. Increased access to CT would also allow for international teleneurology/teleradiology collaborations through a spoke-and-hub model similar to models used in high-resource settings.[89] In the nearer term, collaboration among stroke care champions across a multitude of LMIC settings could lead to pragmatic multicenter clinical trials that characterize the challenges and best practices for stroke unit implementation. Engagement with national health ministries by local leaders in stroke care can advance the creation of national stroke care plans and context-specific care guidelines. Data sharing among clinical sites can facilitate the dissemination of innovative and effective interventions. Such collaborations are likely not only to improve stroke care in LMICs but also to yield innovations that will inform high-quality, cost-effective stroke care in HICs.

ARTICLE INFORMATION

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